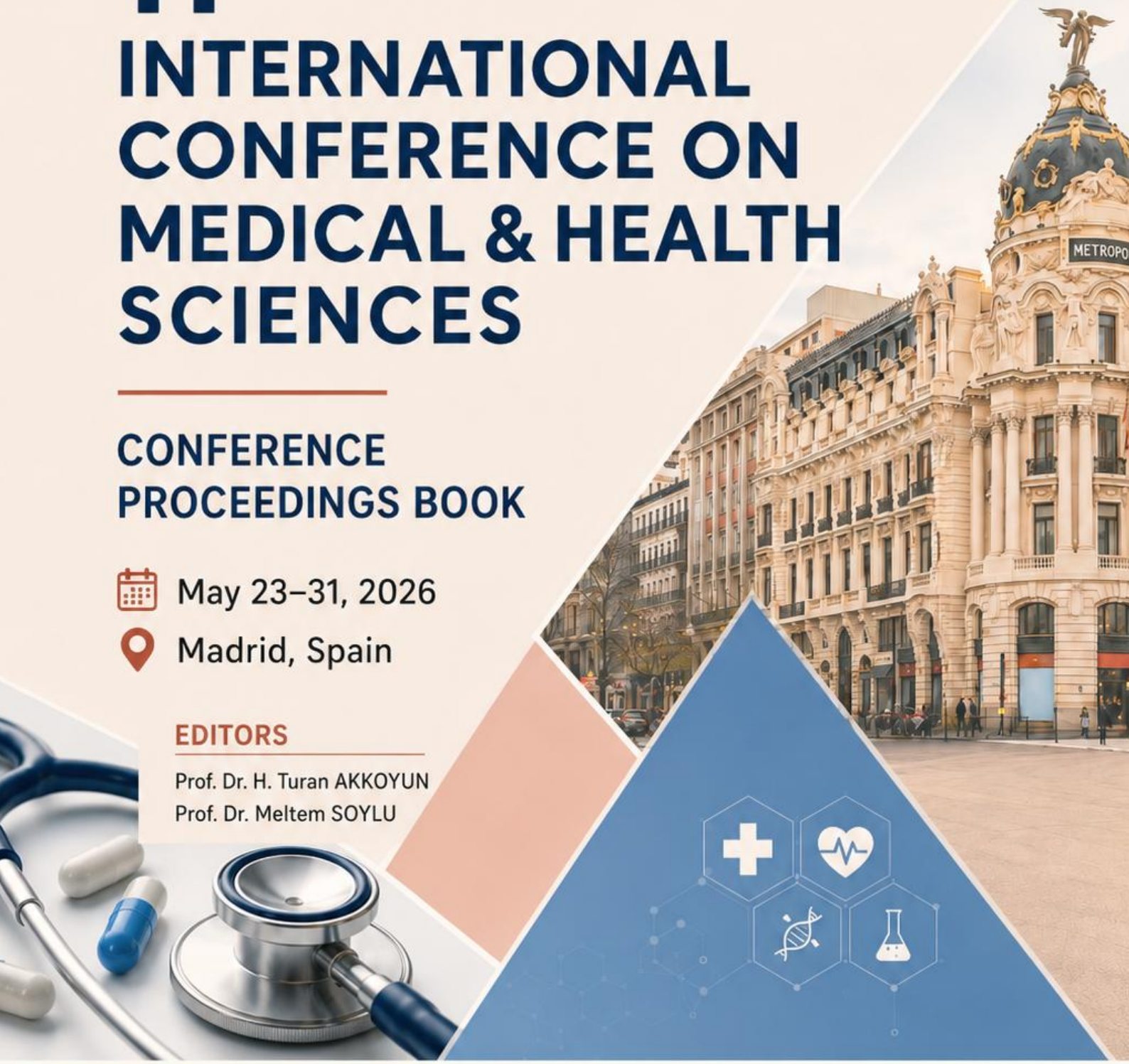
ISPEC

11th INTERNATIONAL CONFERENCE ON MEDICAL & HEALTH SCIENCES

CONFERENCE PROCEEDINGS BOOK

May 23–31, 2026

Madrid, Spain



EDITORS

Prof. Dr. H. Turan AKKOYUN

Prof. Dr. Meltem SOYLU

ISPEC • Madrid, Spain • 2026

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adopted by Mariam Rasulan

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ISPEC
11th INTERNATIONAL CONGRESS ON MEDICINE AND HEALTH SCIENCES

MAY 23- 31, 2026 / MADRID, SPAIN

CONFERENCE
PROCEEDINGS BOOK
(Abstracts & Full Texts)

EDITORS
Prof. Dr. H. Turan AKKOYUN
Prof. Dr. Meltem SOYLU

ISBN: **979-8-89695-449-1**

EVALUATION PROCESS and POLICIES

All applications have undergone double blind peer review process. In addition, cach paper was accepted and the process of publishing in the book was carried out through editorial oversight.

The published papers were presented and discussed at the meting. Full texts and abstracts published in accordance with the Symposium Policy have been prepared in accordance with ethical rules and APA standards. Authors of all papers are both ethically and legally responsible.

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Türkiye, Albania, Algeria, Azerbaijan, Bangladesh, Bulgaria, China, Cyprus, Ethiopia, Georgia, India, Indonesia, Iran, Iraq, Italy, Kazakhstan, Kosovo, Moldova, Morocco, Nigeria, Oman, Pakistan, Poland, Romania, South Korea, Spain

TOTAL ACCEPTED ARTICLES: 226

Number of Accepted Articles from Turkey: 108

Full Number of Articles Accepted from Other Countries: 118

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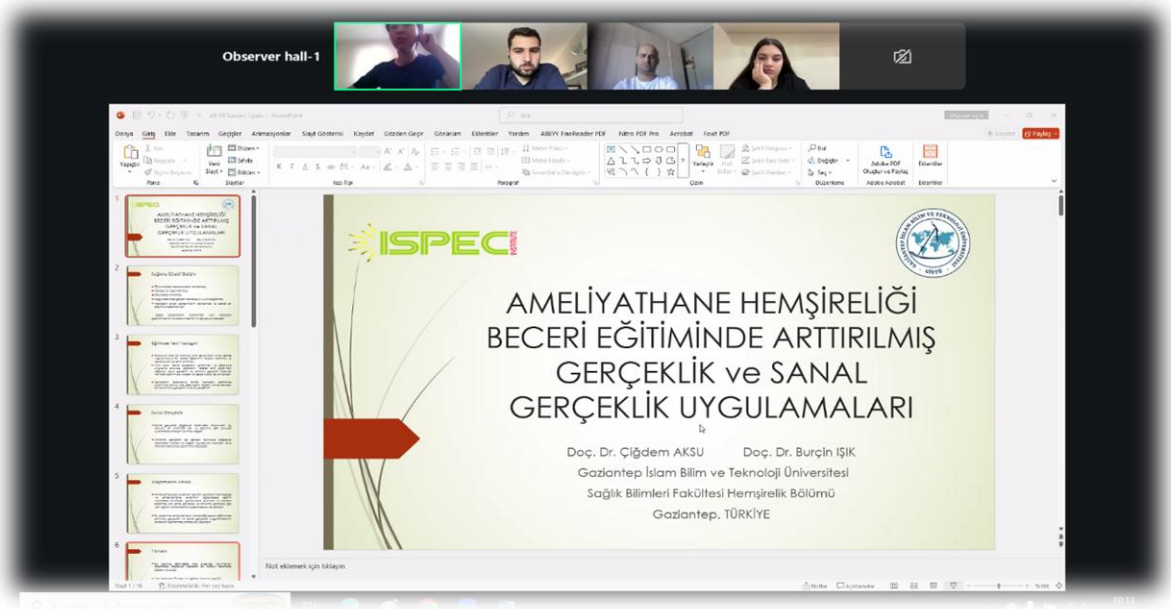

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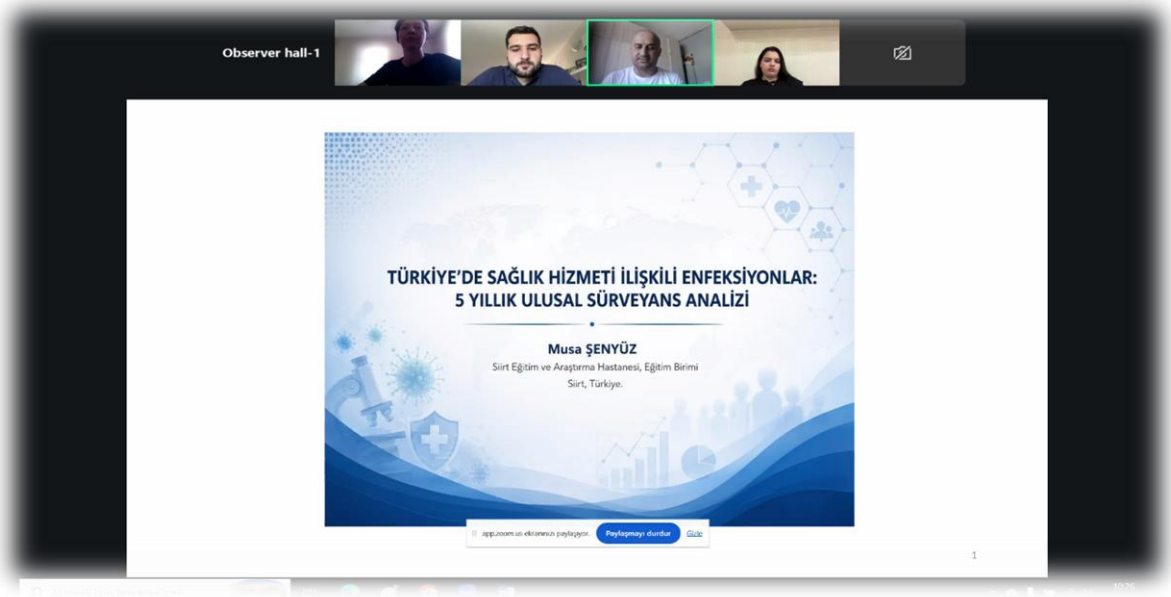



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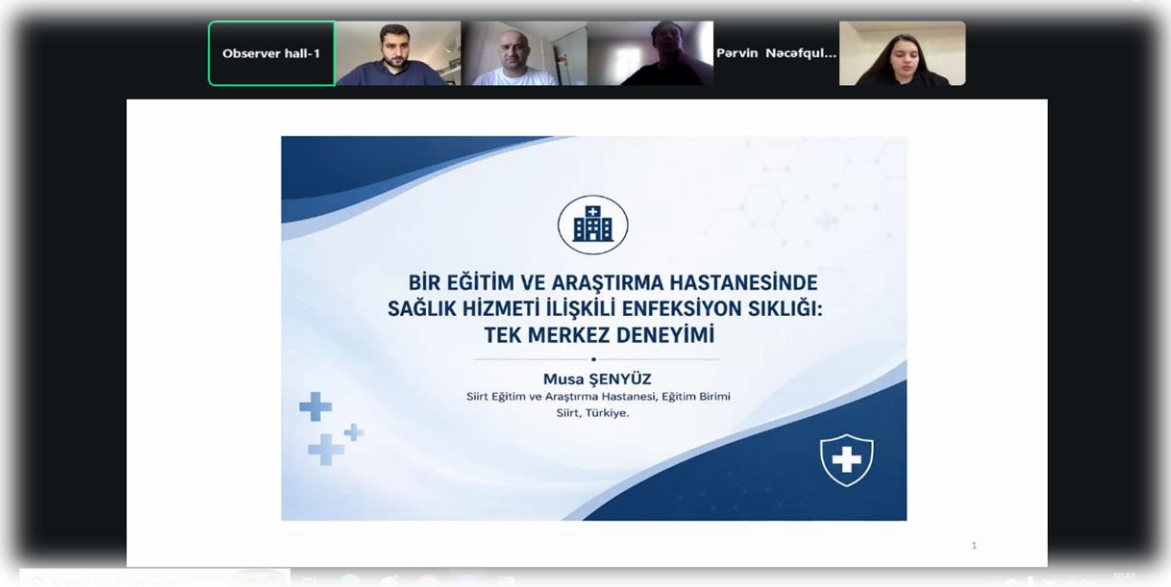

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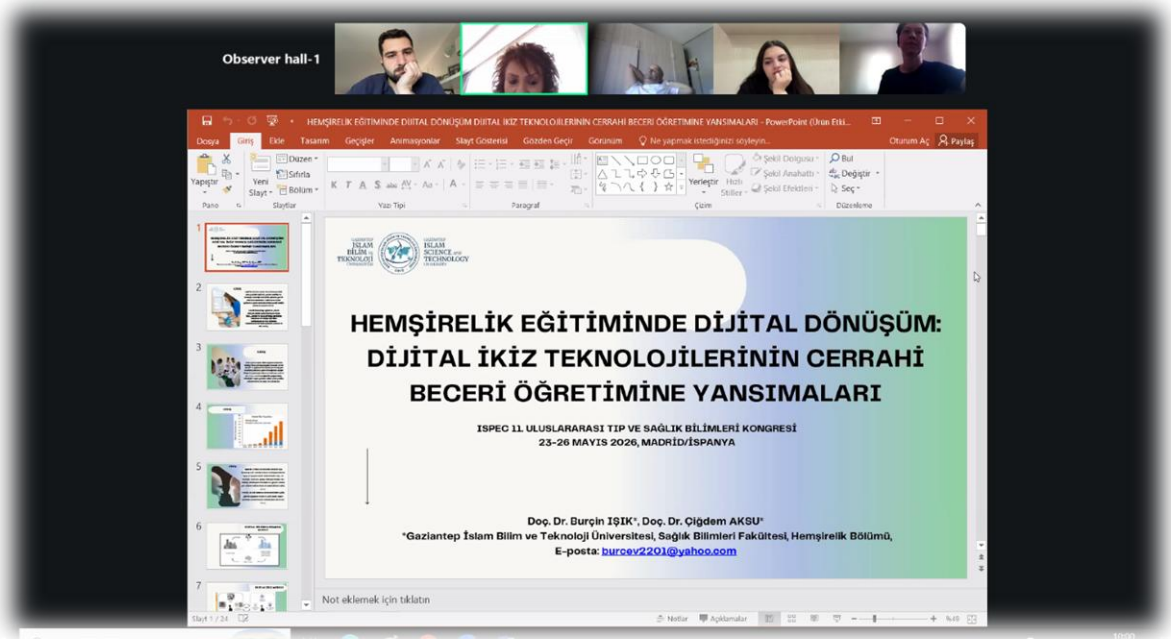

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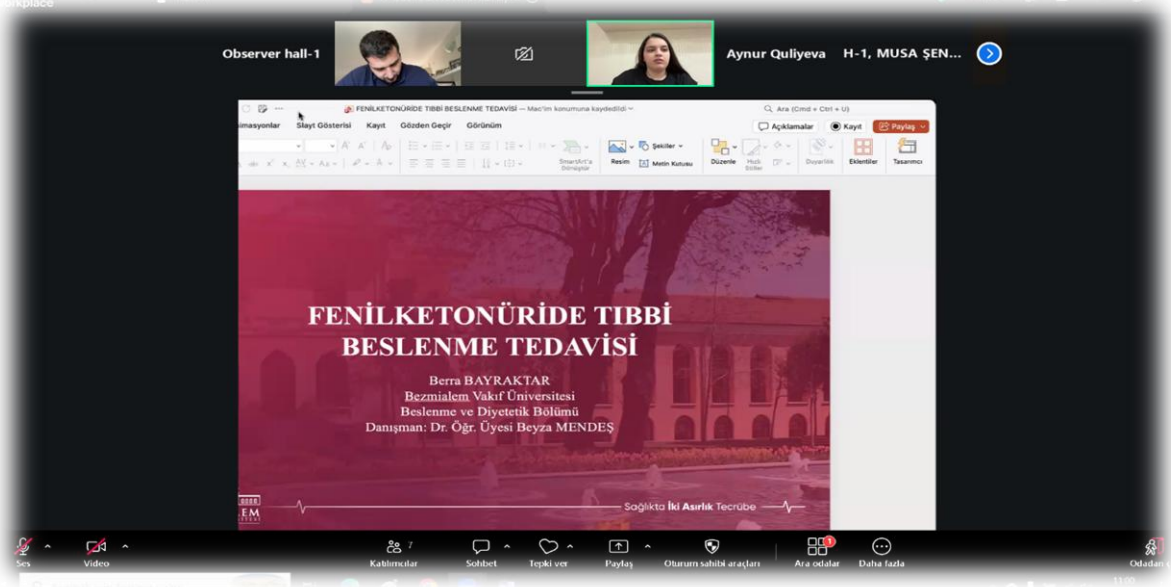

Observer hall-1
ISPEC
AMELİYATHANE HEMŞİRELİĞİ BECERİ EĞİTİMİNDE ARTTIRILMIŞ GERÇEKLİK ve SANAL GERÇEKLİK UYGULAMALARI
Doç. Dr. Çiğdem AKSU
Doç. Dr. Burçin IŞIK
Gaziantep İslam Bilim ve Teknoloji Üniversitesi
Sağlık Bilimleri Fakültesi Hemşirelik Bölümü
Gaziantep, TÜRKİYE
Not eklemek için bilayın


Observer hall-1
TÜRKİYE'DE SAĞLIK HİZMETİ İLİŞKİLİ ENFEKSİYONLAR:
5 YILLIK ULUSAL SÜRVEYANS ANALİZİ
Musa ŞENYÜZ
Siirt Eğitim ve Araştırma Hastanesi, Eğitim Birimi
Siirt, Türkiye.
Paylaşmayı durdur
Git


Observer hall-1
H-1, MUSA ŞEN... Pərvin Nəcəfqul...
Bir Nefes Sıhhat
> "Halk içinde muteber bir nesne yok devlet gibi, olmaya devlet cihanda bir nefes sıhhat gibi."
Kanuni Sultan Süleyman
Türkiye için Sağlıkta Üçüncü Bir Yol: Kooperatif Modeli


Observer hall-1
Pərvin Nəcəfqul...
BİR EĞİTİM VE ARAŞTIRMA HASTANESİNDE SAĞLIK HİZMETİ İLİŞKİLİ ENFEKSİYON SIKLIĞI: TEK MERKEZ DENEYİMİ
Musa ŞENYÜZ
Siirt Eğitim ve Araştırma Hastanesi, Eğitim Birimi
Siirt, Türkiye.


Observer hall-1
HEMŞİRELİK EĞİTİMİNDE DİJİTAL DÖNÜŞÜM: DİJİTAL İKİZ TEKNOLOJİLERİNİN CERRAHİ BECERİ ÖĞRETİMİNE YANSIMALARI
ISPEC 11. ULUSLARARASI TIP VE SAĞLIK BİLİMLERİ KONGRESİ
23-26 MAYIS 2026, MADRİD/İSPANYA
Doç. Dr. Burçin IŞIK*, Doç. Dr. Çiğdem AKSU*
*Gaziantep İslam Bilim ve Teknoloji Üniversitesi, Sağlık Bilimleri Fakültesi, Hemşirelik Bölümü,
E-posta: burcev2201@yahoo.com


Observer hall-1
Aynur Quliyeva
H-1, MUSA ŞEN...
FENİLKETONÜRİDE TIBBİ BESLENME TEDAVİSİ
Berra BAYRAKTAR
Bezmialem Vakıf Üniversitesi
Beslenme ve Diyetetik Bölümü
Danışman: Dr. Öğr. Üyesi Beyza MENDEŞ
Sağlıkta İki Asırlık Tecrübe

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11th INTERNATIONAL CONGRESS ON MEDICINE AND HEALTH SCIENCES

MAY 23 - 31, 2026 / MADRID, SPAIN

CONGRESS PROGRAM

In-person and Online Participation



25.05.2026 / IN-PERSON SESSION-1 / HALL-1

Madrid Local Time/ 09:00-10:30

Hotel Galaico Madrid (Avenida Juan Carlos I, 45 28400 Collado Villalba – Spain)

HEAD OF SESSION: Prof. Dr. Emrah YERLİKAYA

Authors	*Affiliation*	*Presentation Title*
Nagihan Merve SOYLEMEZ Selin SOYUNMEZ	*Kırşehir Ahi Evran University*	Mindfulness-Based Interventions in Children: A Review
Tuğba KANMAZ	*Kırşehir Ahi Evran University*	AI-Supported Parenting in Early Childhood
Adem YAĞAN Zelal YAYLA KALAY Musa YAĞAN Mücahit ÖNAL	*Van Yuzuncu Yil University*	Relationship Between HbA1c Levels and Demographic Factors in Newly Diagnosed Diabetes Patients in a Tertiary Hospital: The Case of Van Province
Elif KAYA Umut CINDILOGLU	*Kırşehir Ahi Evran University*	A Machine Learning Approach With Explainable Artificial Intelligence for Predicting Depression Risk in Adolescents: A Model Proposal From a Psychiatric Nursing Perspective
Kevser AVCI KABAL Murat Gokhan KABAL	*Kırşehir Ahi Evran University*	Current and Innovative Methods in the Education of Pregnant Women With Gestational Diabetes and the Role of the Nurse: A Literature Review
Selin SOYUNMEZ Nagihan Merve SOYLEMEZ	*Kırşehir Ahi Evran University*	A Review on the Effects of Laughter-Based Interventions on Child Health
Emrah YERLİKAYA Hasan KARAGEÇİLİ Kübra ASLAN Mesut SIRRI Veysel TAHİROĞLU İlhami GÜLÇİN	*Siirt University*	A Comparative Polyphenolic Profile of Centaurea Species by LC-MS/MS and Evaluation of Their Antioxidant, Antidiabetic, Antibacterial, Antialzheimer and Antiglaucoma Activities
Hasan KARAGEÇİLİ Emrah YERLİKAYA Adem ERTÜRK Kübra ASLAN İlhami GÜLÇİN	*Siirt University*	Assessment of Peonidin Compound's Antioxidant, Antidiabetic, Antimicrobial, Antialzheimer and Antiglaucoma Activities and Molecular Docking of Peonidin

Moderator is responsible for ensuring the smooth running of the presentation, managing the group discussion and dynamics.

25.05.2026 / IN-PERSON SESSION-1 / HALL-2

Madrid Local Time/ 09:00-10:30

Hotel Galaico Madrid (Avenida Juan Carlos I, 45 28400 Collado Villalba – Spain)

HEAD OF SESSION: Prof. Dr. İbrahim TEĞİN

Authors	Affiliation	Presentation Title
Pınar GÜVENÇ Deniz ÇETİN Asli SİLKÜ OFLİOĞLU Hülya ERTEN	*Dokuz Eylul University*	Adaptation of the Halitosis Associated Life-Quality Test (HALT) Into Turkish: Preliminary Results
Berfin KORKUT AZAN Adem YAĞAN	*Van Yüzüncü Yıl Üniversitesi*	Knowledge and Awareness Levels of Family Physicians and Family Medicine Residents in Van Province About Autism Spectrum Disorder
Mesut GÖK İbrahim TEGIN	*Siirt University*	Determination of the Fatty Acid Composition of the Hexane Extract of Cold-Pressed Fennel Seed Waste by GC-MS
İbrahim TEGIN Mesut GÖK	*Siirt University*	GC-MS Analysis of Hexane-Extracted Pine Gum (Pinus spp.): Chemical Composition and Bioactive Potential
Sevinç AYDIN	*Tunceli University*	Biochemical Composition and Antioxidant Activities of *Gundelia munzurensis* Seeds Growing in the Tunceli Region
Tuba OKUTAN Ökkeş YILMAZ	*Fırat University*	Effect of Cannabidiol Derived from Cannabis Indica Lam. Callus Culture on Plasma Oxidative Stress Parameters in DMBA-Induced Rats
Tuba OKUTAN Ökkeş YILMAZ	*Fırat University*	Modulatory Effects of Cannabidiol Isolated from Cannabis Indica Lam. Callus Culture on Lipophilic Compounds and Fatty Acid Composition in a DMBA-Induced Rat Model

Moderator is responsible for ensuring the smooth running of the presentation, managing the group discussion and dynamics.

25.05.2026 / IN-PERSON SESSION-2 / HALL-1

Madrid Local Time/ 11:30-13:00

Hotel Galaico Madrid (Avenida Juan Carlos I, 45 28400 Collado Villalba – Spain)

HEAD OF SESSION: Prof. Dr. Mahire BAYRAMOĞLU AKKOYUN

Authors	Affiliation	Presentation Title
Edanur ÇAK ÜÇLER Aysun ERDAL Naile BİLGİLİ	*Gazi University*	Post-traumatic stress disorder, psychological resilience, and meaning in life among adults who have experienced a disaster: the case of the 2023 Kahramanmaras earthquake
Sinan ÖZCAN Gamze SAATÇİ	*Kırşehir Ahi Evran University*	Space, memory, and well-being: the psychosocial dimension of cultural heritage in nursing students
Eslem Berra KİLECİ Sevda ARSLAN	*Düzce University*	Bibliographic analysis of postgraduate theses on obesity in the field of pediatric health and diseases nursing in turkey
Elif ŞAHİN	*Istanbul Okan University*	The predictive effect of childhood traumas and attachment styles on psychopathology
Deniz TOPRAK Şeyda Maide BATMAZ	*Kırşehir Ahi Evran University*	An innovative perspective in promoting child mental health: a review on philosophy for children (p4c)
Merve Safa KURT	*Van Yuzuncu Yil University*	The endocrine system and longevity: the role of hormones in nutrition
Şeyda Maide BATMAZ Deniz TOPRAK	*Ankara University*	The effect of picture books on cognitive inference and meaning-making processes in early childhood: a literature review
Berfin ÖKSÜZ	*Van Yuzuncu Yil University*	The relationship between obesity and oxidative stress

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Önemli, Dikkatle Okuyunuz Lütfen

- Kongremizde Yazım Kurallarına uygun gönderilmiş ve bilim kurulundan geçen bildiriler için online (video konferans sistemi üzerinden) sunum imkanı sağlanmıştır.
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- Moderator is responsible for the presentation and scientific discussion (question-answer) section of the session.

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***

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27.05.2026 / ONLINE SESSION-1 / HALL-1

Madrid Local Time/ 09:00-11:00 | **Ankara** Local Time/ 10:00-12:00

Zoom Meeting ID: 897 0755 8402 / Zoom Passcode: 123456

Head of Session: Musa ŞENYÜZ

Authors	*Affiliation*	*Presentation Title*
Ertuğrul GÜREŞCİ Yılmaz AKGÜNDÜZ	*Kırşehir Ahi Evran University*	The Health Services Cooperatives as a Third Way in the Health Sector in Turkey
Ersin Özer	*Ordu University*	Diagnosis and Management of Chronic Venous Insufficiency in Primary Care: Current Approaches
Berra BAYRAKTAR Beyza MENDEŞ	*Bezmialem Vakıf University*	Medical Nutrition Therapy in Fenilketonuria
Burçin IŞIK Çiğdem AKSU	*Gaziantep Islamic Science and Technology University*	Digital Transformation in Nursing Education: Implications of Digital Twin Technologies for Surgical Skills Training
Çiğdem AKSU Burçin IŞIK	*Gaziantep Islamic Science and Technology University*	Augmented Reality and Virtual Reality Applications in Operating Room Nursing Skills Training
Musa ŞENYÜZ	*Dicle University*	Healthcare-Associated Infections in Turkey: A Five-Year National Surveillance Analysis
Musa ŞENYÜZ	*Dicle University*	Frequency of Healthcare-Associated Infections in a Training and Research Hospital: A Single-Center Experience
Anıl EKER Tansu DEĞIRMENCI	*Izmir City Hospital*	Comparison of Perioperative Outcomes of RIRS and PNL in 15–25 mm Renal Pelvic Stones
Aynur Quliyeva	*Scientific Surgery Center of M.A. Topchubashov*	Laser Treatment of Pilonidal Sinus: Current Approaches and Clinical Experiences

(All speakers required to be connected to the session 10 min before the session starts)

Moderator is responsible for ensuring the smooth running of the presentation, managing the group discussion and dynamics.

27.05.2026 / ONLINE SESSION-1 / HALL-2

Madrid Local Time/ 09:00-11:00 | **Ankara** Local Time/ 10:00-12:00

Zoom Meeting ID: 897 0755 8402 / Zoom Passcode: 123456

Head of Session: Şeyma YILMAZ GÜNEŞ

Authors	*Affiliation*	*Presentation Title*
Orhan Ay Pelin Bahçeci Ali Acar	*Necmettin Erbakan University*	Clinicopathological Predictors of Recurrence and Mortality in Uterine Leiomyosarcoma: The Potential Role of Preoperative Inflammatory Markers
Cahidenur KOÇAK ORUÇ Esra PEHLİVAN	*Istanbul Esenyurt University*	Early Integration of Palliative Care in Non-Small Cell Lung Cancer: A Systematic Review of Patient-Reported Quality of Life Outcomes
Bilge MERACI YILDIRAN Nuray ERCAN	*Bolu Abant Izzet Baysal University*	Evaluation of Awareness and Educational Practices of Dental Educators Toward Left-Handed Students
Ulvi NOVRUZOV Songül CÖMERT KILIÇ Binali ÇAKIR	*Ataturk University*	Retrospective Evaluation of the Association of Petrotympanic Fissure Type and Presence of Tympanic Foramen with Otologic Symptoms and Radiological Findings in Patients with Temporomandibular Joint Osteoarthritis
Şeyma ÖZTÜRK Zeynep KURT	*Kırıkkale University*	Primary Ciliary Dyskinesia and Lobe-Limited Bronchiectasis: A Case Report
Merve Nur TEPE Kayıhan KARAÇOR Hakan SOYLU	*Düzce University*	Research of the Histopathological Effect of Oxymatrine in Ischemia/Reperfusion Injury Due to Testicular Torsion/Detorsion
Mehmet DEMİR	*Çiğli Training and Research Hospital*	Prenatal Diagnosis and Postnatal Management of Bochdalek Hernia in a Fetus of a Pregestational Diabetic Mother: A Case Report
Mehmet DEMİR	*Çiğli Training and Research Hospital*	Prenatal and Postnatal Course of a Fetus With Maternal Hydatid Cyst, Insulin-Treated Gestational Diabetes Mellitus, and Left Pes Equinovarus
Şeyma Öztürk Şeyma Yılmaz Güneş	*Kırıkkale University*	Well-Differentiated Papillary Mesothelial Tumor in Hydrocele Sac: A Rare Paratesticular Lesion

(All speakers required to be connected to the session 10 min before the session starts)
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27.05.2026 / ONLINE SESSION-1 / HALL-3

Madrid Local Time/ 09:00-11:00 | **Ankara** Local Time/ 10:00-12:00

Zoom Meeting ID: 897 0755 8402 / Zoom Passcode: 123456

Head of Session: Osman Gökhan GÖKDERE

Authors	*Affiliation*	*Presentation Title*
Tülay MORTAŞ	*Kırıkkale University*	Comparing the Performance of Gemini Advanced and Medical Students in Histology Question Answering
Osman Gökhan GÖKDERE	*Malatya Turgut Özal University*	The Relationship Between Inflammatory and Nutritional Indices and Lymph Node Metastasis in Gastric Cancer: A Retrospective Analysis in Patients Undergoing Gastrectomy
Seda ÖZBEY Semra TÜRKOĞLU	*Fırat University*	Metabolic Effects of Fermented Beetroot Beverage on Type 2 Diabetes
Sevgi ARSLAN Elif KETEN EDİS	*Amasya University*	Determination of Nursing Students' Sexual Health Literacy and Their Beliefs in Sexual Myths
Elif KETEN EDİS Sevgi ARSLAN	*Amasya University*	Reversal Request After Tubal Ligation: A Case Series at the Intersection of Different Motivations
Fırat DEMİR Sıddık KESKİN	*Van Yuzuncu Yıl University*	Oncological Data Analysis: Model Robustness in a 30-Variable Simulation Scenario Comparing GLMM and ANOVA
Onur Aydoğan	*Kırıkkale University*	Model Robustness in Oncological Data Analysis: Comparison of GLMM and ANOVA in a 30-Variable Simulation
Rabia Duman Tepe Buğra Doğan Nihan Aksakallı	*Istanbul University*	Osteosarcoma of the Anterior Mandible: A Case Report
İlay BURAN KAVURAN Sena DEVECİ	*Fırat University*	Cuproptosis in Hepatocellular Carcinoma: Current Molecular Approaches and Therapeutic Perspectives

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27.05.2026 / ONLINE SESSION-1 / HALL-4

Madrid Local Time/ 09:00-11:00 | **Ankara** Local Time/ 10:00-12:00

Zoom Meeting ID: 897 0755 8402 / Zoom Passcode: 123456

Head of Session: Fatjona KRAJA

Authors	*Affiliation*	*Presentation Title*
Shahed DAWOUD Gözde CANIK	*Near East University*	Conservative Biomimetic Repair of Multiple Anterior Class III Composite Restorations: A Case Report
Gheorghe GIURGIU Manole COJOCARU	*Deniplant-Aide Sante Medical Center*	The Gut-Brain-Skin Axis in Acne: Impact of Polenoderm
Fleura SHKËMBI Silva IBRAHIMI Ervin IBRAHIMI	*Mediterranean University of Albania*	A Comparative Analysis of Mindfulness and Hypnosis Techniques in Reducing Fear in Adults
Hasti BALALI Ali MORABBI	*University of Milan*	Prognostic and Pharmacogenomic Relevance of SLC7A11 in Hepatocellular Carcinoma
Fatjona KRAJA	*University of Milan*	Paget's disease or bone metastasis? The pivotal role of advanced imaging in prostate cancer diagnosis
Fatjona KRAJA Bledar KRAJA	*University of Milan*	Determinants of quality of life after cancer diagnosis in Albania: A prospective cohort study
Fatjona KRAJA Aurel JANKO Erald KARAULL Rezart XHANI	*University of Milan*	Prostate cancer in a real-world cohort: Clinical characteristics and prognostic determinants
Baraa ALKHATIB Mohamad Talal RADWAN	*Near East University*	Direct 3D-Printed Aligners in Orthodontics: Current Progress Toward a Promising Alternative to Thermoformed Aligners
Shahir Chowdhury Tanwi Dey Md. Sakhawat Hossain	*Sylhet Agricultural University*	Dietary Guanosine Monophosphate Supplementation Effects on Growth, Blood Chemistry, Stress Tolerance, and Disease Resistance of Stinging Catfish *Heteropneustes fossilis*

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27.05.2026 / ONLINE SESSION-1 / HALL-5

Madrid Local Time/ 09:00-11:00 | **Ankara** Local Time/ 10:00-12:00

Zoom Meeting ID: 897 0755 8402 / Zoom Passcode: 123456

Head of Session: Munevver PAZHARBEK

Authors	*Affiliation*	*Presentation Title*
Munevver PAZHARBEK	*Saken seifullin kazakh agro-technical university*	Stress and Academic Pressure on Student Mental Health
Munevver PAZHARBEK	*Saken seifullin kazakh agro-technical university*	Polycystic Ovary Syndrome (PCOS) in Young Women: Awareness and Management
Munevver PAZHARBEK	*Saken seifullin kazakh agro-technical university*	Sleep Deprivation and Its Effects on Adolescent Health
Munevver PAZHARBEK	*Saken seifullin kazakh agro-technical university*	Vaccine Hesitancy and Its Impact on Public Health
Munevver PAZHARBEK	*Saken seifullin kazakh agro-technical university*	Vitamin D Deficiency as a Public Health Issue
Oumaima BOUCHRA Amina ESSALIHI Soukaina BARIGOU Zineb KHADROUF Khadija KHADIR Mehdi KARKOURI	*Hassan II University of Casablanca*	Long-Term Survival in a 47-Year-Old Glioblastoma Patient with Multiple Recurrences : A Case Report
Muchamad DAFIP Ali Zainal ABIDIN Nina Sakina LESSY Alik SANDER Aprilia Indra KARTIKA Didik Setyo HARIYANTO Suci WIDHIANTI Dewi Kartikawati PARAMITA Sofia Mubarika HARYANA Tri WIBAWA	*Universitas Gadjah Mada*	Altered Lung Mycobiome Reflects a Tumor-Associated Microenvironment Remodelingin Lung Cancer
Habiba Khan ILHAM Tanwi DEY MD. Sakhawat HOSSAIN	*Sylhet Agricultural University*	Inclusion Effects of Guanosine Monophosphate in Fishmeal-Replaced Alternative Protein Diets on the Growth and Health of Climbing Perch (*Anabas testudineus*)
Cuşnir MAGDALENA Şcerbatiuc CRISTINA	*1 Moldovan State University of Medicine and Pharmacy*	The role of modern biometry in IOL calculation in patients with Down syndrome

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27.05.2026 / ONLINE SESSION-1 / HALL-6

Madrid Local Time/ 09:00-11:00 | **Ankara** Local Time/ 10:00-12:00

Zoom Meeting ID: 897 0755 8402 / Zoom Passcode: 123456

Head of Session: Qinfeng ZHOU

Authors	*Affiliation*	*Presentation Title*
Qinfeng ZHOU	*Shanghai University of Traditional Chinese Medicine*	Doppler Ultrasonography and Multi-Omics Profiling Reveal the Therapeutic Response of Qichuan Jingnaoning Formula in Rats with Vertebral Artery-Type Cervical Spondylosis
Muhammad Safi ASLAM Shahnila TARIQ Anum Arif BUTT	*University of Management and Technology*	Idle Thoughts Management Scale
E. MUKESH S.Tharun KRISHNAN K. SUJATHA N.P.G. BHAVANI Tatireddy Omsai REDDY	*Dr. M.G.R. Educational and Research Institute*	Automated Kidney Tumor Classification from CT Images with Grad-CAM Visualization and Deep learning Neural Networks
Zdravka HARIZANOVA Ferihan POPOVA Sabri SABRI Fanka GERGINSKA Lilia GROZLEKOVA Zlatizara TODOROVA Vyara ZAYKOVA Polina IVANOVA Atanas BALTADJIEV	*Medical University of Plovdiv*	Topographical and morphometric evaluation of the femoral nerve and its anatomical association with the femoral vessels
Dr. Padmalosani DAYALAN Dr. Edukondala Rao JETTI	*University of Technology and Applied Sciences*	Entrepreneurship Education as a Driver of Venture Creation Intentions: Evidence from Oman
Pooja RASAL Gaurav KASAR	*JES's SND College of Pharmacy*	Emerging Roles of Bioactive Compounds in the Prevention and Management of Neuropathy
S. M. Rejbanul ISLAM Jannatul FERDOUSI	*Sylhet Agricultural University*	Assessing the Biological Efficiency, Vitamin Profile, and Antioxidant Properties of Summer Mushroom Species
Saima SHAHEEN Nabila SHER Kalsoom TARIQ	*Khyber Girls Medical College*	Thyroid Hormone Levels and Their Association With Plasma Zinc Levels Among Adolescent Afghan Refugees: A Cross-Sectional Study
Fasika MELESE Destaw DAMTIE Sissay MENKIR Mulugeta KIBRET	*Bahir Dar University*	Effects of Soil Physicochemical Properties on Distribution and Composition of Fungal Species Isolated From Different Ecosystems of Amhara Region, North West Ethiopia

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27.05.2026 / ONLINE SESSION-1 / HALL-7

Madrid Local Time/ 09:00-11:00 | **Ankara** Local Time/ 10:00-12:00

Zoom Meeting ID: 897 0755 8402 / Zoom Passcode: 123456

Head of Session: Aishwarya S

Authors	*Affiliation*	*Presentation Title*
LIJOKA, Kehinde OSEMAWE Y. MUHAMMED S. JIBRIN	*Federal University of Technology*	Adoption of Improved Postharvest Management Practices Developed by the Nigerian Stored Products Research Institute (NSPRI) Among Tomato Marketers in Kwara State, Nigeria
Huma IKRAM Rumaisa ZAKIR Darakhshan J. HALEEM	*University of Karachi*	Neuroprotective Effects of Green Tea Extract on Age-Related Cognitive Decline in a Rat Model
Ranti EKASARI Maghfirah Insan SAKINAH Suci RAHMI Nur SASMITA Muh. Abdul WAHAB	*Universitas Islam Negeri*	Work Climate and Occupational Fatigue in Furniture Workers
Zouhir BOUMOUS, Samira BOUMOUS Hamou NOURI	*University of Souk Ahras*	Smart Grid-Based Hybrid Wind and Photovoltaic Energy Modeling for Sustainable Power Supply in Healthcare Facilities
Adigun OLUWADAMILOLA VICTORIA Y. Muhammed S. Jibrin	*Federal University of Technology*	Gender Participation in Agricultural Extension Activities and Its Effects on Rice Output in Niger State, Nigeria
Aishwarya S	*R.M.K. Engineering College*	Health Sciences
Moses Adeolu AGOI Andrew Ayanfeoluwa OKE Victor Oluwapelumi OGONGO Olajuwon Victor OLAYINKA	*Lagos State University of Education*	Immersive Game-Based Simulation Technologies for Interprofessional Healthcare Education, Clinical Decision-Making, and Collaborative Practice
Derra MOURAD	*Ibn Zohr University*	Ultrasonic Detection of Water Adulteration in Milk for Food Quality and Consumer Health Protection
Anga Peter INALEGWU	*Federal University of Technology*	Development and Implementation of a Virtual Chemistry Laboratory For Enhancing Learning Outcomes Among Senior Secondary School Students in Abuja, Nigeria

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27.05.2026 / ONLINE SESSION-2 / HALL-1

Madrid Local Time/ 11:30-13:30 | **Ankara** Local Time/ 12:30-14:30

Zoom Meeting ID: 897 0755 8402 / Zoom Passcode: 123456

Head of Session: Büşra ÇALIŞIR

Authors	*Affiliation*	*Presentation Title*
Büşra ÇALIŞIR	*Bursa Uludağ University*	Distribution of Aspergillus Species Across Clinical Specimens and Hospital Departments
Ayşe AYGÜN Meral KEKEÇOĞLU Fatih DEMİR	*Düzce University*	The Effects of Different Propolis Extracts on Testicular Histomorphology in Prepubertal Male Rats
Şebnem YILDIRIMCAN KADIÇEŞME	*Kafkas University*	Bioinformatic Analysis of TSPAN8 Expression in Lung Adenocarcinoma: Prognostic Value and Metastasis-Associated Mechanisms
İsmail AĞI Ümmühan Tuğba TÜMÜKLÜ	*Yerköy State Hospital*	Relationship Between Clinical and Laboratory Parameters and Clinical Outcomes in Patients with Carbon Monoxide Poisoning: A Three-Month Retrospective Analysis
Fatih Bedir Muhammet Karadaş	*Recep Tayyip Erdoğan University*	Effect of Different Tea Types on the Color Stability of a Microhybrid Resin Composite: An In Vitro Study
Cafer BARAN Merve ÖTER	*Dicle University*	Industry 5.0 in Healthcare Management: A Systematic Review on the Integration of Artificial Intelligence and Collaborative Robots (Cobots) into Healthcare Services
Mahi BALCI Ayşe Nur EVLEKSİZ	*Kırıkkale University*	Micropapillary Adenocarcinoma of the Ampulla of Vater: A Rare Case Report with a Review of the Literature
Pınar Seçmen	*Sakarya University*	Decision Support Systems in Post-Disaster Health Management: Modeling the Flood-Health Action Plan
Pınar Seçmen	*Sakarya University*	An Analysis of the Effects of Climate Change on Health Tourism

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27.05.2026 / ONLINE SESSION-2 / HALL-2

Madrid Local Time/ 11:30-13:30 | **Ankara** Local Time/ 12:30-14:30

Zoom Meeting ID: 897 0755 8402 / Zoom Passcode: 123456

Head of Session: İhsan NALKIRAN

Authors	*Affiliation*	*Presentation Title*
Burcu YILMAZ Derya ŞİMŞEKLİ	*Ardahan University*	Emotional and Behavioral Issues Among Parents Who Have Lost Their Children: The Role of Pediatric Nurses in End-of-Life Care
Burcu YILMAZ Derya ŞİMŞEKLİ	*Ardahan University*	The Physical and Psychosocial Effects of Problematic Digital Media Use in Children and Adolescents
Derya ŞİMŞEKLİ Burcu YILMAZ	*Ardahan University*	Sleep Disorders and Nursing Care in Patients with Asthma
Derya ŞİMŞEKLİ Burcu YILMAZ	*Ardahan University*	Factors Affecting Treatment Adherence in Patients with Diabetes and Nursing Care
Melike Nur Özçelik Merve Kılıç Tekin	*Tekirdağ Namık Kemal University*	Comparison of Methicillin-Susceptible and Methicillin-Resistant Staphylococcus aureus Bacteremia in a Tertiary Care Hospital: Distribution Across Hospital Units
İhsan NALKIRAN	*Recep Tayyip Erdoğan University*	Assessment of the Binding Interaction Between Honokiol and MDM2
İhsan NALKIRAN	*Recep Tayyip Erdoğan University*	Investigation of Celastrol-MMP14 Binding Interaction
Mefküre DURMUŞ Davut AYDIN	*Karadeniz Technical University*	The Retrospective Evaluation of Therapy Regimens and Clinical Outcomes of Patients with Myasthenia Gravis in an Intensive Care Unit
Melike DEMİR DOĞAN	*Gümüşhane University*	Examination of Studies on Therapeutic Touch: A Bibliometric Study

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27.05.2026 / ONLINE SESSION-2 / HALL-3

Madrid Local Time/ 11:30-13:30 | **Ankara** Local Time/ 12:30-14:30

Zoom Meeting ID: 897 0755 8402 / Zoom Passcode: 123456

Head of Session: İlknur KABA

Authors	*Affiliation*	*Presentation Title*
Elif KURKCUOGLU Omer KARATAS Emel Hulya YUKSELOGLU	*Istanbul University-Cerrahpasa*	The Role of Short Tandem Repeat (STR) Variants in Neurobiological Disorders
Elif KURKCUOGLU Omer KARATAS Emel Hulya YUKSELOGLU	*Istanbul University-Cerrahpasa*	Artificial Intelligence's Advances and Limitations in Forensic Science
Ali Hakan GÜNAYDIN Öykü SARAYDEMİR Yeşim YAMAN AKTAŞ	*Giresun University*	A Nursing Practice Framework for Septic Shock: From Early Recognition to Continuity of Care Based on Evidence-Based Guidelines
Öykü SARAYDEMİR Ali Hakan GÜNAYDIN Yeşim YAMAN AKTAŞ	*Giresun University*	Digital Health Technologies in Monitoring Surgical Patients
İlknur KABA	*Hitit University*	The Fatal Condition Behind the Mask: Two Cases of Meningococcemia with Distinct Clinical Courses
Tülay GÜRSOY Necdet KARAKOYUN	*Van Yuzuncu Yıl University*	Evaluation Of Van Province Air Quality In Terms Of Co (COBALT), Zn (ZINC), Ni (NICKEL), Ag (SILVER), AND Se (SELENIUM)
Ayşe Nur EVLEKSİZ Şeyma ÖZTÜRK	*Kırıkkale University*	Squamous Cell Carcinoma in a Case Operated on with a Preliminary Diagnosis of Inverted Papilloma: Clinical and Pathological Correlation
Ergün ÖZTAŞ Süleyman BAHAR Nazmi DEMIREL	*Özel Aritmi Hospital*	Diagnostic and Treatment Process in a Case of Septic Shock Associated with Liver Failure
Husameddin ASIDE Tuba UNVER	*Inonu University*	Automated Systems Used in Bacterial Identification and Their Working Principles
Cansu YATMAZ Neriman ARAL	*Ankara University*	Teachers' Knowledge and Awareness of Neurodevelopmental Disorders: A Review of Studies in Turkey

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27.05.2026 / ONLINE SESSION-2 / HALL-4

Madrid Local Time/ 11:30-13:30 | **Ankara** Local Time/ 12:30-14:30

Zoom Meeting ID: 897 0755 8402 / Zoom Passcode: 123456

Head of Session: Yousra ANWAR

Authors	*Affiliation*	*Presentation Title*
Faria NAWAB Mohammad AHSAN	*1 State Unani Medical College*	Effect of Physical Activity on Cardiovascular Health: A Critical Review of Current Evidence
Umar Baba SHAABA	*Ahman Pategi University*	The Role of Management Accounting in Enhancing Decision-Making in Nigerian Public Sector Organizations
Sumayya AKRAM Muhammad Nouman MAJEED	*Government College University*	ANN-Driven Optimization of Zinc Oxide Nanoparticles (ZnO-NPs) for Anti-Diabetic Drug Delivery
Kiran KULKARNI	*JES's SND College of Pharmacy*	Semaglutide: Transforming Metabolic Health in Diabetes and Obesity Management
Mohammed MERZOUKI Ahmed CHETOUANI	*University Mohamed Premier*	ADMET, Molecular Docking, and Molecular Dynamics Analysis of Flavone Derivatives as SARS-CoV-2 RdRp Inhibitors
Zaina IDIR Rhizlane ABDNIM Soukaina TERROUFI Ilham ABIDI Fatima AOUINTI Nadia GSEYRA	*Mohammed First University*	Evaluation of the In Vitro Antioxidant and Antidiabetic Activities of Quino (Chenopodium quinoa Willd.) Seed Extracts and the quantification of their bioactive compounds
Yousra ANWAR	*David Tvildiani Medical University*	Emerging Non-Invasive Biomarkers for Psoriasis Severity Assessment: A Review of Current Evidence
Vahid MOLABASHI Ebrahim Yar MOHAMMADI Nazli RABINEJAD Saeed BASHIRIAN Elaheh EZZATI	*David Tvildiani Medical University*	Studying the prevalence of musculoskeletal disorders and mental health among dentists in the west of the country
Khalid TALEBALI Ahmed AARAB	*Abdelmalek Essaadi University*	Quantitative Ethnobiological Analysis of Lkhel Sahraoui: Structural Core and Biocultural Resilience of a Saharan Polyherbal Formulation for Digestive Disorders in Southern Morocco

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27.05.2026 / ONLINE SESSION-2 / HALL-5

Madrid Local Time/ 11:30-13:30 | **Ankara** Local Time/ 12:30-14:30

Zoom Meeting ID: 897 0755 8402 / Zoom Passcode: 123456

Head of Session: Shalvi PAWAR

Authors	*Affiliation*	*Presentation Title*
Sibari BOUTAINA Souirti ZOUHAYR	*Hassan II University Hospital Center*	Extreme Sleep Spindles in a Child with Psychomotor Retardation: Clinical: A Case report
Mohammad Amin ROSTAMIAN Mohammad KARIMIAN	*University of Mazandaran*	Association of rs8052394 polymorphism with increased risk of preeclampsia
FELLAKI Anas ABOUROUH Mohamed ELYACOUBI Houda ELYAMANI Asmaa Aboukhalaf Abdelghani ROCHDI Atmane	*Ibn Tofail University*	Ecology of Ceps: A Mini-Review
Emmanuel Tomisin BELLO Majekodunmi Rachael ADEDAYO	*Newland Polytechnic and College of Health Technology*	Gold Nanoparticle–Based Lateral Flow Immunoassays for Tuberculosis Diagnosis: Mechanistic Insights, Optimization Strategies, and Translational Prospects
Rabiu Musa ISAH Mahdi Gambo DISSI Muhammad Ali SALIM	*College of Medical Sciences*	Chronic Artificial Light at Night Exposure Disrupts Circadian Rhythms and Modulates P53 Gene Expression in a Rat Model of Colorectal Cancer
Jogendra KUMAR Harshit BHANDARI Harshdeep GAUR Anuj CHAMOLI Vedansh TOMAR	*GBPIET Ghurdauri Pauri Garhwal Uttarakhand*	Detection of Face-Swap Deepfake Videos Using Deep Learning and Machin Learning Models
Mariami MANAGADZE	*Tbilisi State Medical University*	The problem of microplastics in environmental medicine
Muhammad ZUBAIR	*Government College University*	Synthesis of 5-phenyl-N-(pyridin-3-ylmethyl) furan-2-carboxamide derivatives through Pd (0) catalyzed reaction.
Shalvi PAWAR	*JES's SND College of Pharmacy*	Zoonotic Diseases: A Comprehensive Review of Toxoplasmosis and Its Impact on Public Health

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27.05.2026 / ONLINE SESSION-2 / HALL-6

Madrid Local Time/ 11:30-13:30 | **Ankara** Local Time/ 12:30-14:30

Zoom Meeting ID: 897 0755 8402 / Zoom Passcode: 123456

Head of Session: Atia SANZIDA

Authors	*Affiliation*	*Presentation Title*
Hamza EL KISSANY Hicham EL-BOUKHARY Hicham EL KISSANI Adil LAAZIZ Abdelouahed HAJJAJI	*Sultan Moulay Slimane University*	Drought stress and its influence on morphological, physiological, and biochemical traits of medicinal and aromatic plants. A review
Nodar SULASHVILI Gocha CHANKSELIANI Lali PATSIA	*Medicine at Alte University*	Comprehensive Scientific Evaluation of the Principal Clinical, Diagnostic, and Therapeutic Dimensions of Endovascular Interventional Management in Gastrointestinal and Duodenal Ulcer Hemorrhage: A Concise Case-Based Analytical Report
Iram LIAQAT	*Government College University*	QS Inhibition by Algal Compounds against Marine Biofilms
Atia SANZIDA	*Pabna University of Science and Technology*	Photocatalytic Degradation of Pefloxacin and Ciprofloxacin Using PPy-NiO-MoO_3 Composite: Performance, Kinetics Study and Reusability
Dr Lakshmi Devi GOTTEMUKKULA Dr Ravindra NAGASURI Dr Sunitha SAMPATHI	*Joginpally B.R. Pharmacy College*	Formulation, Development and Comparative Evaluation of Solid Dispersions, Nanosuspensions, and Self-Nano Emulsifying Drug Delivery Systems (SNEDDS) for Enhanced Oral Delivery of an Antiretroviral Drug
Sara SOULAIMANI	*Chouaib Doukkali University of El Jadida*	Analysis of Deterministic and Stochastic Alcohol Consumption Models: Stability and Sensitivity
Monika LOPUSZANSKA-DAWID	*Józef Piłsudski University of Physical Education in Warsaw*	The Impact of Socioeconomic and Macroeconomic Factors on Physical Activity Levels in Polish Women
SAID AIT MESSAAD	*Higher Institute of Nursing Professions and Health Techniques*	Study of the prevalence of malnutrition in relation to socioeconomic factors among children in the city of Salé, Morocco
Anna Kopiczko Patrycja Widłak Joanna Cieplińska	*Józef Piłsudski University of Physical Education in Warsaw*	Musculoskeletal Health Risk Profiling İn Elite Athletes: Interactions Between Bone Mineral Density, Lean Tissue And Stress-Related Bone Injuries
Patrycja Widłak Anna Kopiczko Aspasia Dania Piotr Bartnicki	*Józef Piłsudski University of Physical Education in Warsaw*	Beyond Fms: Integrating Functional, Morphological, And Biochemical Markers In Sport Injury Risk Assessment
P.H. NAJAFGULIYEVA	*Azerbaijan Medical University*	Long-Term Clinical and Metabolic Outcomes of Laparoscopic Sleeve Gastrectomy in Patients with Morbid Obesity: A Retrospective Single-Center Experience

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27.05.2026 / ONLINE SESSION-2 / HALL-7

Madrid Local Time/ 11:30-13:30 | **Ankara** Local Time/ 12:30-14:30

Zoom Meeting ID: 897 0755 8402 / Zoom Passcode: 123456

Head of Session: Soukaina AMEUR

Authors	*Affiliation*	*Presentation Title*
Abah, David UNEKWUOJO Faith AGIOUNIM	*Federal University Lokoja*	Anthelmintic Drug Resistance and the Potential of Plant-Based Alternatives: The Case of *Azadirachta indica* (A Review)
Imane ELBELGHITI Noureddine SLIMANI Zohra LEMKHENTE Fatima BOUBRIK Ahmed BELMOUDEN	*Ibn Zohr University*	Isolation, Characterization and Therapeutic Applications of Bacteriophages against Pathogenic Bacteria of the ESKAPE group
Səriyyə Abidova Elşən qızı	*Elmi Araşdırmalar*	The Importance of the Silk Road in the Formation of Turkish Civilization
Najiba SULTANI Subhashini SRIVATSA	*Mangalore University*	Healthcare Employee Wellbeing as a Predictor of Quality Patient Care: A Systematic Literature Review
Soukaina AMEUR	*Chouaib Doukkali University*	MEDT and Molecular Dynamics Investigation of 1,3-Dipolar Cycloaddition Reactions of Fused Pyrrole-2,3-diones with Diphenylnitrone
Tamanna T Ara I Siddika A Amin R Ahmmed M.S Sikder M.M Alam M.N	*Jahangirnagar University*	Phylogenetic characterization and in vitro control of Aspergillus fumigatus: a concerned fungal contaminant of shrimp balachao in Bangladesh
Zagane Mohammed EL SALLAH Moulgada ABDELMADJID Baltach ABDELGHANI	*University of Tiaret*	Study of the fracture behavior of different structures by the extended finite element method
Alaekwe I. O.	*Federal University Gusau*	Microplastic Pollution and Human Health
Youssra ECH-CHAHDI Hicham ZAITAN Fouad KHALIL	*Sidi Mohamed Ben Abdellah University*	AI-Driven and In Silico Investigation of Novel Tetrahydropyrazolo Scaffolds as Promising Selective Pim-1 Kinase Inhibitors Against Prostate Cancer

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27.05.2026 / ONLINE SESSION-3 / HALL-1

Madrid Local Time/ 14:00-16:00 | **Ankara** Local Time/ 15:00-17:00

Zoom Meeting ID: 897 0755 8402 / Zoom Passcode: 123456

Head of Session: Merih ŞİMŞEK

Authors	*Affiliation*	*Presentation Title*
Merih ŞİMŞEK Muhammed Zahid ASLAN	*Afyonkarahisar Health Sciences University*	Statement of Scientific Consensus on the Diagnosis and Treatment of Spinal Implant Infections: Literature Review
Merih ŞİMŞEK Muhammed Zahid ASLAN	*Afyonkarahisar Health Sciences University*	Extended and Combined Antibiotic Treatment Due to Spinal Involvement in Brucellosis: Current Approach
Melise İPHAR	*Bilecik Şeyh Edebali University*	Removal of Pharmaceutical Residues by Fungal Mechanisms
Özge Kuşcu Betül Taşpınar Ferruh Taşpınar	*İzmir Democracy University*	Cystic Fibrosis and Exercise Training
Zeyneb ÖZTÜRK Merve YÜRÜK	*Erciyes University*	Comparative Transcriptomic Analysis of Developmental Stage of Lucilia Sericata with Next Generation RNA Sequencing
Beyza ÇELEN İmren ESENTÜRK-GÜZEL Evren ALGIN YAPAR Ebrar İNAL-KILIÇARSLAN Murat KARTAL Cemre ÖZKANCA Sibel DÖŞLER	*University of Health Sciences*	Development and In Vitro Assessment of Ginger (Zingiber Officinale) Essential Oil-Loaded Nanoemulsion and Nanoemulgel Formulations for Topical Application
Selim ÖĞÜT	*Bandırma Onyedi Eylül University*	Radiotherapy-Induced MicroRNA Expression Changes and Their Effects on Radiosensitivity in Breast Cancer
Sinan KORKMAZ Hamdiye ARDA	*Dicle University*	Nursing-Based Non-Pharmacological Interventions in Thyroid Fine Needle Aspiration Biopsy
Deniz ALMAK	*Balıkesir Bandırma Family Medicine*	Attention Deficit Hyperactivity Disorder in Family Medicine: A Current Review from Diagnosis to Treatment

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27.05.2026 / ONLINE SESSION-3 / HALL-2

Madrid Local Time/ 14:00-16:00 | **Ankara** Local Time/ 15:00-17:00

Zoom Meeting ID: 897 0755 8402 / Zoom Passcode: 123456

Head of Session: Tilbe ERTEN ALMAK

Authors	*Affiliation*	*Presentation Title*
Semanur GÖZ Kevser KARAMAN Armağan YÜRÜK Kanykei KANATBEKOVA	*Erciyes University*	Effect of Germination and/or Fermentation Processes Applied to White Quinoa Seeds (Chenopodium Quinoa Willd.) on Total Phenolic Content
Tilbe ERTEN ALMAK	*Bandırma Onyedi Eylül University*	Screen Time, Sleep Disorders, and Chronotype in Children and Adolescents with Autism Spectrum Disorder: A Recent Review
İbrahim YEL Sedat Ozan KARAKIŞI Doğuş HEMŞINLI	*Recep Tayyip Erdoğan University*	Mid-Term Anchoring Zone–Related Complications After Thoracic Endovascular Aortic Repair: A Report of Two Cases
Sedat Ozan KARAKIŞI Doğuş HEMŞINLI İbrahim YEL	*Recep Tayyip Erdoğan University*	Emergency Surgical Repair of a Large Apical Muscular Ventricular Septal Defect in an Elderly Patient with Reduced Ejection Fraction: A Case Report
Sevde Nur BİLTEKİN KALELİ	*Istanbul Medipol University*	Evaluation of the Inhibitory Effects of Imidazole-Thiazole Derivatives on COX-1/2 and 5-LOX Enzymes
Taha GÜVEN	*Van Training and Research Hospital*	Postpartum Facial Valsalva Purpura: A Case Report
Meltem ASAN-OZUSAGLAM Ali SAGLAM Mehmet COBANOĞLU Merve ALAN	*University of Aksaray*	Developing Soaps For Health-Related Industries Using Caper Extract and Its Antimicrobial Activity
Taha GÜVEN	*Van Training and Research Hospital*	Preauricular Accessory Auricle: A Case Report
Yeşim Ceylantekin Dudu Zeynep Arı Tuğçe Erdal	*Afyonkarahisar Health Sciences University*	The Relationship Between Adults' Sense of Meaning in Their Lives and Their Perception of Life, and Their Awareness of Cardiovascular Disease Risk
Nurten NAS KIRDAR Abdülhalim AKAR	*Bandırma Onyedi Eylül University*	Optimal Rehabilitation Strategies After Total Knee Arthroplasty: A Systematic Review of Accelerated Protocols and Telerehabilitation in Light of Current Evidence

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Head of Session: Suleiman SAMBO

Authors	*Affiliation*	*Presentation Title*
Mahira Firudin kizi Amirova	*Azerbaijan Medical University*	Leptin and Adiponectin Signal Paths at the Obesity-related Breast Cancer
Mahira Firudin kizi Amirova Kamila Talibova	*Azerbaijan Medical University*	Search for Early Detection and Precision Monitoring of Breast Cancer
Suleiman SAMBO	*Modibbo Adama University*	Prevalence and Preventive Strategies of Child Abuse and Neglect Among Social Welfare Workers in Yola Metropolis
Jan Sadur Rahman Moon Soikot Kawria Ismat Ara Begum	*Affiliated with University of Rajshahi*	Increasing Burden of Multidrug-Resistant Klebsiella Pneumoniae in Community and Hospital-Acquired UTIs
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Wiktoria Pietrzak	*Józef Piłsudski University of Physical Education in Warsaw*	Determinants Of Bone Mineral Density In The Forearm Of Young Gymnasts And Swimmers
Saadatu IBRAHIM Ibrahim ABDULRAHMAN	*Federal University of Technology Minna*	Antenatal Care Factors Influencing Babies' Weight at Birth
Sama BOROUNMAND Ayda PADASH Majed J. AMRO Şensu DINÇER Berivan Beril KILIÇ	*Biruni University*	The Effect Of Regular Fitness Activity On Pain, Functional Disability, Core Endurance, Functional Capacity, And Quality Of Life in Individuals With Non-Specific Low Back Pain
Fouzia BENOUDJIT Djihad CHERIFI Fatma Zohra BENYOUCEF Imene HAMOUDI	*M'hamed Bougara University*	Upcycling Agricultural By-products: Essential Oil and Hydrosol from Pruning Biomass in Topical Formulation

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Head of Session: K. Vaishnavi

Authors	*Affiliation*	*Presentation Title*
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Head of Session: Adriana QAFA

Authors	*Affiliation*	*Presentation Title*
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Kamal SMIMIH Omar EL HIBA	*Sultane Moulay Slimane University*	Developmental neurotoxicity of prenatal ethanol exposure: implications for working memory dysfunction in mice
BELLIL Dassine GHAROUT-SAIT Alima DJOUDI Ferhat BELLIL Zahra MENDIL Ouidad MANSEUR Lyticia DIB-SAIT Sabrina	*Université de Bejaia*	Overview and Epidemiology of Non-tuberculous Mycobacteria Isolated from Wild Animals in Africa
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Aurel NURO Ilirjana OSMANI Arben HAZIRI Bledar MYRTAJ Kleva SHPATI Aurora NAPUCE Aurora NURO Ardit SHEHI Indrit BRAHOLLARI Doriana BEQIRAJ	*University of Tirana*	Occurrence and Risk Assessment of Organochlorine Pesticides and PCB Markers in Liver and Muscle Tissues of the Endemic Belushka (Salmo ohridanus) from Lake Ohrid
Vjollca BERISHA Sevdije GOVORI	*University of Prishtina*	Novel Co(II) and Ni(II) Pyrimidine Schiff Base Complexes as Potential Anticancer Agents
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Head of Session:

Authors	*Affiliation*	*Presentation Title*
Mohamed EL MORSY Laila AFIA	Ibnou Zohr University	Environmental Health Implications of Brine Management in Industrial Water Softening Systems
H. MABCHOUR H. AKARNI L. EL AARABI S. MORDANE	Hassan II University	Analytical Study of Wave-Current Interaction with Double Rectangular Trenches
Samiha BOUAOUICH Abdelali BALAHBIB Souad BOUHOUT El Bachir ADLAOUI Fatima AMARIR	Hassan II University	Distribution and Dynamics of Bulinus truncatus Populations in the Drâa-Tafilalt Region: Implications for Schistosomiasis Transmission
Janani S.S Preethi B Ragul R David G Jayaramakani N R. Srinivasan	Bharath Institute of Higher Education and Research	Herbal Medicines
Hawraa Abdulameer Ali Najlaa Abdulameer Ali	*University of Kufa*	Epidemiological Survey of Viral Infections Among Blood Donors and Their Association with Blood Groups in Al-Najaf Province, Iraq
A F M Faridul Islam Eun-Bi Kim M. Shaheer Akhtar Sadia Ameen	*Jeonbuk National University*	Zinc Stannate@Graphene Oxide Nanocomposite for Electrochemical Sensing of Aquatic Microplastics
Adamu Amanu Asari Ameyu Godesso Zewdie Birhanu	*Jimma University*	Health literacy among adolescents in Ethiopia: Evidence for policy and interventions
S. Deepak A. Palanisamy S. Kalaivanan Lavanya Babu C.Ravi G.David.	*Bharath Institute of Higher Education and Research*	Optimizing Cefazolin Prophylaxis in Obese Adults Undergoing Surgery
Safinez BOUTRID	*University of Batna*	Protective effect of the flavonoid extract of Ranunculus repens against hyperglycemia and pancreatic damage in an experimental model of glucotoxicity

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Head of Session: Kübra Geçmez Cahan

Authors	*Affiliation*	*Presentation Title*
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Mehmet Ali Dursun	*Tavsanli State Hospital, Dept. of Orthopedics and Traumatology*	Relationship between chronic lateral epicondylitis and erectile dysfunction: a prospective cross-sectional comparative study
Deniz Taşkıran	*Giresun University*	Association between maternal tsh levels and neonatal birth weight: a retrospective cohort study
Zahide Yüsra Yıldız Mahire Bayramoğlu Alkoyun Kıvanç Irak	*Siirt University*	The Potential Protective Effects of Polydatin Against Oxidative Stress and Ferroptosis
Fatima Qasim Bushra Parveen Kulsoom Ghulam Ali	*Government College University Faisalabad*	Synthesis, Characterization and Biological Applications of Mixed Ligand Metal Complexes with a Ligand derived from 2-amino-4-chlorophenol and 5-bromo Salicylaldehyde and 1,10 phenanthroline as a Co-ligand
Maria Fareed Siddiqui Umar Raees Aiman Mehmood	*University of Lahore*	Association of Oral and Parenteral Antidiabetic Therapy with Acute Myocardial Infarction in Patients with Diabetes Mellitus
Zahra ORDUDARI	*Isfahan University of Medical Science*	The Health–Labour Nexus: A Critical Review of Occupational Health Challenges, Theoretical Frameworks, and Multilevel Strategies for Sustainable Worker Well-being
Ndidi M, Ofole OKESIJI L.A	*University of Ibadan*	Therapeutic Impact Of Social Skills-Based Intervention On Hiv Self-Stigma Among Newly Diagnosed Patients In Oyo State, Nigeria
Loichita Mihai Petre Ion Furau Marius Faur Ionut Bobora Razvan Mirica Nicoleta Voinea Oana Petre Izabella	*University of Medicine and Pharmacy Timisoara*	The relationship between endometrial cancer and Lynch syndrome
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Head of Session: Melike POSTALLI

Authors	*Affiliation*	*Presentation Title*
Melike Postallı Yusuf AYKEMAT	*Nuh Naci Yazgan University*	The Emerging Role of GLP-1 Analogs in Nutrition and Obesity Management: Current Perspectives and Nutritional Considerations
Ümit Ünsal Yusuf AYKEMAT	*Nuh Naci Yazgan University*	Food Noise: Neurobehavioral Mechanisms, Appetite Regulation, and Nutritional Perspectives
Rabia Çiçek Yusuf AYKEMAT	*Nuh Naci Yazgan University*	Mindful Eating: Current Perspectives on Eating Awareness and Nutritional Behavior
Rümeysa Karapınar Yusuf AYKEMAT	*Nuh Naci Yazgan University*	Ultra-Processed Foods and Appetite Regulation: Current Evidence and Nutritional Perspectives
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Merve Nur Demir Yusuf AYKEMAT	*Nuh Naci Yazgan University*	The Potential Role of Bitter Hop Extract in Obesity Management: Current Evidence and Nutritional Perspectives
Yusuf Erdoğan Yusuf AYKEMAT	*Nuh Naci Yazgan University*	The Effects of Whey Protein Supplementation on Appetite Control: Current Evidence and Nutritional Perspectives
Fatma Aybike Bozoklu Yusuf AYKEMAT	*Nuh Naci Yazgan University*	The Role of Akkermansia muciniphila in Obesity Management: Current Insights and Nutritional Perspectives
Reshma Kanwal Preet Singh Attwal	*Punjabi University*	A Review on Feature Extraction Techniques for Medicinal Plant Identification

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ÇOCUKLARDA MİNDFULNESS TEMELLİ MÜDAHALELER: BİR DERLEME

Nagihan Merve Söylemez

Kırşehir Ahi Evran Üniversitesi, Sağlık Bilimleri Fakültesi, Hemşirelik Bölümü, Kırşehir, Türkiye

ORCID ID: https://orcid.org/0000-0002-3430-7241

Selin Söyünmez

Kırşehir Ahi Evran Üniversitesi, Sağlık Bilimleri Fakültesi, Hemşirelik Bölümü, Kırşehir, Türkiye

ORCID ID: https://orcid.org/0000-0001-5671-6444

ÖZET

Mindfulness yaklaşık 2500 yıl önce Budist meditasyon uygulamalarından doğan, günümüzde dikkat, farkında olma ve anı yargısız biçimde deneyimleme becerilerini içeren çok boyutlu bir kavram olarak tanımlanmaktadır. Türkçede "bilinçli farkındalık" olarak ifade edilen bu yaklaşım, bireyin dikkatini kasıtlı olarak içinde bulunduğu ana yönlendirmesi ve deneyimlerini kabul edici bir tutumla gözlemlemesini temel alır. Son yıllarda okul öncesi dönemden yaşlılığa kadar geniş bir yaş aralığında mindfulness temelli müdahalelere yönelik bilimsel ilgi belirgin biçimde artmıştır. Mevcut literatür, bilinçli farkındalık uygulamalarının en yoğun olarak ilkokul çağı (6–12 yaş) ve erken ergenlik döneminde, çoğunlukla okul temelli programlar kapsamında ele alındığını göstermektedir. Buna karşın, okul öncesi dönem ve orta ergenlikte yürütülen çalışmaların sayısı giderek artmakla birlikte, bu yaş gruplarına ilişkin kanıtlar hem nicelik hem de yöntemsel tutarlılık açısından daha sınırlı ve heterojen bir yapı sergilemektedir. Özellikle 6–12 yaş arası çocuklarda yürütülen meta-analizler, mindfulness temelli programların dikkat, duygu ve davranış düzenleme, olumlu duygular ve sosyal beceriler üzerinde küçük ancak istatistiksel olarak anlamlı iyileşmeler sağladığını göstermektedir. Okul temelli mindfulness ve bilişsel davranışçı yaklaşımlar, çocuklarda duygu farkındalığını artırmakta, pozitif duyguları desteklemekte ve depresif belirtilerde azalma ile ilişkilendirilmektedir. Ayrıca anksiyete ve stres düzeylerinde anlamlı ancak sınırlı düzeyde düşüşler rapor edilmektedir. Mindfulness temelli müdahale uygulanan çocukların ebeveynlerinin raporları, çocuklarda olumsuz duygu dışavurumunun azaldığını ortaya koyarken; öğretmenlerinin değerlendirmeleri, dikkat problemlerinde azalma, duygu düzenleme ve prososyal davranışlarda artış ile akran sorunları ve duygusal belirtilerde azalmaya işaret etmektedir. Buna karşın, çocukların öz-bildirimlerinde depresif belirtilerde belirgin bir değişim gözlenmemekle birlikte, dispozisyonel mindfulness ve yaşam doyumu düzeyinde artış, psikolojik katılık ve anksiyetede azalma bildirilmektedir. Bu çerçevede, mevcut bulguların genel olarak olumlu bir eğilime işaret ettiği görülmekle birlikte, farklı örneklemler ve uygulama koşullarından elde edilen sonuçlardaki çeşitlilik dikkate alındığında, bilinçli farkındalık temelli müdahalelerin etkililiğine ilişkin daha dengeli ve kapsamlı değerlendirmelere ihtiyaç olduğu söylenebilir.

Anahtar Kelimeler: Çocuk, Bilinçli farkındalık, Müdahale programları

MINDFULNESS-BASED INTERVENTIONS IN CHILDREN: A REVIEW

ABSTRACT

Mindfulness, which originated approximately 2,500 years ago from Buddhist meditation practices, is currently defined as a multidimensional concept encompassing attention, awareness, and the nonjudgmental experience of the present moment. Referred to in Turkish as *bilinçli farkındalık*, this approach is based on the intentional direction of attention to the present moment and the observation of one's experiences with an accepting attitude. In recent years, scientific interest in mindfulness-based interventions has increased markedly across a wide age range, from preschool children to older adults. The existing literature indicates that mindfulness practices have been most extensively examined during

middle childhood (6–12 years) and early adolescence, predominantly within school-based programs. In contrast, although the number of studies conducted during the preschool period and middle adolescence has gradually increased, the evidence for these age groups remains more limited and heterogeneous in terms of both quantity and methodological consistency.

Particularly, meta-analyses conducted among children aged 6–12 years have demonstrated that mindfulness-based programs produce small but statistically significant improvements in attention, emotional and behavioral regulation, positive emotions, and social skills. School-based mindfulness and cognitive behavioral approaches have been shown to enhance emotional awareness, support positive emotions, and be associated with reductions in depressive symptoms in children. Furthermore, significant but modest decreases in anxiety and stress levels have been reported. Parent reports of children receiving mindfulness-based interventions indicate reductions in children's negative emotional expression, whereas teacher evaluations point to decreases in attention problems, peer difficulties, and emotional symptoms, as well as improvements in emotion regulation and prosocial behaviors. In contrast, children's self-reports have not demonstrated marked changes in depressive symptoms; however, increases in dispositional mindfulness and life satisfaction, along with decreases in psychological inflexibility and anxiety, have been reported.

Within this framework, although the existing findings generally indicate a positive trend, it can be stated that more balanced and comprehensive evaluations are needed regarding the effectiveness of mindfulness-based interventions, considering the variability in findings obtained from different samples and implementation conditions.

Keywords: Child, Mindfulness, Intervention programs

ERKEN ÇOCUKLUK DÖNEMİNDE YAPAY ZEKA DESTEKLİ EBEVEYNLİK

Tuğba KANMAZ

Dr. Öğr. Üyesi Kırşehir Ahi Evran Üniversitesi, Eğitim Fakültesi, Okul Öncesi Eğitimi ABD

ORCID:0000-0003-0810-6304

Amaç

Günümüzde yapay zeka teknolojilerinin ebeveynlik pratiklerine giderek daha fazla entegre olması, çocukların öğrenme ve gelişim deneyimlerinin dolaylı olarak algoritmik sistemler tarafından şekillenmesine yol açmaktadır. Bu bağlamda çalışma, erken çocukluk döneminde (3–6 yaş) çocuğu olan ebeveynlerin yapay zeka (YZ) destekli araçları ebeveynlik süreçlerinde nasıl kullandıklarını ve bu süreçte geliştirdikleri pedagojik karar alma, güven değerlendirmesi ve etik muhakeme biçimlerini incelemeyi amaçlamaktadır. Ayrıca çalışma, yapay zeka kullanımının çocukların gelişimsel süreçleriyle ilişkisini ebeveyn perspektifinden analiz etmeyi hedeflemektedir.

Materyal ve Yöntem

Bu araştırma, nitel araştırma yaklaşımı çerçevesinde fenomenoloji deseni ile yürütülmüştür. Çalışma grubunu, ölçüt örnekleme yöntemiyle belirlenen, 3–6 yaş aralığında çocuğa sahip ve en az bir kez yapay zeka temelli araç kullanmış 19 ebeveyn oluşturmaktadır. Veri toplama sürecinde yarı yapılandırılmış görüşme formu kullanılarak ebeveynlerin yapay zeka kullanım deneyimleri, pedagojik karar alma süreçleri, güven algıları ve etik değerlendirmeleri derinlemesine incelenmiştir. Elde edilen veriler tematik analiz yöntemi kullanılarak sistematik biçimde çözümlenmiştir.

Bulgular

Bulgular, ebeveynlerin yapay zekayı ağırlıklı olarak bilgi edinme ve araştırma amacıyla kullandıklarını göstermektedir. Kullanım alanları; çocukların gelişim düzeyine ilişkin değerlendirmeler, sağlık konuları, yaratıcı etkinlik ve materyal önerileri, dijital içeriklerin uygunluğu ve çocukların sorularına yanıt bulma gibi pratik ebeveynlik süreçlerinde yoğunlaşmaktadır. Ebeveynler, yapay zekanın hızlı, pratik ve yaratıcı çözümler sunmasını önemli bir avantaj olarak değerlendirirken, elde edilen bilgileri çoğu zaman çocuklarının gelişim özelliklerine göre uyarladıklarını ifade etmiştir. Bununla birlikte, içeriklerin zaman zaman yüzeysel ya da yetersiz olduğu, doğruluğunun her zaman kontrol edilemediği ve veri gizliliğine ilişkin kaygılar taşıdıkları belirlenmiştir. Ayrıca yapay zekanın düşünme süreçlerini sınırlayabileceği, yanlış yönlendirme riski taşıdığı ve bağımlılık oluşturabileceği de öne çıkan riskler arasındadır.

Sonuç

Sonuç olarak, yapay zekanın ebeveynlik süreçlerinde işlevsel ve destekleyici bir araç olarak konumlandığı, ancak kullanımının eleştirel değerlendirme ve pedagojik uyarlama gerektirdiği söylenebilir. Bu doğrultuda, ebeveynlerin yapay zekayı daha bilinçli ve eleştirel bir biçimde kullanabilmelerini desteklemek amacıyla dijital okuryazarlık ve yapay zeka farkındalığına yönelik eğitim programlarının geliştirilmesi önerilmektedir.

Anahtar Kelimeler: Erken çocukluk, Yapay zeka, Ebeveyn

AI-SUPPORTED PARENTING IN EARLY CHILDHOOD

Aim

The increasing integration of artificial intelligence (AI) technologies into parenting practices has led to the indirect shaping of children's learning and developmental experiences through algorithmic systems. In this context, the present study aims to examine how parents of children in early childhood (aged 3–6) utilize AI-supported tools in their parenting processes, as well as the pedagogical decision-making, trust evaluations, and ethical reasoning they develop in this process. Additionally, the study seeks to

analyze the relationship between AI use and children's developmental processes from the parental perspective.

Materials and Methods

This study was conducted within the framework of a qualitative research approach using a phenomenological design. The study group consisted of 19 parents, selected through criterion sampling, who have children aged 3–6 and have used at least one AI-based tool in parenting or child development processes. Data were collected using a semi-structured interview form, enabling an in-depth examination of parents' experiences with AI use, their pedagogical decision-making processes, perceptions of trust, and ethical evaluations. The collected data were analyzed systematically using thematic analysis.

Findings

The findings indicate that parents primarily use AI tools for information seeking and research purposes. Areas of use include evaluating children's developmental levels, addressing health-related issues, generating creative activities and materials, assessing the appropriateness of digital content, and responding to children's questions. Parents emphasized the advantages of AI in providing fast, practical, and creative solutions, while also stating that they frequently adapt AI-generated information according to their children's developmental characteristics. However, it was found that the content may sometimes be superficial or insufficient, that its accuracy is not always verified, and that parents have concerns regarding data privacy. In addition, potential risks such as limiting critical thinking, the possibility of misinformation, and the risk of dependency were identified as prominent concerns.

Conclusion

In conclusion, AI is positioned as a functional and supportive tool in parenting processes; however, its use requires critical evaluation and pedagogical adaptation. Accordingly, it is recommended to develop digital literacy and AI awareness programs to support parents in using AI more consciously and critically.

Keywords: Early childhood, Artificial intelligence, Parenting.

ÜÇÜNCÜ BASAMAK BİR HASTANEDE YENİ TANI DİYABET HASTALARINDA HBA1C DÜZEYLERİ VE DEMOGRAFİK FAKTÖRLERİN İLİŞKİSİ: VAN İLİ ÖRNEĞİ

Dr. Öğr. Üyesi Adem Yağan

Arş. Gör. Dr. Zelal Yayla Kalay

Arş. Gör. Dr. Musa Yağan

Arş. Gör. Dr. Mücahit Önal

Amaç: Bu çalışmada, Van'da üçüncü basamak bir hastaneye başvuran yeni tanı tip 2 diyabet hastalarında HbA1c düzeyleri ile demografik faktörler arasındaki ilişkinin değerlendirilmesi amaçlandı.

Yöntem: Retrospektif ve tanımlayıcı tipte planlanan çalışmada, 2010-2025 yılları arasındaki hastane kayıtları incelendi. Yaşı 18-90 arasında olan ve HbA1c verisi bulunan 22.255 hastanın, hastaneye ilk kayıt anındaki sonucu analize dahil edildi. Yaş, cinsiyet, ikamet ve biyokimyasal parametreler değerlendirildi.

Bulgular: Hastaların yaş ortalaması 53,2±16,2 yıl olup %59,7'si kadındı. Ortalama HbA1c düzeyi 6,35±1,73 olarak saptandı. Hastaların %43,9'unda HbA1c <5,7, %29,9'unda 5,7-6,4 ve %26,2'sinde ≥6,5 idi. Erkeklerde HbA1c düzeyi kadınlara göre daha yüksekti. Yaş arttıkça HbA1c düzeyinin anlamlı biçimde yükseldiği görüldü. HbA1c ile açlık glukozu arasında güçlü pozitif korelasyon saptandı. Ayrıca trigliserid ve LDL ile pozitif, HDL ile negatif ilişki izlendi.

Sonuç: Bulgular, yenitanı tip 2 diyabet hastalarında kötü glisemik kontrolün özellikle ileri yaş, erkek cinsiyet ve olumsuz metabolik profil ile ilişkili olduğunu göstermektedir. Bölgesel risk gruplarının tanımlanması, erken müdahale ve hedefe yönelik izlem stratejileri açısından önemlidir.

Anahtar kelimeler: Tip 2 diyabet, HbA1c, glisemikkontrol, demografik faktörler, metabolikprofil, Van

ADOLESAN BİREYLERDE DEPRESYON RİSKİNİN TAHMİNİNDE AÇIKLANABİLİR YAPAY ZEKA İLE MAKİNE ÖĞRENİMİ YAKLAŞIMI: PSİKİYATRİ HEMŞİRELİĞİ PERSPEKTİFİYLE BİR MODEL ÖNERİSİ

Elif KAYA

Erciyes Üniversitesi, Sağlık Bilimleri Enstitüsü, Ruh Sağlığı ve Hastalıkları Hemşireliği Anabilim Dalı (Doktora Programı), Kayseri, Türkiye

Kırşehir Ahi Evran Üniversite, Sağlık Bilimleri Fakültesi, Psikiyatri Hemşireliği Bölümü, Kırşehir, Türkiye

ORCID: 0000-0002-8700-5538

Umut Cindiloğlu

Endüstri Mühendisliği Bölümü, Mühendislik Fakültesi, Gazi Üniversitesi, Ankara, Türkiye

ORCID: 0000-0002-1600-2006

ÖZET

Amaç: Bu çalışmanın amacı, adolesan bireylerde depresyon riskini yüksek doğrulukla tahmin edebilen, aynı zamanda klinik olarak yorumlanabilir bir makine öğrenmesi tabanlı karar destek modeli geliştirmektir. Psikiyatri hemşireliği perspektifiyle ele alınan çalışma, dijital davranışlar, yaşam tarzı ve psikososyal değişkenlerin depresyon riski üzerindeki etkileşimlerini açıklanabilir yapay zeka yaklaşımıyla ortaya koymayı hedeflemektedir.

Materyal ve Yöntem: Kesitsel ve öngörücü tasarıma sahip bu araştırmada, 2.500 adolesanı temsil eden Kaggle kaynaklı *Teen Mental Health Dataset* kullanılmıştır. Bağımlı değişken depresyon riski (düşük-orta-yüksek) olarak tanımlanmıştır. Bağımsız değişkenler demografik özellikler, dijital davranışlar, uyku ve fiziksel aktivite düzeyleri, stres ve anksiyete gibi psikososyal parametreler ile akademik performansı kapsamaktadır. Veri seti ön işleme aşamasında etiketleme, normalizasyon ve sınıf dengeleme teknikleri uygulanmıştır. K-En Yakın Komşu, Lojistik Regresyon, Karar Ağacı, Random Forest ve Naive Bayes algoritmaları eğitilmiş; performans değerlendirmesinde doğruluk, F1 skoru ve çok sınıflı AUC ölçütleri kullanılmıştır.

Bulgular: Analiz sonuçları, ağaç tabanlı algoritmaların lineer ve olasılıksal modellere kıyasla anlamlı düzeyde üstün performans sağladığını göstermiştir. Karar Ağacı modeli %91,7 doğruluk ve 0,917 F1 skoru ile en başarılı sınıflandırmayı gerçekleştirirken, Random Forest modeli 0,989 AUC değeri ile sınıfları ayırt etmede neredeyse kusursuz bir kapasite sunmuştur. Bu bulgular, depresyon riskinin çok değişkenli ve doğrusal olmayan yapısını doğrulamaktadır.

Sonuç: Çalışma, açıklanabilir makine öğrenmesi modellerinin psikiyatri hemşireliğinde erken risk tanılama, vaka önceliklendirme ve kişiselleştirilmiş bakım planlamasında etkili bir karar destek aracı olarak kullanılabileceğini ortaya koymaktadır. Özellikle Karar Ağacı temelli modeller, hemşirelik uygulamalarında klinik gerekçelendirmeyi güçlendirme potansiyeline sahiptir.

Anahtar Kelimeler: Açıklanabilir yapay zeka, adolesan, depresyon, makine öğrenmesi, psikiyatri hemşireliği.

CURRENT AND INNOVATIVE METHODS IN THE EDUCATION OF PREGNANT WOMEN WITH GESTATIONAL DIABETES AND THE ROLE OF THE NURSE: A LITERATURE REVIEW

Kevser AVCI KABAL

Nurse, Kırşehir Training and Research Hospital, Department of Obstetrics and Gynecology Nursing, kvsrrvci@gmail.com, 05362342534, ORCID: 0009-0007-0595-4291

Murat Gökhan KABAL

Research Assistant, Kırşehir Ahi Evran University, Faculty of Health Sciences, Department of Nursing, Department of Internal Medicine Nursing, murat.kabal@ahievran.edu.tr, 05519756132, ORCID: 0000-0002-2580-6858

ABSTRACT

Gestational Diabetes Mellitus (GDM) is a significant metabolic disorder that occurs during pregnancy, affecting approximately 14-18% of pregnancies worldwide. Uncontrolled hyperglycemia increases the risk of preeclampsia, cesarean delivery, and subsequent type 2 diabetes in the mother, while leading to severe complications in the neonate such as macrosomia, hypoglycemia, and preterm birth. In supporting patient education and self-management, which are the core components of GDM management, traditional methods based on one-way communication remain inadequate in providing personalized feedback. The aim of this review is to examine innovative interventions used in GDM education and the changing roles of nurses in the digitalized care process in light of the literature.

To bridge the gaps in traditional education methods, innovative interventions such as mobile health (mHealth) applications, telemedicine platforms, web-based educational systems, social media support networks, psychoeducational interventions, group care models, and artificial intelligence (AI)-supported systems have come to the forefront. These innovative methods have been shown to yield positive clinical and psychosocial outcomes, including improvements in fasting and postprandial blood glucose levels, reductions in anxiety, and enhancements in self-efficacy and self-care behaviors. It has been established that integrating these innovative interventions with various health theories and quality management tools further strengthens clinical success.

In this process, nurses assume key roles that go beyond mere clinical monitoring, such as educational counseling, digital coordination, and providing psychosocial support. Nevertheless, conditions such as a lack of digital health literacy, alongside language and cultural barriers, remain the primary obstacles restricting the adoption of innovative applications. Consequently, integrating approaches into clinical practice that blend technology-supported care with the empathetic and emotional support—an indispensable element of face-to-face communication—as well as incorporating the digital competencies of nurses into the core nursing curriculum, are of paramount importance.

Keywords: Gestational Diabetes, Nursing, Patient Education, Digital Health, Psychoeducation, Self-Management

GESTASYONEL DİYABETLİ GEBELERİN EĞİTİMİNDE GÜNCEL VE YENİLİKÇİ YÖNTEMLER VE HEMŞİRENİN ROLÜ: LİTERATÜR DERLEMESİ

ÖZET

Gestasyonel Diyabetes Mellitus (GDM), gebelik sürecinde ortaya çıkan ve dünya genelinde gebeliklerin yaklaşık %14-18'ini etkileyen önemli bir metabolik bozukluktur. Kontrol altına alınamamış hiperglisemi; annede preeklampsi, sezaryen doğum ve ilerleyen dönemde tip 2 diyabet riskini artırırken yenidoğanda makrozomi, hipoglisemi ve erken doğum gibi ciddi komplikasyonlara yol açmaktadır.

GDM yönetiminin temel bileşeni olan hasta eğitimi ve öz-yönetimin desteklenmesinde, tek yönlü iletişime dayalı geleneksel yöntemler kişiselleştirilmiş geri bildirim sağlama açısından yetersiz kalmaktadır. Bu derlemenin amacı, GDM eğitiminde kullanılan yenilikçi müdahaleleri ve dijitalleşen bakım sürecinde hemşirenin değişen rollerini literatür ışığında incelemektir.

Geleneksel eğitim yöntemlerinin açıklarını kapatmak amacıyla mobil sağlık uygulamaları, tele-tıp platformları, web tabanlı eğitim sistemleri, sosyal medya destek ağları, psikoeğitimsel müdahaleler, grup bakım modelleri ve yapay zeka destekli sistemler gibi yenilikçi müdahaleler ön plana çıkmaktadır. Söz konusu yenilikçi yöntemlerin, açlık-tokluk kan glukozu düzeylerinde iyileşme, anksiyetede azalma, öz-yeterlilik ve öz-bakım davranışlarında artış gibi olumlu klinik ve psikososyal çıktılar sağladığı görülmektedir. Bu yenilikçi müdahalelerin çeşitli sağlık kuramları ve kalite yönetim araçları ile bütünleştirilmesinin klinik başarıyı daha da güçlendirdiği saptanmıştır.

Bu süreçte hemşireler, salt klinik izlemi aşan; eğitim danışmanlığı, dijital koordinatörlük ve psikososyal destek sağlama gibi kilit roller üstlenmektedir. Bununla birlikte dijital sağlık okuryazarlığı eksikliği, dil ve kültürel bariyerler gibi durumlar yenilikçi uygulamaların benimsenmesini sınırlayan başlıca engellerdir. Sonuç olarak, teknoloji destekli bakımı, yüz yüze iletişimin vazgeçilmez bir unsuru olan empatik ve duygusal destekle harmanlayan yaklaşımların klinik sahada hayata geçirilmesi ve hemşirelerin dijital yetkinliklerinin hemşirelik eğitimi müfredatına dahil edilmesi büyük önem taşımaktadır.

Anahtar Kelimeler: Gestasyonel Diyabet, Hemşirelik, Hasta Eğitimi, Dijital Sağlık, Psikoeğitim, Öz-Yönetim

KAHKAHA TEMELLİ MÜDAHALELERİN ÇOCUK SAĞLIĞI ÜZERİNDEKİ ETKİSİ ÜZERİNE DERLEME

Selin Söyünmez

Kırşehir Ahi Evran Üniversitesi, Sağlık Bilimleri Fakültesi, Hemşirelik Bölümü, Kırşehir, Türkiye

ORCID ID: https://orcid.org/0000-0001-5671-6444

Nagihan Merve Söylemez

Kırşehir Ahi Evran Üniversitesi, Sağlık Bilimleri Fakültesi, Hemşirelik Bölümü, Kırşehir, Türkiye

ORCID ID: https://orcid.org/0000-0002-3430-7241

ÖZET

Gülmek insan yaşamının doğal bir parçası, uyarana karşı verilen samimi ve doğuştan gelen evrensel bir tepkidir. Kahkaha yogası diğer adıyla kahkaha terapisi tıp doktoru olan Madan Kataria ve yoga eğitmeni eşi tarafından, 1995 yılında, kahkahanın iyileştirici gücünün nefes egzersizleriyle birleştirilmesiyle oluşturulmuş fizyolojik, psikolojik ve sosyal yönden olumlu etkileri olan tamamlayıcı alternatif bir terapi şeklidir. Sadece gülümsemek ya da mutluymuş gibi davranmak bile vücudun mutlulukla ilgili salgısal süreçleri başlatmasını sağlamaktadır. Kahkaha yogasında gülmek için bir nedene ya da mizaha gerek duyulmamaktadır. Ayrıca gülmenin yanında nefes egzersizleri, esneme egzersizleri ve meditasyon gibi yoga egzersizlerini de içermektedir. Literatür, kahkaha yogasının çocuklarda fiziksel, psikolojik ve sosyal alanlarda çok yönlü olumlu etkiler oluşturduğunu göstermektedir. Fizyolojik açıdan kahkaha yogasının oksijenlenmeyi artırdığı, solunum kapasitesini desteklediği, tükrük IgA'da artış sağladığı; kan şekeri, trigliserit, total kolesterol, kan basıncı, nabız, stresle ilişkili fizyolojik yanıtları azalttığı ve postoperatif ağrı kontrolünde etkili olduğu bildirilmiştir. Psikolojik olarak çocuklarda stres, anksiyete ve gerginlik düzeylerini azaltırken; olumlu duygulanımı, mutluluk hissini ve duygusal dayanıklılığı artırmaktadır. Sosyal boyutta ise grup temelli uygulanması sayesinde iletişim becerilerini güçlendirdiği, sosyal etkileşimi artırdığı ve akran ilişkilerini desteklediği belirtilmektedir. Bununla beraber özel gruplarla yapılan çalışmalarda kahkaha yogasının lösemili çocuklarda yalnızlık ve umutsuzluk düzeyini azalttığı, fiziksel engelli adölesanlarda psikolojik sağlamlığı artırdığı, görme engelli çocuklarda sözel çalışma belleği düzeyini artırdığı, hafif gelişimsel yetersizliği olan adölesanlarda süreğen kaygı ve yalnızlık düzeyini azalttığı bildirilmiştir. Sağlıklı çocuklarda ise okul tükenmişliğini azalttığı, okul yaşamına uyumu, umut, mutluluk ve benlik saygısını artırdığı belirtilmiştir. Sonuç olarak, kahkaha yogası çocuklarda bütüncül gelişimi destekleyen, düşük maliyetli ve yan etkisiz bir tamamlayıcı yöntem olup; oyun temelli yapısı sayesinde çocukların katılımını artırarak sürdürülebilir bir uygulama niteliği taşımaktadır.

Anahtar Kelimeler: Çocuk, Kahkaha Yogası, Kahkaha Terapisi, Tamamlayıcı Terapiler

A REVIEW ON THE EFFECTS OF LAUGHTER-BASED INTERVENTIONS ON CHILD HEALTH

ABSTRACT

Laughter is a natural part of human life and an innate, sincere, and universal response to stimuli. Laughter yoga, also known as laughter therapy, is a complementary and alternative therapeutic approach developed in 1995 by medical doctor Madan Kataria and his yoga instructor wife. It was created by combining the healing power of laughter with breathing exercises and has physiological, psychological, and social beneficial effects. Even simply smiling or acting as if one is happy can initiate the body's secretion processes related to happiness. In laughter yoga, there is no need for a reason or humor to laugh. In addition to laughter, it also includes yoga practices such as breathing exercises, stretching exercises, and meditation. The literature demonstrates that laughter yoga has multifaceted positive

effects on children in physical, psychological, and social domains. Physiologically, it has been reported to increase oxygenation, support respiratory capacity, and increase salivary IgA levels; reduce blood glucose, triglycerides, total cholesterol, blood pressure, pulse rate, and stress-related physiological responses; and be effective in postoperative pain control. Psychologically, it reduces stress, anxiety, and tension levels in children while increasing positive affect, feelings of happiness, and emotional resilience. Socially, due to its group-based implementation, it strengthens communication skills, enhances social interaction, and supports peer relationships. Moreover, studies conducted with special groups have shown that laughter yoga reduces loneliness and hopelessness in children with leukemia, increases psychological resilience in physically disabled adolescents, improves verbal working memory in visually impaired children, and decreases chronic anxiety and loneliness in adolescents with mild developmental disabilities. In healthy children, it has been reported to reduce school burnout and improve school adjustment, as well as increase hope, happiness, and self-esteem. In conclusion, laughter yoga is a low-cost, side-effect-free complementary method that supports holistic development in children. Its play-based structure increases children's participation and makes it a sustainable intervention.

Keywords: Child, Laughter Yoga, Laughter Therapy, Complementary Therapies

A COMPARATIVE POLYPHENOLIC PROFILE OF *CENTAUREA* SPECIES BY LC-MS/MS AND EVALUATION OF THEIR ANTIOXIDANT, ANTIDIABETIC, ANTIBACTERIAL, ANTIALZHEIMER AND ANTIGLAUCOMA ACTIVITIES

Emrah YERLİKAYA

Professor, Siirt University, Faculty of Health Sciences, Nutrition and Dietetics Department, 56100, Siirt, Türkiye, ORCID ID: https://orcid.org/0000-0003-4050-0790, Biochemistry

Hasan KARAGEÇİLİ

Associate Professor Siirt University, Faculty of Health Sciences, Nursing Department, 56100, Siirt, Türkiye

ORCID ID: https://orcid.org/0000-0001-6912-3998, Biochemistry

Kübra ASLAN

Research Assistant Department of Chemistry, Faculty of Science, Atatürk University, 25240 Erzurum, Türkiye

ORCID ID: https://orcid.org/0000-0001-8388-5470, Biochemistry

Mesut SIRRI

Assistant Professor Siirt University, Kurtalan Vocational School, Department of Plant and Animal Production, 56100, Siirt, Türkiye

ORCID ID: https://orcid.org/0000-0001-9793-9599, Weed Science

Veysel TAHİROĞLU

Associate Professor Şırnak University, Faculty of Health Sciences, Nursing Department, 73100, Şırnak, Türkiye

ORCID ID: https://orcid.org/0000-0003-3516-5561, Biochemistry

İlhami GÜLÇİN

Professor Department of Chemistry, Faculty of Science, Atatürk University, 25240 Erzurum, Türkiye

ORCID ID: https://orcid.org/0000-0001-5993-1668, Biochemistry

ABSTRACT

Aim: Plants have been used as folk remedies for treating various diseases for many years. Therefore, plants are considered a key target for the discovery of drug candidates due to their bioactive compounds and are actively researched worldwide. It has been determined that 80% of 122 plant-based medicines are derived from traditionally used plants[1]. The *genus Centaurea L.* belongs to the Asteraceae family and has over 600 species worldwide. It has a wide distribution in Europe and the Mediterranean. *Centaurea L.* is the third most common genus in Türkiye, with 255 taxa and 194 species, 118 of which are endemic. The endemic rate is 68% [2]. This study aims to evaluate the polyphenolic profiles, antioxidant properties, and enzyme inhibition activities of ethanol and aqueous extracts of *Centaurea spectabilis var. spectabilis* (C1)*, Centaurea nemecii* (C2), and *Centaurea gigantea* (C3).

Materials and Methods: In this study, the polyphenolic profiles and antioxidant, antimicrobial, antidiabetic, anti-alzheimer's, and antiglaucoma potentials of ethanol extracts obtained from *Centaurea spectabilis var. spectabilis*, *Centaurea nemecii* and *Centaurea gigantea* were evaluated using an integrated approach. After determining the total phenolic content and total flavonoid content of the extracts, their phytochemical compositions were comprehensively characterized by LC–MS/MS analysis.

Findings: The LC–MS/MS results revealed that the C1 extract was rich in phenolic acids, the C2 extract was distinguished by a high diversity of flavonoids and flavonoid glycosides, while the C3 extract exhibited a more selective composition dominated by quercetin. Antioxidant activity assays (ABTS, DPPH, CUPRAC, FRAP, and Fe^{3+} reducing power) demonstrated that all extracts exerted concentration-dependent antioxidant effects, with the overall antioxidant capacity ranked as C1 ≥ C2 > C3. In enzyme

inhibition studies, the C3 extract showed the strongest inhibitory activity against acetylcholinesterase, whereas the C2 extract exhibited the most pronounced inhibition of butyrylcholinesterase and α-glucosidase. Antimicrobial activity results indicated that the ethanol extracts of *Centaurea* species produced concentration-dependent inhibitory effects, particularly against multidrug-resistant Gram-negative bacteria. Among the tested extracts, the C1 extract exhibited the broadest antimicrobial spectrum, showing activity against *Escherichia coli, Pseudomonas aeruginosa, Klebsiella pneumoniae*, and *Staphylococcus aureus*.

Conclusion: In conclusion, this study demonstrates that *Centaurea* species, owing to their rich phytochemical compositions, represent natural sources capable of modulating multiple biological targets. Their notable antioxidant, enzyme inhibitory, and antimicrobial properties highlight their promising potential for the development of pharmaceutical and functional products.

Keywords: *Centaurea spectabilis var. spectabilis; Centaurea gigantea; Centaurea nemecii;* Antioxidant; α-glycosidase; Acetylcholinesterase; Carbonic Anhydrase; Phenolic Compounds.

Acknowledgement: This study are supported by Siirt University Scientific Research Projects Coordination (2025-SİÜSBF-03).

References:

1. Yırtıcı, Ü., Ergene, A., Atalar, M. N., & Adem, Ş. (2022). Phytochemical composition, antioxidant, enzyme inhibition, antimicrobial effects, and molecular docking studies of *Centaurea sivasica*. South African Journal of Botany, 144, 58–71. https://doi.org/10.1016/j.sajb.2021.08.043
2. Guven, L., Ugur Kaplan, A. B., Yesilyurt, F., Cetin, M., Lacin, B. B., Ozkaraca, M., Yilmaz, M. A., Hacimuftuoglu, A., & Kaya, Y. (2024). The methanol extract of *Centaurea depressa* M. Bieb. -Containing nanoemulsion formulation: In vitro characterization and scratch assay. Journal of Drug Delivery Science and Technology, 99(February), 105923. https://doi.org/10.1016/j.jddst.2024.105923

ASSESMENT OF PEONIDIN COMPOUND'S ANTIOXIDANT, ANTIDIABETIC, ANTIMICROBIAL, ANTIALZHEIMER AND ANTIGLAUCOMA ACTIVITIES AND MOLECULAR DOCKING OF PEONIDIN

Hasan KARAGEÇİLİ

Associate Professor Siirt University, Faculty of Health Sciences, Nursing Department, 56100, Siirt, Türkiye, ORCID ID: https://orcid.org/0000-0001-6912-3998, Biochemistry

Emrah YERLİKAYA

Professor Siirt University, Faculty of Health Sciences, Nutrition and Dietetics Department, 56100, Siirt, Türkiye, ORCID ID: https://orcid.org/0000-0003-4050-0790, Biochemistry

Adem ERTÜRK

Asistant Professor Department of Chemistry, Faculty of Science, Ataturk University, 25240 Erzurum, Türkiye, ORCID ID: https://orcid.org/ 0000-0002-1750-1966, Biochemistry

Kübra ASLAN

Research Assistant Department of Chemistry, Faculty of Science, Atatürk University, 25240 Erzurum, Türkiye, ORCID ID: https://orcid.org/0000-0001-8388-5470, Biochemistry

İlhami GÜLÇİN

Professor Department of Chemistry, Faculty of Science, Atatürk University, 25240 Erzurum, Türkiye

ORCID ID: https://orcid.org/0000-0001-5993-1668, Biochemistry

ABSTRACT

Aim: Anthocyanins are water-soluble plant pigments. They give many plants, fruits, vegetables, and cereal kernels their red, purple, and blue colors [1]. Aim of this study is to reveal the biological properties of peonidin, an anthocyanin.

Materials and Methods: To comprehend the antioxidant capabilities of peonidin 2,2'-azino-bis-3-ethylbenzthiazoline-6-sulphonic acid radical ($ABTS^{\bullet+}$), N,N-dimethyl-p-phenylenediamine dihydrochloride radical ($DMPD^{\bullet+}$), and 1,1-diphenyl-2-picrylhydrazyl free radical ($DPPH^{\bullet}$), Fe^{3+}-2,4,6-tris(2-pyridyl)-s-triazine (TPTZ) and Cu^{2+} reducing assays were recorded. The IC_{50} values for peonidin for $ABTS^{\bullet+}$ and $DPPH^{\bullet}$ scavenging capabilities were resolved to compare with standard antioxidants [2].

Findings: $ABTS^{\bullet+}$ radical scavenging activity of peonidin had a IC_{50} value of 15.40 µg/mL, while the IC_{50} values for BHA, BHT, Trolox, and α-Tocopherol were 12.82, 11.78, 12.67, and 10.83 µg/mL, accordingly. $DPPH^{\bullet}$ radical scavenging activity of peonidin had an IC_{50} value of 43.32 µg/mL, while the IC_{50} values for BHA, BHT, Trolox, and α-Tocopherol were 8.45, 23.10, 6.30, and 18.73 µg/mL, respectively. Inhibitions of enzymes were studied to investigate the effects of peonidin. The K_i values of peonidin exhibited 114.33, 63.02, 2.99, 9.76 and 15.14 nM toward hCA I, hCA II, AChE, BChE, and α-glycosidase, respectively. Furthermore, peonidin's interactions with target enzymes BChE, hCA II, AChE, and α-glycosidase were investigated by molecular docking.

Conclusion: The results postulated that antioxidant-rich peonidin is a plant-based compound with potential use in the remedy of glaucoma, Alzheimer's and diabetes diseases.

Keywords: peonidin; antioxidant; α-glycosidase; antimicrobial; acetylcholinesterase; carbonic anhydrase; flavonoid compounds; molecular docking

Acknowledgement: This study are supported by Siirt University Scientific Research Projects Coordination (2025-SİÜSBF-02).

References

1. HE L, KANG Z, HAIQIN J, et al. Current advances in anthocyanins- structure, bioactivity and human health. *J Food Nutr Res*. 2021;60(1336-8672):203-216.

2. Durmaz L, Karageçili H, Erturk A, et al. Hamamelitannin's Antioxidant Effect and Its Inhibition Capability on α-Glycosidase, Carbonic Anhydrase, Acetylcholinesterase, and Butyrylcholinesterase Enzymes. *Processes*. 2024;12(11). doi:10.3390/pr12112341

ADAPTATION OF THE HALITOSIS ASSOCIATED LIFE-QUALITY TEST (HALT) INTO TURKISH: PRELIMINARY RESULTS

PINAR GÜVENÇ

Deü Diş Hekimliği Fakültesi Restoratif Diş Tedavisi Ana Bilim Dalı, İzmir, Türkiye, ORCID: 0000-0002-9410-8391

DENİZ ÇETİN

Deü Diş Hekimliği Fakültesi Restoratif Diş Tedavisi Ana Bilim Dalı, İzmir, Türkiye, ORCID: 0009-0005-0681-8879

ASLI SİLKÜ OFLİOĞLU

Deü Diş Hekimliği Fakültesi Restoratif Diş Tedavisi Ana Bilim Dalı, İzmir, Türkiye, ORCID: 0009-0009-1210-9867

HÜLYA ERTEN

Deü Diş Hekimliği Fakültesi Restoratif Diş Tedavisi Ana Bilim Dalı, İzmir, Türkiye, ORCID: 0000-0001-7823-7145

Objective

Halitosis is an important condition that can affect individuals' social and psychological well-being, and there is a need for valid and reliable measurement tools to assess this impact. The aim of this study was to perform the cultural adaptation of the Halitosis Associated Life-Quality Test (HALT) into Turkish and to present the preliminary evaluation findings.

Materials and Methods

This methodological study was conducted in accordance with international guidelines for scale adaptation (Beaton et al., WHO). The HALT scale was independently translated into Turkish by two translators, and the resulting translations were reconciled by the research team to obtain a single version. Subsequently, a back-translation procedure was applied to evaluate linguistic and conceptual equivalence with the original scale. Content validity was assessed by a panel of five experts experienced in the field. The comprehensibility and cultural appropriateness of the scale were evaluated through a pilot study conducted with 30 volunteer participants. Feedback regarding the clarity and understandability of the items was obtained from the participants, and minor linguistic revisions were made to a limited number of items based on this feedback.

Results

The results of the pilot study indicated that the Turkish version of the HALT scale was generally found to be understandable and applicable by the participants. Minor linguistic revisions were made to some items in line with participant feedback. Positive findings were obtained regarding the comprehensibility of the scale in the target population. Factor analysis revealed that the scale had a unidimensional structure and explained a substantial proportion of the total variance. The Cronbach's alpha coefficient was found to be 0.95.

Conclusion

The Turkish version of the HALT scale appears to be appropriate in terms of comprehensibility and applicability based on the preliminary findings. However, further advanced psychometric analyses with larger sample sizes are required to establish the validity and reliability of the scale.

Keywords

Halitosis, quality of life, scale adaptation, cultural adaptation, HALT

HALITOSIS ASSOCIATED LIFE-QUALITY TEST (HALT) ÖLÇEĞİNİN TÜRKÇE'YE UYARLANMASI: ÖN ÇALIŞMA SONUÇLARI

ABSTRACT

Amaç

Halitozis, bireylerin sosyal ve psikolojik yaşamını etkileyebilen önemli bir durum olup, bu etkinin değerlendirilmesine yönelik geçerli ve güvenilir ölçüm araçlarına ihtiyaç duyulmaktadır.Bu çalışmanın amacı, Halitosis Associated Life-Quality Test (HALT) ölçeğinin Türkçe'ye kültürel adaptasyonunun gerçekleştirilmesi ve ön değerlendirme bulgularının sunulmasıdır.

Gereç ve Yöntem

Bu metodolojik çalışma, ölçek uyarlama çalışmalarına yönelik uluslararası kılavuzlar (Beaton ve ark., WHO) doğrultusunda yürütülmüştür. HALT ölçeği iki bağımsız çevirmen tarafından Türkçe'ye çevrilmiş ve elde edilen çeviriler araştırma ekibi tarafından uzlaştırılarak tek bir versiyon oluşturulmuştur. Daha sonra geri çeviri yöntemi uygulanarak orijinal ölçek ile dilsel ve kavramsal eşdeğerlik değerlendirilmiştir. İçerik geçerliği, alanında deneyimli 5 uzmandan oluşan bir ekip tarafından değerlendirilmiştir. Ölçeğin anlaşılabilirliği ve kültürel uygunluğu, 30 gönüllü birey üzerinde gerçekleştirilen pilot uygulama ile incelenmiştir. Katılımcılardan maddelerin açıklığı ve anlaşılabilirliği hakkında geri bildirim alınmış ve bu geri bildirimler doğrultusunda gerekli görülen sınırlı sayıda maddede dilsel düzenlemeler yapılmıştır.

Bulgular

Pilot uygulama sonuçları, HALT ölçeğinin Türkçe versiyonunun katılımcılar tarafından genel olarak anlaşılır ve uygulanabilir bulunduğunu göstermiştir. Katılımcı geri bildirimleri doğrultusunda bazı maddelerde küçük dilsel düzenlemeler yapılmıştır. Ölçeğin hedef popülasyonda anlaşılabilirliğine ilişkin olumlu bulgular elde edilmiştir. Faktör analizi sonucunda ölçeğin tek faktörlü yapıda olduğu ve varyansın önemli bir kısmını açıkladığı belirlendi. Cronbach alfa değerinin 0.95 olduğu tespit edildi.

Sonuç

HALT ölçeğinin Türkçe versiyonu, ön değerlendirme bulgularına göre anlaşılabilirlik ve uygulanabilirlik açısından uygun görünmektedir. Bununla birlikte, ölçeğin geçerlik ve güvenirliğinin belirlenebilmesi için daha geniş örneklem gruplarında yapılacak ileri düzey psikometrik analizlere ihtiyaç bulunmaktadır.

Anahtar Kelimeler

Halitozis, yaşam kalitesi, ölçek uyarlama, kültürel adaptasyon, HALT

VAN İLİNDE AİLE HEKİMLERİNİN VE AİLE HEKİMLİĞİ ASİSTANLARININ OTİZM SPEKTRUM BOZUKLUĞU HAKKINDAKİ BİLGİ VE FARKINDALIK DÜZEYLERİ

Berfin KORKUT AZAN

Dr., Van Yüzüncü Yıl Üniversitesi Tıp Fakültesi, Aile Hekimliği Anabilim Dalı, Van, Türkiye,

ORCID:0009-0008-6577-7183

Adem YAĞAN

Dr. Öğr. Üyesi, Van Yüzüncü Yıl Üniversitesi Tıp Fakültesi, Aile Hekimliği Anabilim Dalı, Van, Türkiye,

ORCID: 0000-0001-9216-8254

ÖZET

Amaç: Otizm Spektrum Bozukluğu (OSB), erken çocukluk döneminde başlayan; sosyal iletişimde yetersizlik, sınırlı ilgi alanları ve tekrarlayıcı davranışlarla seyreden nörogelişimsel bir bozukluktur. Bu çalışmada, Van ilindeki aile sağlığı merkezlerinde çalışan hekimler ile Van Yüzüncü Yıl Üniversitesi Tıp Fakültesi Aile Hekimliği asistanlarının OSB hakkındaki bilgi ve farkındalık düzeylerinin değerlendirilmesi amaçlandı.

Yöntem: Tanımlayıcı ve kesitsel tipteki çalışma, 01.10.2024–15.11.2024 tarihleri arasında yürütüldü. Çalışmaya 183 gönüllü hekim dahil edildi. Veriler, sosyodemografik veri formu ve Sağlık Çalışanlarının Çocukluk Çağı Otizmi Hakkında Bilgi Anketi ile çevrim içi ortamda toplandı. Analizlerde MS Excel ve SPSS 27 kullanıldı; grup karşılaştırmalarında bağımsız örneklem t testi ve One-way ANOVA uygulandı. Anlamlılık düzeyi $p<0,05$ kabul edildi.

Bulgular: Katılımcıların ölçek puanları 7 ile 19 arasında değişti; ortalama puan 13,78 olarak bulundu. Ortalama doğru yanıt oranı yaklaşık %72,5 idi. Cinsiyet, medeni durum, çocuk sahibi olma, yaş, mesleki deneyim, aile hekimliğindeki çalışma süresi, çocuk psikiyatrisi stajı alma ve çocuk psikiyatrisi rotasyonuna katılma durumlarına göre bilgi düzeylerinde anlamlı fark saptanmadı ($p>0,05$). Buna karşılık görev türü, kişinin kendi bilgi düzeyini değerlendirmesi, OSB tanılı çocukla klinik değerlendirme sürecinde karşılaşma, çevresinde OSB tanılı birey bulunması, otizm eğitimi alma ve Sağlık Bakanlığı Otizm Tarama ve Takip Programı hakkında bilgi sahibi olma durumlarına göre anlamlı fark saptandı ($p<0,05$).

Sonuç: Katılımcıların OSB bilgi ve farkındalık düzeyleri orta-iyi düzeyde bulunmakla birlikte, birinci basamakta erken tanı ve doğru yönlendirme açısından daha güçlü eğitimlere ihtiyaç vardır.

Anahtar Kelimeler: Otizm, Otizm Spektrum Bozukluğu, Otizm Farkındalığı, Aile Hekimliği, Birinci Basamak

KNOWLEDGE AND AWARENESS LEVELS OF FAMILY PHYSICIANS AND FAMILY MEDICINE RESIDENTS IN VAN PROVINCE ABOUT AUTISM SPECTRUM DISORDER

ABSTRACT

Objective: Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder that begins in early childhood and is characterized by impaired social communication, restricted interests, and repetitive behaviors. This study aimed to evaluate the knowledge and awareness levels of physicians working in family health centers in Van province and family medicine residents of Van Yüzüncü Yıl University Faculty of Medicine regarding ASD.

Methods: This descriptive cross-sectional study was conducted between October 1 and November 15, 2024. A total of 183 volunteer physicians were included. Data were collected online using a sociodemographic data form and the Healthcare Workers' Knowledge Questionnaire on Childhood

Autism. MS Excel and SPSS version 27 were used for statistical analysis. Independent samples t-test and One-way ANOVA were used for group comparisons. Statistical significance was accepted as $p<0.05$.

Results: The participants' scale scores ranged from 7 to 19, with a mean score of 13.78. The average correct response rate was approximately 72.5%. No significant difference was found in ASD knowledge levels according to sex, marital status, having children, age, professional experience, duration of work in family medicine, child psychiatry internship during medical education, or child psychiatry rotation during residency ($p>0.05$). However, significant differences were found according to professional role, self-perceived knowledge level, involvement in the evaluation process of a child diagnosed with ASD, having a person diagnosed with ASD in the participant's environment, receiving autism-related training, and awareness of the Autism Screening and Follow-up Program conducted by the Ministry of Health ($p<0.05$).

Conclusion: Participants had a moderate-to-good level of knowledge and awareness regarding ASD. However, stronger training programs are needed to improve early recognition and appropriate referral in primary care.

Keywords: Autism, Autism Spectrum Disorder, Autism Awareness, Family Medicine, Primary Care.

BİOCHEMİCAL COMPOSİTİON AND ANTİOXİDANT ACTİVİTİES OF *GUNDELİA MUNZURENSİS* SEEDS GROWİNG İN THE TUNCELİ REGİON

Sevinç AYDIN[1],

Munzur University, Tunceli Vocational School, Tunceli, Turkey

İbrahim Akın TEMİZER[2],

Fırat Universtiy, Science Faculty, Biology Department, Elazığ, Turkey

Tuba OKUTAN[2],

Fırat Universtiy, Science Faculty, Biology Department, Elazığ, Turkey

Arzu KARATEPE[3],

Fırat Universtiy, Science Faculty, Chemistry Department, Elazığ, Turkey

Celal Can ÇAKAN[2],

Fırat Universtiy, Science Faculty, Biology Department, Elazığ, Turkey

Elif Sema TEMİZER[2],

Fırat Universtiy, Science Faculty, Biology Department, Elazığ, Turkey

Ökkeş YILMAZ[2]

Fırat Universtiy, Science Faculty, Biology Department, Elazığ, Turkey

ABSTRACT

Wild edible plants are widely used throughout the world for their nutritional and functional properties. One of these plants, *Gundelia munzurensis*, known colloquially as Kenger, is a perennial milky plant growing in the Tunceli region and a member of the Asteraceae family. The leaves and stems of this plant are commonly used as food, especially in salads and soups. The aim of this study is to determine the amounts of some biochemical components of Gundelia munzurensis seeds collected from the Tunceli region and to demonstrate their antioxidant activities. For this purpose, fatty acids in the lipid extract were converted to methyl esters and then analyzed by gas chromatography. Total protein, total phenolic and flavonoid content were analyzed using a spectrophotometer, while ADEK vitamins and phytosterols were analyzed using HPLC (high-performance liquid chromatography). At the end of the study, the total protein value was determined to be 36.87 mg/g, the total phenolic value 19.94 µgE/1g, and the total flavonoid value 4.27 µgE/1g. While the amount of palmitic acid (16:00, 11.63%), a saturated fatty acid, was observed to be high, the unsaturated fatty acids oleic acid (18:1, n9c, 22.59%) and linoleic acid (18:2, n-6c, 54.58%) were found to be significantly high. When examined in terms of vitamins, high amounts of Alpha-tocopherol (82.50 µ/g), K2 (35.23 µ/g), and K1 (39.17 µ/g) were observed, respectively, while from the phytosterol group, significantly higher amounts of Stigmasterol (51.60 µ/g) and β-sitosterol (beta-sitosterol) (40.57 µ/g) were detected. Furthermore, our results revealed that *Gundelia munzurensis* possesses free radical scavenging properties (DPPH: 86.48%, ABTS: 97.94%), which are indicators of antioxidant activity.In conclusion, the findings obtained in this study support the traditional use of *Gundelia munzurensis* and present an idea demonstrating its potential as a new biopharmaceutical agent candidate for public health problems.

Keywords: Protein, fatty acid, vitamin-phytosterol, phenolic, flavonoid, antioxidant

TUNCELİ BÖLGESİNDE YETİŞEN KENGER (*GUNDELİA MUNZURENSİS*) BİTKİSİNİN TOHUMLARININ BİYOKİMYASAL BİLEŞİMİ VE ANTİOKSİDAN AKTİVİTELERİ

ÖZET

Yabani yenebilir bitkiler tüm dünyada besinsel ve fonksiyonel özelliklerinden dolayı yaygın olarak kullanılmaktadır. Bu bitkilerden biri olan ve halk arasında kenger otu ismiyle bilinen *Gundelia munzurensis* Tunceli yöresinde yetişen, çok yıllık sütlü bitki olup Asteraceae familyasının bir üyesidir. Halk arasında bu bitkinin yaprakları ve sapları gıda olarak kullanılmakta, özellikle salata ve çorbalara katılmaktadır. Bu çalışmanın amacı, Tunceli bölgesinden toplanan *Gundelia munzurensis*'in tohumunun bazı biyokimyasal içeriklerinin miktarlarının belirlenerek antioksidan aktivitelerinin gösterilmesidir. Bu amaçla çalışmada, lipit ekstraktı içindeki yağ asitleri metil esterlerine dönüştürüldükten sonra gaz kromatografisi ile analiz edildi. Total protein, total fenolik ve flavonoid içeriği spektrofotometre cihazı ile analiz edilirken, ADEK vitamin ve fitosteroller ise HPLC (yüksek performanslı sıvı kromatografisi) cihazı ile analiz edildi. Çalışmanın sonunda total protein değerinin 36,87 mg/g, total fenolik değerinin 19,94 µgE/1g ve total flavonoid değerinin 4,27 µgE/1g olduğu tespit edildi. Doymuş yağ asitlerinden özellikle palmitik asit (16:00, %11,63) miktarı yüksek miktarda gözlenirken, doymamış yağ asitlerinden ise oleik asit (18:1, n9c, % 22,59) ve lineoleik asit (18:2, n-6c, % 54,58) 'in belirgin düzeyde yüksek olduğu tespit edildi. Vitamin bakımından incelendiğinde sırasıyla Alfa-tokoferol (82,50 µ/g) , K2 (35,23 µ/g) ve K1 (39,17 µ/g) yüksek miktarlarda gözlenirken, fitosterolerden ise sırasıyla Stigmasterol (51,60 µ/g) ve β-sitosterol (beta-sitosterol) (40,57 µ/g) miktarlarının belirgin düzeyde fazla olduğu tespit edildi. Ayrıca sonuçlarımız *Gundelia munzurensis*'in antioksidan aktivitenin göstergesi olan serbest radikal temizleme (DPPH:% 86,48, ABTS: % 97,94) özelliklerine sahip olduğunu ortaya koymuştur.

Sonuç olarak, bu çalışmada elde edilen bulgular, *Gundelia munzurensis* 'nın geleneksel kullanımını destekleyerek, halk sağlığı sorunları için yeni bir biyofarmasötik ajan adayı olarak potansiyelini gösteren bir fikir sunmaktadır.

Anahtar kelimeler: Protein, yağ asidi, vitamin-fitosterol, fenolik, flavonoid, antioksidan

YETİŞKİNLERDE TRAVMA SONRASI STRES BOZUKLUĞU, PSİKOLOJİK DAYANIKLILIK VE HAYATTA ANLAM DÜZEYİ: 2023 KAHRAMANMARAŞ DEPREMİ ÖRNEĞİ

Edanur ÇAK ÜÇLER

Arş. Gör. Gazi Üniversitesi, Hemşirelik Fakültesi, Halk Sağlığı Hemşireliği Anabilim Dalı,

0000-0002-7048-2311

Aysun ERDAL

Arş. Gör. Gazi Üniversitesi, Hemşirelik Fakültesi, Halk Sağlığı Hemşireliği Anabilim Dalı

0000-0002-8767-3982

Naile BİLGİLİ

Prof. Dr. Gazi Üniversitesi, Hemşirelik Fakültesi, Halk Sağlığı Hemşireliği Anabilim Dalı

0000-0002-7639-0303

ÖZET

Amaç: Bu araştırma Kahramanmaraş depreminden bir yıl sonra hayatta kalan yetişkin bireylerde Travma Sonrası Stres Bozukluğu (TSSB) sıklığını belirlemeyi, TSSB'nin oluşumu ile psikolojik dayanıklılık ve hayattan anlam değişkenleri arasındaki ilişkiyi incelemek amacıyla yapılmıştır.

Materyal ve Yöntem: Kesitsel analitik tipteki çalışmanın örneklemini, deprem sonrası sosyal konutlara yerleştirilen 307 yetişkin birey oluşturdu. Veriler, kişisel bilgi formu, Hayatta Anlam Anketi, Connor-Davidson Psikolojik Dayanıklılık Ölçeği ve DSM-5 için Travma Sonrası Stres Bozukluğu Kontrol Listesi kullanılarak toplanmıştır. Verilerin analizinde Mann Whitney U testi, Kruskal Wallis H testi ve Spearman korelasyon analizi uygulanmıştır. Anlamlılık düzeyi tüm analizlerde p<0,05 olarak kabul edilmiştir.

Bulgular: Yetişkinlerin hayatta anlam toplam puan ortalaması 49.27 (*SD*=9.94), psikolojik dayanıklılık toplam puan ortalaması 24.89 (*SD*=7.52) ve travma sonrası stres bozukluğu toplam puan ortalaması 43.42 (*SD*=19.40) bulunmuştur. Travma sonrası stres bozukluğu görülme sıklığı %43,64'tür. Spearman korelasyon analizi sonuçlarına göre, hayatta anlam ve psikolojik dayanıklılıkları arasında pozitif yönde istatiksel olarak anlamlı, zayıf düzeyde bir ilişki saptanmıştır (r=0.283; p <0.001). Ayrıca hayatta anlam ile travma sonrası stres bozukluğu (r=0.002; p=0.966) ve psikolojik dayanıklılık ile travma sonrası stres bozukluğu (r=-0.055; p=0.336) arasında anlamlı bir ilişki saptanmamıştır.

Sonuç: Araştırma bulguları, Kahramanmaraş depremini yaşayan yetişkinlerin yaklaşık yarısında TSSB görüldüğünü göstermektedir. Hayatta anlam puanları orta düzeyin biraz üzerinde, psikolojik dayanıklılık puanları ise orta düzeydedir. Bu sonuçlar doğrultusunda, yetişkinlerin ruh sağlığını desteklemek ve depremin uzun vadeli olumsuz etkilerini azaltmak amacıyla destek programlarının geliştirilmesi önerilmektedir.

Anahtar Kelimeler: deprem, hayatta anlam, psikolojik dayanıklılık, stres bozukluğu, hemşirelik

POST-TRAUMATIC STRESS DISORDER, PSYCHOLOGICAL RESILIENCE, AND MEANING IN LIFE AMONG ADULTS WHO HAVE EXPERIENCED A DISASTER: THE CASE OF THE 2023 KAHRAMANMARAŞ EARTHQUAKE

ABSTRACT

Aim: This study was conducted to determine the prevalence of Post-Traumatic Stress Disorder (PTSD) among adult survivors one year after the Kahramanmaraş earthquake and to examine the relationship between the development of PTSD and the variables of psychological resilience and meaning in life.

Materials and Methods: The sample of this cross-sectional analytical study consisted of 307 adults placed in social housing after the earthquake. Data were collected using a personal information form, the Meaning in Life Questionnaire, the Connor-Davidson Resilience Scale, and the DSM-5 Posttraumatic Stress Disorder Checklist. The Mann-Whitney U test, the Kruskal-Wallis H test, and the Spearman correlation analysis were used to analyze the data. The significance level was set at $p<0.05$ for all analyses.

Results: The mean total score for meaning in life among adults was 49.27 (SD=9.94), the mean total score for psychological resilience was 24.89 (SD=7.52), and the mean total score for post-traumatic stress disorder was 43.42 (SD=19.40). The prevalence of post-traumatic stress disorder was 43.64%. According to the Spearman correlation analysis, a statistically significant, weak positive correlation was found between meaning in life and psychological resilience ($r = 0.283$; $p < 0.001$). Furthermore, no significant relationship was found between meaning in life and post-traumatic stress disorder ($r=0.002$; $p=0.966$) or between psychological resilience and post-traumatic stress disorder ($r=-0.055$; $p=0.336$).

Conclusion: Research findings indicate that approximately half of adults who experienced the Kahramanmaraş earthquake have PTSD. Meaning in life scores are slightly above average, while psychological resilience scores are average. Based on these results, it is recommended that support programs be developed to support adults' mental health and reduce the long-term negative effects of the earthquake.

Keywords: earthquake, meaning in life, psychological resilience, stress disorder, nursing

MEKÂN, BELLEK VE İYİLİK HALİ: KÜLTÜREL MİRASIN HEMŞİRELİK ÖĞRENCİLERİNDE PSİKOSOSYAL BOYUTU

Sinan ÖZCAN

Uzm. Arkeolog / Eğitim Koordinatörü, Anturia Arkeoloji ve Sosyal Çevre Etiği Okulu, Kütahya, Türkiye, ORCID: 0000-0001-6480-9907

Gamze SAATÇİ

Arş. Gör. Kırşehir Ahi Evran Üniversitesi Sağlık Bilimleri Fakültesi, Hemşirelik Esasları ABD., Kırşehir, Türkiye, ORCID: 0000-0002-3612-2961

Amaç

Bu çalışmanın amacı, kültürel miras alanlarının hemşirelik öğrencilerinin mekânsal bellek oluşumu, toplumsal hafıza ile kurdukları bağ ve psikososyal iyilik halleriyle nasıl ilişkilendirilebileceğini incelemektir. Hemşirelik eğitimi bağlamında mekân–bellek–iyilik hali ilişkisinin olası rolleri değerlendirilerek, kültürel miras temelli deneyimlerin öğrencilerin mesleki kimlik gelişimi, aidiyet duygusu ve ruhsal dayanıklılıkları üzerindeki potansiyel katkılarına odaklanılmaktadır.

Materyal ve Yöntem

Çalışma, hemşirelik eğitimi ve bakım bilimleriyle ilişkilendirilen disiplinler arası bir kuramsal çerçeve doğrultusunda kurgulanmıştır. Veri kaynağı olarak UNESCO'nun yaşayan miras yaklaşımı, hemşirelikte çevre ve bakım ilişkisini ele alan kuramsal yaklaşımlar, toplumsal bellek çalışmaları ve salutogenez modeli esas alınmıştır.

Literatür taraması, son on yıl içerisinde kültürel mirasın sağlık, eğitim ve bakım meslekleri öğrencileri üzerindeki psikososyal boyutlarını ele alan çalışmalar üzerinden yürütülmüş; kavramsal analiz yöntemiyle kültürel miras-bellek-iyilik hali ilişkisini hemşirelik öğrencileri bağlamında yorumlamaya olanak tanıyan temalar belirlenmiştir.

Bulgular

Yapılan görüşmeler, kültürel miras alanlarının hemşirelik öğrencileri açısından yalnızca estetik ve tarihsel değerler bağlamında değil, aynı zamanda duygusal denge, mesleki aidiyet ve bakım anlayışının gelişimiyle ilişkili olabileceğini düşündürmektedir. Ritüellerin yeniden üretimi, kültürel simgelerin anlamlandırılması ve kuşaklararası deneyim paylaşımının; hemşirelik öğrencilerinde öz-etkililik algısı, topluluk hissi, empati ve psikolojik dayanıklılıkla ilişkilendirilebilecek etkiler oluşturduğu görülmektedir. Mekânla kurulan süreklilik içeren ilişkilerin, öğrencilerin bilişsel tutarlılığı, mesleki kimlik oluşumu ve öznel iyilik halleri üzerinde destekleyici bir rol oynayabileceği değerlendirilmiştir.

Sonuç

Elde edilen bulgular, kültürel mirasın hemşirelik öğrencilerinin psikososyal iyilik halleri açısından destekleyici bir unsur olarak ele alınabileceğini göstermektedir. Bu doğrultuda, hemşirelik eğitiminde kültürel miras temelli öğrenme ortamlarının yalnızca kültürel farkındalık kazandırma amacıyla değil; aynı zamanda öğrencilerin ruhsal dayanıklılığı, mesleki aidiyeti ve bakım odaklı değerlerinin gelişimini destekleyebilecek bir araç olarak değerlendirilmesi önerilmektedir. Mekân-bellek-iyilik hali etkileşimi; hemşirelik eğitimi, sağlık hizmetleri ve sosyal bakım uygulamaları için yenilikçi ve tamamlayıcı bir pedagojik çerçeve sunmakta; kültürel mirasın bakım bilimleri açısından bütüncül iyilik hali yaklaşımlarıyla ilişkilendirilebilecek bir kaynak olduğu sonucuna ulaşılmaktadır.

Anahtar Kelimeler: Kültürel Miras, Hemşirelik Öğrencileri, Mekânsal Bellek, Psikososyal İyilik Hali, Mesleki Kimlik, Kuşaklararası Aktarım.

TÜRKİYE'DE ÇOCUK SAĞLIĞI VE HASTALIKLARI HEMŞİRELİĞİ ALANINDA OBEZİTE KONULU LİSANSÜSTÜ TEZLERİN BİBLİYOGRAFİK ANALİZİ

(2009–2025)

Eslem Berra KİLECİ

Düzce Üniversitesi, Lisansüstü Eğitim Enstitüsü, Çocuk Sağlığı ve Hastalıkları Hemşireliği Programı, Yüksek Lisans Öğrencisi, Düzce / Türkiye, https://orcid.org/0009-0007-3881-2185

Sevda ARSLAN

Düzce Üniversitesi, Sağlık Bilimleri Fakültesi, Çocuk Sağlığı ve Hastalıkları Hemşireliği Düzce / Türkiye, https://orcid.org/0000-0003-1961-1496

ÖZET

Amaç: Bu araştırma Türkiye'de Çocuk Sağlığı ve Hastalıkları Hemşireliği alanında, obezite konulu lisansüstü tezlerin bibliyografik özelliklerini ve eğilimlerini incelemek amacıyla yapılmıştır.

Gereç ve Yöntem: Bibliyografik analiz türündeki araştırmanın verileri Mart 2026'da "Yükseköğretim Kurulu Ulusal Tez Merkezi" veri tabanından gerçekleştirilmiştir. Tarama sürecinde "obezite", "obesity", "çocuk sağlığı ve hastalıkları hemşireliği" ve "child health and diseases nursing" anahtar kelimeleri kullanılarak tezler sorgulanmıştır. Kriterlere uyan 13 lisansüstü tez çalışması; yılları, üniversiteleri, illeri, danışman unvanları, türleri, anahtar kelimeleri, örneklem büyüklükleri ve araştırma desenlerine göre incelenmiştir.

Bulgular: Çocuk sağlığı ve hastalıkları hemşireliği alanında obezite konusunda hazırlanan lisansüstü çalışmalar incelendiğinde; en fazla çalışmanın 2020 ve 2016 yıllarında (%23,07) olduğu belirlenmiştir. Üniversitelere göre dağılımları incelendiğinde en fazla çalışmanın Dokuz Eylül Üniversitesi'nde (%23,07) üretildiği görülmüştür. Tez çalışmaları en fazla, İzmir (%23,07), Ankara ve İstanbul (%15,38) illerinde dağılım göstermiştir. Tezlerin %53,84'ü doktora, %46,15'i yüksek lisans, tezinden oluşmuştur. Tezlerde 43 farklı anahtar kelime kullanılmıştır ve en sık "Obezite" (%15) ile "Çocuk" (%10) kelimeleri tercih edilmiştir. Örneklem büyüklüğü bakımından %38,46 oranıyla 1–100 kişi arasında örneklem grubu ile çalışmıştır. Araştırma desenlerinin %46,15'i tanımlayıcı tipte olduğu belirlenmiştir.

Sonuç: Türkiye'de çocuk sağlığı ve hastalıkları hemşireliği alanında obezite konulu lisansüstü tezlerin sayısının yıllara göre dengeli dağılım gösterdiği ve çoğunlukla tanımlayıcı tasarımlarla olduğu görülmektedir. Çocukluk ve adolesan dönemlerinde obezitenin prevalansındaki artışlar sonucunda alan yazında daha kapsamlı ve analitik çalışmaların arttırılması, obezite ile ilişkilendirilebilecek hastalıklar ve önlemeye yönelik çalışmaların arttırılması önerilebilir.

Anahtar Kelimeler: Çocuk sağlığı; Hemşirelik; Obezite

BİBLİOGRAPHİC ANALYSİS OF POSTGRADUATE THESES ON OBESİTY İN THE FİELD OF PEDİATRİC HEALTH AND DİSEASES NURSİNG İN TÜRKİYE

(2009–2025)

ABSTRACT

Objective: This study aimed to examine the bibliographic characteristics and research trends of postgraduate theses focusing on obesity within the field of pediatric health and nursing in Türkiye.

Materials and Methods: Data for this bibliometric analysis were obtained in March 2026 from the "YÖK National Thesis Database." The search was conducted using the keywords "obezite,"obesity", "çocuk sağlığı ve hastalıkları hemşireliği" and "child health and disease nursing." A total of 13

postgraduate theses that met the inclusion criteria were analyzed according to publication year, university, province, advisor title, thesis type, keywords, sample size, and research design.

Findings: The analysis showed that the highest number of theses on obesity in pediatric nursing were completed in 2020 and 2016 (23.07%). Dokuz Eylül University produced the largest proportion of these theses (23.07%). Geographically, most theses originated from İzmir (23.07%), followed by Ankara and İstanbul (15.38%). Of the theses, 53.84% were doctoral dissertations and 46.15% were master's theses. Across all theses, 43 different keywords were identified, with "Obesity" (15%) and "Child" (10%) being the most frequently used. Regarding sample size, 38.46% of the studies included 1–100 participants. Nearly half of the research designs (46.15%) were descriptive.

Conclusion: Postgraduate theses on obesity in the field of pediatric health and nursing in Türkiye show a relatively balanced distribution across years and predominantly employ descriptive research designs. Considering the increasing prevalence of obesity during childhood and adolescence, there is a need to expand the literature with more comprehensive and analytical studies, as well as research addressing obesity-related health conditions and preventive approaches.

Keywords: Child health; Nursing, Obesity

ÇOCUKLUK ÇAĞI TRAVMALARI VE BAĞLANMA STİLLERİNİN PSİKOPATOLOJİ ÜZERİNDEKİ YORDAYICI ETKİSİ

Elif ŞAHİN

Uygulamalı Psikoloji, İstanbul Okan Üniversitesi, Lisansüstü Eğitim Birimi, Uygulamalı Psikoloji Doktora Programı, ORCID: https://orcid.org/0000-0002-2411-8498

ÖZET

Amaç: Bu çalışma, bireylerin çocukluk döneminde maruz kaldıkları travmatik yaşantıların ve kurdukları bağlanma örüntülerinin, yetişkinlik dönemindeki psikopatolojik semptomların şiddeti üzerindeki yordayıcı rolünü incelemeyi amaçlamaktadır. Erken dönem ilişkisel deneyimlerin, yetişkinlikteki duygu düzenleme becerileri ve ruhsal iyi oluş üzerindeki kalıcı etkilerinin anlaşılması hedeflenmiştir.

Materyal ve Yöntem: Araştırmanın örneklemini, 18-55 yaş aralığında bulunan ve farklı sosyo-demografik geçmişe sahip bireyler oluşturmaktadır. Veri toplama sürecinde demografik bilgi formu, Çocukluk Çağı Travmaları Ölçeği ve İlişki Ölçekleri Anketi kullanılmıştır. Elde edilen veriler SPSS 26.0 paket programı ile analiz edilmiştir. Değişkenler arasındaki korelasyon ilişkilerini saptamak amacıyla Pearson korelasyon analizi; çocukluk çağı travmaları ve bağlanma stillerinin psikopatolojiyi yordama düzeyini belirlemek amacıyla ise hiyerarşik çoklu regresyon analizi yöntemine başvurulmuştur.

Bulgular: Araştırma sonuçları, fiziksel, duygusal ve cinsel istismar ile ihmal gibi çocukluk çağı travmalarının, yetişkinlikteki psikolojik sağlık üzerinde anlamlı ve negatif bir etkiye sahip olduğunu göstermiştir. Bağlanma stilleri açısından yapılan analizlerde, özellikle saplantılı ve korkulu bağlanma biçimlerinin, psikopatolojik belirtilerle pozitif yönde ve yüksek düzeyde ilişkili olduğu saptanmıştır. Saplantılı bağlanmaya sahip bireylerdeki reddedilme hassasiyeti ve korkulu bağlanmaya özgü yakınlıktan kaçınma davranışlarının, travmatik geçmişle birleştiğinde psikolojik kırılganlığı önemli ölçüde artırdığı gözlemlenmiştir.

Sonuç: Elde edilen bulgular, erken dönem travmatik yaşantıların ve güvensiz bağlanma örüntülerinin, yetişkinlikte depresyon, anksiyete ve somatizasyon gibi psikopatolojik süreçlerin temel belirleyicileri olduğunu desteklemektedir. Bu durum, klinik psikoloji uygulamalarında ve koruyucu ruh sağlığı politikalarında, sadece mevcut semptomlara odaklanmak yerine, bağlanma odaklı müdahalelerin ve travma temelli iyileşme yaklaşımlarının hayati bir önem taşıdığını ortaya koymaktadır.

Anahtar Kelimeler: Çocukluk Çağı Travmaları, Bağlan Stilleri, Psikopatoloji

ÇOCUK RUH SAĞLIĞININ GELİŞTİRİLMESİNDE YENİLİKÇİ BİR BAKIŞ AÇISI: ÇOCUKLAR İÇİN FELSEFE (P4C) ÜZERİNE BİR DERLEME

Deniz Toprak

Arş. Gör., Kırşehir Ahi Evran Üniversitesi, Orcid: https://orcid.org/0009-0006-8611-7796

Şeyda Maide Batmaz

Yüksek Lisans Öğrenci, Ankara Üniversitesi, Orcid: https://orcid.org/0009-0007-1342-7950

Amaç: P4C, Çocuklar için Felsefe (Philosophy for Children) veya Topluluklar için Felsefe (Philosophy for Communities) olarak ifade edilmektedir. P4C' deki 4 simgesi ile eleştirel (critical), yaratıcı (creative), iş birliğine açık (collaborative) ve özenli (caring) kavramları belirtilmektedir. P4C, Matthew Lipman tarafından geliştirilmiş, çocukların gruplar içinde farklı konu ve kavramları eleştirel ve yaratıcı bir şekilde tartışarak düşünme becerilerini geliştirmeyi hedefleyen diyalog temelli bir eğitim yöntemidir. Çocuk ruh sağlığı alanında önleyici yaklaşımların önemi artarken; P4C'nin de bu alandaki rolünün anlaşılması, çocuk ve gençlere uygun yaklaşım ve girişimlerle yeni ufukların açılması hedeflenmektedir.
Materyal ve Yöntem: Bu çalışma, Çocuklar için Felsefe (P4C) yaklaşımının çocuk ve ergen ruh sağlığı üzerindeki potansiyel etkilerini inceleyen bir literatür derlemesidir. Bir derleme çalışması olarak hazırlanan bu bildiri, P4C'nin teorik çerçevesini ve uygulamaları özetleyerek mevcut ampirik ve teorik literatürü analiz etmektedir. P4C, bir kolaylaştırıcı liderliğinde felsefi bir uyaran etrafında yapılandırılarak, çocukların kendi sorularını oluşturup birlikte tartıştığı oturumlar şeklinde uygulanmaktadır. Bu uygulamalar, çocukların düşünsel özerklik kazanmalarına ve karmaşık kavramları analiz etmelerine olanak tanımaktadır.
Bulgular: P4C uygulamalarında bilişsel kazanımların yanı sıra, sosyal ve duygusal gelişim alanlarında da önemli pozitif etkilerinin varlığı çeşitli çalışmaların bulgularında belirtilmiştir. Mevcut araştırmalar ışığında P4C katılımının benlik saygısında, eleştirel düşünmede ve iletişimlerde duyarlılık artışı gibi çıktılarla ilişkili olduğunu göstermektedir. Bu bulgular, P4C'nin bireyin kendine dair algısını ve kabulünü olumlu yönde etkileyerek kişisel potansiyelini geliştirmesini desteklediğini göstermektedir.
Sonuç: Bu veriler ışığında P4C' nin okullar, topluluklar ve gruplar gibi evrensel erişim noktalarında uygulanabilecek, ruhsal iyi oluşu destekleyerek önleyici bir strateji olabileceğini düşündürmektedir. Bu çalışmada, Çocuklar için Felsefe (P4C)' nin çocuk ruh sağlığını koruma ve geliştirmede dikkate değer bir potansiyele sahip, yenilikçi bir araç olarak değerlendirilerek, çocuk ve ergen sağlığına dair olumlu çıktılarını derinlemesine incelenmesi hedeflenmektedir.
Anahtar Kelimeler: Çocuklar için Felsefe, P4C, Çocuk Ruh Sağlığı, Erken Müdahale

ENDOCRINE SYSTEM AND LONGEVITY: THE ROLE OF HORMONES IN NUTRITION

Merve Kurt

Van Yuzuncu Yil University, Faculty of Medicine, Department of Physiology, Van, 65100, Turkey,

Sermin Algul

Van Yuzuncu Yil University, Faculty of Medicine, Department of Physiology, Van, 65100, Turkey,

ABSTRACT

Longevity is a holistic concept that extends beyond increasing lifespan and aims to promote healthy, functional, and high-quality aging throughout life . This approach focuses on delaying age-related chronic diseases, preserving physical and cognitive functions, and maintaining independence during aging. With the increasing elderly population worldwide, longevity has evolved from a purely biomedical concept into a multidisciplinary model integrating nutrition, lifestyle, and environmental factors.

Among the major determinants of healthy aging are regular physical activity, adequate sleep, stress management, social engagement, and continuous cognitive stimulation. In this context, the endocrine system plays a central role in regulating metabolic homeostasis and aging-related physiological processes.

Hormones such as insulin, cortisol, melatonin, and thyroid hormones significantly influence energy metabolism, oxidative stress, circadian rhythm, and cellular repair mechanisms. Maintaining these hormonal pathways within physiological ranges is essential for sustaining metabolic resilience and healthy aging. Dysregulation of endocrine balance has been associated with chronic inflammation, metabolic disorders, and accelerated biological aging.

Nutrition represents one of the fundamental pillars of longevity. Anti-inflammatory and antioxidant-rich dietary patterns, particularly plant-based nutrition models, contribute to reducing oxidative stress and supporting endocrine balance. Increased consumption of vegetables, fruits, whole grains, and healthy fats, together with reduced intake of refined sugars, ultra-processed foods, and trans fats, has been associated with improved metabolic and hormonal health.

Current studies evaluating longevity-related nutritional and endocrine factors commonly utilize demographic data, anthropometric measurements, biochemical parameters, dietary intake records, and validated questionnaire forms. These parameters provide important insights into the interaction between nutrition, hormonal regulation, and healthy aging.

In conclusion, longevity should be considered not merely as lifespan extension, but as a comprehensive strategy aimed at achieving metabolic, physiological, and psychosocial well-being during aging. Evidence-based nutritional and lifestyle interventions that support endocrine homeostasis may play a key role in promoting healthspan and preventing age-related diseases.

Keywords: Longevity; Endocrine system; Healthy aging; Nutrition; Hormonal regulation; Oxidative stress; Metabolic health

ERKEN ÇOCUKLUK DÖNEMİNDE SESSİZ KİTAPLARIN BİLİŞSEL ÇIKARIM VE ANLAM KURMA SÜREÇLERİNE ETKİSİ: BİR LİTERATÜR DERLEMESİ

Şeyda Maide Batmaz

Yüksek Lisans Öğrenci, Ankara Üniversitesi, Orcid: https://orcid.org/0009-0007-1342-7950

Deniz Toprak

Arş. Gör., Kırşehir Ahi Evran Üniversitesi, Orcid: https://orcid.org/0009-0006-8611-7796

Giriş: Erken çocukluk döneminde (0-8 yaş) görsel işlemleme ve anlamlandırma becerilerinin, bilişsel gelişimin önemli bileşenleri arasında yer aldığı kabul edilmektedir. Metin içermeyen resimli kitaplar (sessiz kitaplar); çocuğun sözel destek olmadan, görsel ipuçlarını analiz ederek bir anlatı kurgulamasını gerektiren bilişsel bir yapı sunmaktadır. Mevcut literatürde, bu etkileşimli sürecin çocukların sembolik düşünme ve görsel analiz yetkinliklerini desteklediği ifade edilmektedir.

Amaç: Bu çalışma; sessiz kitapların çocuklarda bilişsel çıkarım (inference making) becerileri ve görsel anlam inşa süreçleri üzerindeki etkisini konu alan araştırmaları bir literatür derlemesi kapsamında değerlendirmeyi amaçlamaktadır.

Yöntem: Mevcut çalışma kapsamında; görsel okuryazarlık, bilişsel gelişim ve anlatı üretme odaklı ulusal ve uluslararası yayınlar kuramsal çerçevede değerlendirilecektir.

Bulgular: İncelenen literatürde, sessiz kitapların, çocuklarda görsel detaylardan örtük anlamları keşfetme ve karakterlerin durumlarına dair zihinsel çıkarım yapma süreçlerini desteklediği gözlenmiştir. Yazılı metin sınırlaması olmadan çocuğun kendi anlatısını oluşturmasının; bilişsel esneklik, neden-sonuç ilişkisi kurma ve dikkat yönetimi gibi yürütücü işlevlerle ilişkilendirildiği görülmektedir. Ayrıca, bu materyallerin dil bariyerlerini aşan yapısı sayesinde kapsayıcı eğitim süreçlerinde gelişimsel bir destek aracı olduğu bilinmektedir.

Sonuç: Elde edilen verilerde, sessiz kitaplar, çocukların bilişsel stratejilerini destekleyen esnek ve çok yönlü bir materyal olarak değerlendirilmektedir. Bu sessiz anlatıların sunduğu zengin uyaranların, çocukların anlam inşa süreçlerini analiz etme ve gelişimsel izlem süreçlerinde, destekleyici bir mekanizma olarak kullanılabileceği düşünülmektedir.

Anahtar Kelimeler: Sessiz Kitaplar, Bilişsel Çıkarım, Anlam Kurma, Görsel Okuryazarlık.

THE EFFECT OF PICTURE BOOKS ON COGNITIVE INFERENCE AND MEANING-MAKING PROCESSES IN EARLY CHILDHOOD: A LITERATURE REVIEW

Introduction: It is widely accepted that visual processing and comprehension skills are key components of cognitive development during early childhood (ages 0–8). Picture books without text (silent books) provide a cognitive framework that requires children to construct a narrative by analyzing visual cues without verbal support. The existing literature indicates that this interactive process supports children's symbolic thinking and visual analysis skills. Objective: This study aims to evaluate current academic research examining the effects of silent books on children's cognitive inference-making abilities and visual meaning-construction processes.

Method: This study aims to evaluate research examining the effects of picture books on children's cognitive inference skills and visual meaning-making processes within the scope of a literature review. Findings: In the reviewed literature, it has been observed that wordless books support children's processes of discovering implicit meanings from visual details and making mental inferences about the characters' states. It is noted that allowing children to create their own narratives without the constraints of written text is associated with executive functions such as cognitive flexibility, establishing cause-

and-effect relationships, and attention management. Additionally, due to their structure that transcends language barriers, these materials are known to serve as a developmental support tool in inclusive educational processes.

Conclusion: Based on the data obtained, silent books are evaluated as a flexible and versatile material that supports children's cognitive strategies. It is believed that the rich stimuli offered by these silent narratives can be utilized as a supportive mechanism in analyzing children's meaning-making processes and in developmental monitoring processes.

Keywords: Silent Books, Cognitive Inference, Meaning Construction, Visual Literacy.

OBEZİTE İLE OKSİDATİF STRES ARASINDAKİ İLİŞKİ

Berfin Öksüz

Van Yüzüncü Yıl Üniversitesi

ABSTRACT

Obezite, vücutta aşırı yağ birikimi ile karakterize kronik bir sağlık sorunudur. Günümüzde hem gelişmiş hem de gelişmekte olan ülkelerde yaygınlığı artmaktadır. Obezite yalnızca metabolik hastalıklarla değil, aynı zamanda hücresel düzeyde hasara yol açan oksidatif stres ile de yakından ilişkilidir (WHO, 2023; Hruby & Hu, 2015).

Oksidatif Stres Nedir?

Oksidatif stres, serbest radikaller ile antioksidan savunma sistemi arasındaki dengenin bozulması sonucu ortaya çıkar. Serbest radikaller, hücrelere zarar verebilen reaktif moleküllerdir. Antioksidanlar ise bu zararlı etkileri nötralize ederek hücreyi korur (Sies, 2017; Liguori ve ark., 2018).

Obezitenin Oksidatif Stresi Artırma Mekanizmaları

Obez bireylerde oksidatif stresin artmasının başlıca nedenleri şunlardır:

* Artmış yağ dokusu nedeniyle inflamasyonun yükselmesi (Furukawa ve ark., 2004)

* Mitokondriyal fonksiyon bozuklukları (Rolo & Palmeira, 2006)

* Serbest yağ asitlerinin artışı (Vincent ve ark., 2007)

* Antioksidan savunma sisteminin yetersiz kalması (Marseglia ve ark., 2015)

Bu durum, reaktif oksijen türlerinin (ROS) üretimini artırarak hücresel hasara yol açar (Finkel & Holbrook, 2000).

Oksidatif Stresin Obeziteye Etkileri

Oksidatif stres yalnızca obezitenin sonucu değil, aynı zamanda ilerlemesini hızlandıran bir faktördür:

* İnsülin direncinin gelişimine katkı sağlar (Evans ve ark., 2002)

* Tip 2 diyabet riskini artırır (Ceriello & Motz, 2004)

* Kardiyovasküler hastalıkların oluşumunu tetikler (Madamanchi ve ark., 2005)

* Hücre ve doku hasarını artırır (Halliwell & Gutteridge, 2015)

Sonuç olarak, obezite ve oksidatif stres arasında çift yönlü bir ilişki bulunmaktadır. Obezite oksidatif stresi artırırken, artan oksidatif stres de obeziteye bağlı komplikasyonların gelişimini hızlandırır. Bu nedenle obezite tedavisinde yalnızca kilo kaybı değil, aynı zamanda oksidatif stresin azaltılmasına yönelik stratejiler de önemlidir (Blüher, 2019; Roberts & Sindhu, 2009).

TÜRKİYE'DE SAĞLIK SEKTÖRÜNDE ÜÇÜNCÜ BİR YOL OLARAK SAĞLIK HİZMETLERİ KOOPERATİFÇİLİĞİ

Doç. Dr. Ertuğrul Güreşci

Kırşehir Ahi Evran Üniversitesi, İİBF, İşletme Bölümü, 0000-0002-0977-7233

Yılmaz Akgündüz

0009-0003-7721-332X

ÖZET

Amaç: Bu çalışmada Türkiye'de sağlık sektörünün sorunlarına dikkat çekerek kamu ve özel sağlık hizmetlerine eleştrisel bir gözle bakarak ilgili sektörde üçüncü bir yol olarak sağlık hizmetleri kooperatifçiliğini Türkiye ölçeğinde inceleyerek sonuçları literatüre katkı sağlayacak şekilde değerlendirmektir.

Materyal Metot: Çalışmada sistematik bir literatür taraması yöntemi kullanılmıştır. Bu yöntemde Türkiye'nin sağlık sektörü ile ilgili sorunlar kaynak taramasından geçirilerek çalışmanın alt yapısı oluşturulmuş, kooperatifçilik ile ilgili genel bilgiler ile literatür çalışmanın amacı doğrultusunda, sağlık hizmetleri kooperatifçiliği ile ilgili yerli ve yabancı literatür ile ilişkisi TÜİK gibi çeşitli kamu kurumlarında alınan sayısal verilerin özetlenerek anlamlı bulgulara dönüştürülmesi sağlanmıştır.

Bulgular: Çalışmada sağlığın insan yaşamındaki zorunlu ve ivedilikli önemi bu alanda yapılacak hizmetlerin ulaşılabilirliği ve kalitesine bağlı olacaktır. Bu konuda Türkiye'de kamusal alanda sağlık harcamalarının artması bütçeye ciddi bir mali yük getirmiştir. Benzer şekilde özel sektör sağlık hizmetlerinde ise bir takım insani ve mali istismarların olduğu bulgularına rastlanmıştır. Bu noktadan hareket edilerek sağlık hizmetleri kooperatifçiliğinin alternatif bir yol olarak, bu sektörde kullanılmasına doğru bir adım olacağı ve bunun için gerekli yasal ve idari düzenlemelerin gerekliliğine işaret edilmiştir.

Sonuç: Çalışmada Türkiye'de sağlık sektöründe gerek kamusal alanda gerekse özel sektörde, ciddi mali, insani, idari ve yasal sorunların olduğu tespit edilmiştir. İlgili sektörde üçüncü bir yol olarak sağlık hizmetleri kooperatifçiliğinin geçerli ve önerilebilir olduğu ancak bu alanda başta sağlık hizmetleri kooperatifçiliği ana sözleşmesi olmak üzere ciddi bir yapılanma üzerinde yoğun ve sistematik çalışmalara ihtiyaç duyulacağı sonucuna varılmıştır.

Anahtar Kelimeler: Kooperatif, Sağlık, Sağlık Hizmetleri, Sağlık Hizmetleri Kooperatifçiliği

THE HEALTH SERVICES COOPERATIVES AS A THIRD WAY IN THE HEALTH SECTOR IN TURKEY

ABSTRACT

Objective: This study aims to draw attention to the problems of the Turkish health sector, examine public and private health services from a critical perspective, and examine health care cooperatives as a third option within the relevant sector. The study aims to evaluate the results in a way that contributes to the literature.

Materials and Methods: A systematic literature review method was employed in the study. This method established the basis for the study by reviewing the literature on issues related to Turkey's health sector. General information on cooperatives and its relationship with domestic and international literature on health care cooperatives, in line with the purpose of the study, were summarized and numerical data obtained from various public institutions such as the Turkish Statistical Institute (TSI) were compiled into meaningful findings.

Findings: The study examines the essential and urgent importance of health in human life, which will depend on the accessibility and quality of services provided in this field. Increasing public health spending in Turkey has placed a significant financial burden on the budget. Similarly, some human and financial abuses were found in private health services. Based on this, it was pointed out that healthcare cooperatives would be a step toward utilizing this sector as an alternative, and that the necessary legal and administrative regulations are necessary for this purpose.

Conclusion: The study identified serious financial, humanitarian, administrative, and legal problems in the Turkish healthcare sector, both in the public and private sectors. It was concluded that healthcare cooperatives are viable and recommendable as a third option in this sector, but that intensive and systematic work on a serious structuring, particularly the constitution of healthcare cooperatives, is needed in this area.

Keywords: Cooperative, Health, Health Services, Healthcare Cooperatives

DIAGNOSIS AND MANAGEMENT OF CHRONIC VENOUS INSUFFICIENCY IN PRIMARY CARE: CURRENT APPROACHES

Ersin Ozer

MD, Department of Cardiovascular Surgery, Ordu University Education and Research Hospital
Bucak Neighbourhood, 52200, Altinordu, Ordu, Türkiye, ORCID: https://orcid.org/0000-0002-7065-0004

ABSTRACT

Objective: Chronic venous insufficiency (CVI) is a common chronic condition frequently encountered in primary care settings; however, its diagnosis and management are not always standardized in daily practice. The objective of this review is to systematically evaluate the recognition of chronic venous insufficiency in primary care, clinical assessment strategies, conservative and medical treatment approaches, and indications for referral in light of current evidence and clinical guidelines.

Materials and Methods: This narrative review was conducted based on clinical practice guidelines, systematic reviews, and comprehensive review articles published between 2020 and 2025 focusing on the management of chronic venous insufficiency and chronic venous disease. The literature selection was limited to publications addressing diagnostic approaches, treatment strategies, and referral decision-making relevant to primary care practice. The CEAP classification system, appropriate use criteria, conservative treatment modalities, and recent international guidelines were critically reviewed and synthesized.

Results: The literature review indicates that chronic venous insufficiency can be identified at early stages primarily through detailed history taking and physical examination in most patients. Advanced imaging modalities, particularly duplex ultrasonography, are required only in selected cases. Lifestyle modifications and compression therapy emerge as the cornerstone of management in the primary care setting. Pharmacological treatments play a supportive role in symptom control. The presence of skin changes, venous leg ulcers, rapid disease progression, or lack of response to conservative measures constitutes clear indications for referral to secondary or tertiary care.

Conclusion: Chronic venous insufficiency is a condition in which early diagnosis and appropriate management in primary care can significantly reduce disease progression and prevent complications. A structured clinical assessment, effective use of conservative treatment strategies, and timely referral decisions are essential components of optimal care. Integrating current clinical guidelines into primary care practice may improve patient outcomes and contribute to standardized management of chronic venous insufficiency.

Keywords: Chronic Venous Insufficiency; Primary Health Care; Compression Therapy

TÜRKİYE'DE SAĞLIK HİZMETİ İLİŞKİLİ ENFEKSİYONLAR: 5 YILLIK ULUSAL SÜRVEYANS ANALİZİ

Musa ŞENYÜZ

Dicle University, Faculty of Science, Department of Public Health, Siirt-Türkiye

ORCID: 0009-0002-4853-3060

Amaç: Sağlık hizmeti ilişkili enfeksiyonlar (SHİE), hasta güvenliği ve sağlık hizmet kalitesi açısından küresel ölçekte önemli bir halk sağlığı sorunudur. Bu çalışmada Türkiye'de 2020–2024 yılları arasında bildirilen SHİE hızları, enfeksiyon dansiteleri ve etken dağılımlarının değerlendirilmesi amaçlanmıştır.

Materyal ve Yöntem: Bu çalışma tanımlayıcı ve retrospektif nitelikte ekolojik bir analizdir. Veriler, T.C. Sağlık Bakanlığı tarafından yayımlanan Ulusal Sağlık Hizmeti İlişkili Enfeksiyonlar Sürveyans Ağı (USHIESA) yıllık raporlarından elde edilmiştir. 2020–2024 yıllarına ait SHİE hızı, 1000 hasta günü başına enfeksiyon dansitesi ve etken mikroorganizma dağılımı incelenmiştir. Veriler yıllar arası karşılaştırmalı olarak değerlendirilmiş ve eğilim analizi yapılmıştır.

Bulgular: SHİE hızı 2021 yılında 0,43 ile en düşük düzeye gerilemiş, 2022 sonrası artış eğilimi göstererek 2024 yılında 0,69'a ulaşmıştır. Enfeksiyon dansitesi 2020 yılında 0,90 iken 2024 yılında 1,70 olarak saptanmıştır. En sık görülen enfeksiyon türü kan dolaşım enfeksiyonu olup bunu pnömoni, üriner sistem enfeksiyonu ve cerrahi alan enfeksiyonu izlemiştir. Etken dağılımında gram negatif bakteriler baskın olup en sık Klebsiella spp. (%24,4), Acinetobacter spp. (%16,1) ve Pseudomonas spp. (%10,8) izole edilmiştir.

Sonuç: Türkiye'de SHİE oranlarında pandemi sonrası dönemde artış eğilimi dikkat çekmektedir. Gram negatif dirençli patojenlerin baskınlığı, enfeksiyon kontrol uygulamaları ve antibiyotik yönetim programlarının güçlendirilmesi gerekliliğini ortaya koymaktadır. Ulusal sürveyans sistemlerinin etkin kullanımı, hasta güvenliği ve sağlık hizmet kalitesinin artırılması açısından kritik öneme sahiptir.

Anahtar Kelimeler: Sağlık hizmeti ilişkili enfeksiyon, sürveyans, enfeksiyon dansitesi, hasta güvenliği, antibiyotik direnci

HEALTHCARE-ASSOCIATED INFECTIONS IN TURKEY: A FIVE-YEAR NATIONAL SURVEILLANCE ANALYSIS

Objective: Healthcare-associated infections (HAIs) remain a major global public health concern, significantly affecting patient safety and quality of care. This study aimed to evaluate the incidence rates, infection densities, and pathogen distribution of HAIs reported in Türkiye between 2020 and 2024.

Material and Methods: This descriptive, retrospective ecological study was based on secondary data obtained from the annual surveillance reports published by the Ministry of Health of Türkiye under the National Healthcare-Associated Infections Surveillance Network (USHIESA). HAI incidence rates, infection density per 1,000 patient-days, and pathogen distribution data for the years 2020–2024 were analyzed. Comparative evaluation across years was performed to determine temporal trends.

Results: The HAI rate decreased to its lowest level (0.43) in 2021, followed by a steady increase reaching 0.69 in 2024. Infection density rose from 0.90 in 2020 to 1.70 in 2024 per 1,000 patient-days. Bloodstream infections were the most frequently reported HAI, followed by pneumonia, urinary tract infections, and surgical site infections. Gram-negative bacteria predominated among pathogens, with Klebsiella spp. (24.4%), Acinetobacter spp. (16.1%), and Pseudomonas spp. (10.8%) being the most commonly isolated organisms.

Conclusion: An increasing trend in HAI rates was observed in the post-pandemic period in Türkiye. The predominance of multidrug-resistant gram-negative pathogens underscores the urgent need to

strengthen infection prevention strategies and antimicrobial stewardship programs. Effective utilization of national surveillance systems is essential to reduce HAI burden and enhance patient safety and healthcare quality.

Keywords: Healthcare-associated infection, surveillance, infection density, patient safety, antimicrobial resistance

COMPARISON OF PERIOPERATIVE OUTCOMES OF RIRS AND PNL IN 15–25 MM RENAL PELVIC STONES

Anıl EKER

Izmir City Hospital, Urology Clinic, ORCID: 0000-0003-1603-3336

Tansu Değirmenci

University of Health Sciences, Izmir Faculty of Medicine, Department of Urology, ORCID: 0000-0001-7747-3613

Objective

Urolithiasis is a common health problem worldwide, and treatment strategies are primarily guided by stone size. However, the optimal management of renal pelvic stones measuring 15–25 mm remains controversial. This study aimed to compare the intraoperative and postoperative outcomes of retrograde intrarenal surgery (RIRS) and percutaneous nephrolithotomy (PNL) in this specific patient group.

Materials and Methods

Patients who underwent RIRS or PNL for 15–25 mm renal pelvic stones within the last year were retrospectively analyzed. A total of 70 patients were included: 30 in the RIRS group and 40 in the PNL group. Demographic characteristics, stone density, intraoperative parameters (operation time, fluoroscopy time, irrigation volume), and postoperative outcomes (hemoglobin drop, complications, catheter usage, residual stones, SIRS, and hospital stay) were compared.

Results

There were no significant differences between groups in terms of age, gender, stone laterality, or stone density. Operation time was similar between groups ($p=0.498$). Fluoroscopy time and irrigation volume were significantly higher in the PNL group ($p<0.001$). No patient required blood transfusion. Postoperative hemoglobin drop was observed in 25% of PNL patients but not in the RIRS group ($p=0.003$). Higher-grade complications (Clavien ≥2) were more frequent in the PNL group ($p=0.028$). Residual stone rates were higher in the RIRS group (16.7% vs 2.5%, $p=0.036$). Length of hospital stay was significantly shorter in the RIRS group (1.34±0.66 vs 3.12±1.15 days, $p<0.001$). Additionally, postoperative double-J stent placement was markedly more frequent in the RIRS group. No significant difference was observed in postoperative SIRS.

Conclusion

RIRS is associated with lower morbidity, shorter hospitalization, and reduced radiation exposure compared to PNL in 15–25 mm renal pelvic stones. However, it carries a higher risk of residual stones and potential need for reintervention. Additionally, the higher rate of postoperative double-J stent placement in RIRS may contribute to stent-related morbidity and should be considered in patient counseling. Treatment choice should be individualized, balancing efficacy and safety.

Keywords: Urolithiasis; RIRS; Percutaneous Nephrolithotomy; Renal Stone; Minimally Invasive Surgery

Comparison of Demographic, Intraoperative, and Postoperative Parameters Between Groups

		Group 1 (RIRS, n=30)	Group 2 (PNL, n=40)	p-value
Age (years)		52.13 ± 16.69	46.75 ± 13.78	0.144[Σ]
Gender	**Female**	17 (56.70%)	25 (62.50%)	

	Male	13 (43.30%)	15 (37.50%)	0.622[Δ]
Side of Operation	**Right**	14 (46.70%)	25 (62.50%)	0.187[Δ]
	Left	16 (53.30%)	15 (37.50%)	
Stone Density (HU)		1056.66 ± 305.89	1017.95 ± 363.38	0.639[Σ]
Operation Time (min)		73.10 ± 20.51	77 ± 25.79	0.498[Σ]
Fluoroscopy Time (sec)		1.53 ± 1.45	67.07 ± 43.79	<0.001[Σ]
Irrigation Volume (mL)		1893.33 ± 1146.48	8050.00 ± 5406.31	<0. 001[Σ]
Postoperative Hemoglobin Drop	**No**	30 (100.00%)	30 (75.00%)	0.003[Δ]
	Yes	0 (0.00%)	10 (25.00%)	
Blood Transfusion	**No**	30 (100%)	40 (100%)	
	Yes	0 (0.00%)	0 (0.00%)	
Clavien–Dindo Classification	**Grade 0**	25 (83.30%)	37(92.5%)	0.028[Δ]
	Grade 1	5 (16.70%)	0 (0.00%)	
	Grade 2	0 (0.00%)	2 (5.00%)	
	Grade 3	0 (0.00%)	1 (2.5%)	
	Grade 4	0 (0.00%)	0 (0.00%)	
Postoperative Catheter Use	**None**	1 (3.30%)	0 (0.00%)	<0.001[Δ]
	Ureteral catheter	1 (3.30%)	34 (85.00%)	
	Double-J stent	28 (93.30%)	6 (15.00%)	
Postoperative SIRS	**No**	30 (100%)	38 (95.00%)	0.214[Δ]
	Yes	0 (0.00%)	2 (5.00%)	
Residual Stones	**No**	25 (83.30%)	39 (97.50%)	0.036[Δ]
	Yes	5 (16.70%)	1 (2.50%)	
Length of Hospital Stay (days)		1.34 ± 0.66	3.12 ± 1.15	<0.001[Σ]

[Σ] Student's t-test

[Δ] Chi-square test

PİLONİDAL SİNÜS TEDAVİSİNDE LAZER: GÜNCEL YAKLAŞIMLAR VE KLİNİK DENEYİMLER

Aynur Quliyeva

Orcid: 0009-0008-9143-8433, Akademik M.A. Topçubaşov adına Elmi Cərrahiyyə Mərkəzi

Ümumi cərrah- kiçik elmi işçi

ABSTRACT

Pilonidal sinus disease (PSD) is a chronic condition commonly observed in young adult males, characterized by a high recurrence rate and localization in the sacrococcygeal region. It negatively affects patients' quality of life due to pain, discharge, and recurrent infections. Conventional surgical approaches, including wide excision and flap techniques, are associated with prolonged healing time, postoperative pain, and cosmetic concerns. In recent years, minimally invasive techniques, particularly laser-assisted treatments, have gained popularity due to shorter recovery time, lower complication rates, and improved patient comfort.

This study aims to evaluate current approaches in laser treatment of pilonidal sinus disease and to assess clinical outcomes based on existing literature. A comprehensive review of studies including prospective and retrospective trials, systematic reviews, and meta-analyses was conducted. Techniques such as Sinus Laser Assisted Closure (SiLaC®), laser ablation, and combinations with endoscopic pilonidal sinus treatment (EPSiT) were analyzed.

Findings indicate high healing rates, low recurrence rates, reduced postoperative pain, and faster return to daily activities.

In conclusion, laser-assisted treatment represents a modern, safe, and effective alternative; however, further large-scale studies are needed.

Amaç

Pilonidal sinüs hastalığı (PSH), özellikle genç erişkin erkeklerde görülen, sakrokoksigeal bölgede kronik seyirli ve nüks eğilimi yüksek bir hastalıktır. Ağrı, akıntı ve tekrarlayan enfeksiyonlar nedeniyle hastaların yaşam kalitesini önemli ölçüde düşürmektedir. Geleneksel cerrahi yaklaşımlar geniş eksizyon ve flep tekniklerini içermekte olup, uzun iyileşme süresi, postoperatif ağrı ve kozmetik sorunlar gibi dezavantajlara sahiptir. Son yıllarda minimal invaziv yöntemler, özellikle lazer destekli tedaviler, daha kısa iyileşme süresi ve yüksek hasta konforu sağlaması nedeniyle ön plana çıkmıştır. Bu bildirinin amacı, pilonidal sinüs tedavisinde lazer uygulamalarına ilişkin güncel yaklaşımları incelemek ve klinik deneyimlerle birlikte değerlendirmektir.

Yöntem

Bu çalışma, PubMed ve benzeri bilimsel veri tabanlarında yer alan pilonidal sinüs tedavisinde lazer uygulamalarını konu alan çalışmaların derlenmesi ile hazırlanmıştır. İncelenen çalışmalar arasında prospektif ve retrospektif araştırmalar, sistematik derlemeler ve meta-analizler yer almaktadır. Özellikle Sinus Laser Assisted Closure (SiLaC®), lazer ablasyon teknikleri ve endoskopik pilonidal sinüs tedavisi (EPSiT) ile kombine yöntemler değerlendirilmiştir. Veriler; iyileşme oranları, nüks oranları, postoperatif ağrı, hastanede kalış süresi ve komplikasyonlar açısından analiz edilmiştir.

Bulgular

Lazer tedavisinin etkinliği birçok çalışmada gösterilmiştir. SiLaC® yöntemi ile yapılan uygulamalarda %70'in üzerinde primer iyileşme oranı bildirilmiştir. Lazer tedavisi sonrası hastaların kısa sürede günlük yaşamlarına dönebildiği ve postoperatif ağrının belirgin şekilde azaldığı görülmüştür. Nüks olgularda lazer ablasyonun %70–80 oranında başarı sağladığı rapor edilmiştir. EPSiT ile kombine lazer uygulamalarının özellikle kompleks sinüslerde daha etkili olduğu ve nüks oranlarını azalttığı

bildirilmiştir. Genel olarak iyileşme oranları %80'in üzerinde, nüks oranları ise %5–10 arasında değişmektedir.

Tartışma

Lazer tedavisinin en önemli avantajları minimal invaziv olması, kısa operasyon süresi, düşük ağrı düzeyi ve hızlı iyileşmedir. Bununla birlikte her hasta için uygun olmayabilir. Özellikle geniş ve komplike sinüslerde tek başına yeterli olmayabilir. Ayrıca uzun dönem sonuçlara ilişkin veriler sınırlıdır. Bu nedenle hasta seçimi ve uygulayıcı deneyimi büyük önem taşımaktadır. Lazer tedavisi, klasik cerrahi yöntemlere alternatif veya tamamlayıcı bir seçenek olarak değerlendirilebilir.

Sonuç

Lazer destekli tedavi yöntemleri, pilonidal sinüs hastalığında modern ve etkili bir yaklaşım olarak öne çıkmaktadır. Kısa dönem sonuçlar oldukça olumlu olup hasta konforunu artırmaktadır. Ancak uzun dönem etkinliğin netleşmesi için daha geniş örneklemli ve randomize kontrollü çalışmalara ihtiyaç vardır. Uygun hasta seçimi ile lazer tedavisi güvenli ve etkili bir seçenek olarak kullanılabilir.

Anahtar Kelimeler: Pilonidal sinüs, lazer tedavisi, SiLaC®, minimal invaziv cerrahi, EPSiT

KÜÇÜK HÜCRELİ OLMAYAN AKCİĞER KANSERİNDE PALYATİF BAKIMIN ERKEN ENTEGRASYONU: HASTALAR TARAFINDAN BİLDİRİLEN YAŞAM KALİTESİ SONUÇLARININ SİSTEMATİK BİR İNCELEMESİ

Cahidenur Koçak Oruç

İstanbul Esenyurt Üniversitesi, Sağlık Bilimleri Fakültesi, Fizyoterapi ve Rehabilitasyon Bölümü, İstanbul, Türkiye, ORCID: 0000-0003-3362-2415

Esra Pehlivan

Sağlık Bilimleri Üniversitesi, Hamidiye Sağlık Bilimleri Fakültesi, Fizyoterapi ve Rehabilitasyon Bölümü, İstanbul, Türkiye, ORCİD: 0000-0002-1791-5392

ABSTRACT

Introduction: Advanced non-small cell lung cancer (NSCLC) remains an incurable disease with a poor prognosis for the majority of affected patients; therefore, quality of life and symptom relief are primary goals of treatment. Current evidence suggests that early palliative care (EPC) can improve quality of life for these patients. The aim of this study is to investigate the effect of EPC on quality of life in NSCLC patients.

Material and Methods: From March 2021 to March 2026, searches were conducted across three major databases: PubMed, Web of Science, and Cochrane Library, using the keywords “lung cancer, palliative care, supportive care, quality of life” The search was narrowed to include randomized controlled trials published within the last five years.

Results: A total of four studies meeting the inclusion criteria were reviewed. Quality of life was assessed in three studies using the Functional Assessment of Cancer Treatment-Lung (FACT-L) and in one study using the European Organization for Cancer Research and Treatment Quality of Life Scales (EORTC QLQ-C30/LC13). In three studies, quality of life was found to be higher ($p<0.05$) for patients included in the EPC groups compared to the group receiving oncological care.

Conclusion: Our results demonstrate that early palliative care improves the quality of life for NSCLC patients. Early integration of palliative care can be used as a clinically meaningful and feasible care model for NSCLC patients.

Keywords: Lung cancer, palliative care, quality of life.

KÜÇÜK HÜCRELİ OLMAYAN AKCİĞER KANSERİNDE PALYATİF BAKIMIN ERKEN ENTEGRASYONU: HASTALAR TARAFINDAN BİLDİRİLEN YAŞAM KALİTESİ SONUÇLARININ SİSTEMATİK BİR İNCELEMESİ

ÖZET

Giriş: İleri evre küçük hücreli olmayan akciğer kanseri (KHOAK), etkilenen hastaların çoğunluğu için kötü bir prognoza sahip, tedavi edilemeyen bir hastalık olmaya devam etmektedir; bu nedenle yaşam kalitesi ve semptomlardan kurtulma, tedavinin birincil hedefleridir. Mevcut kanıtlar, bu hastalar için erken palyatif bakımın (EPB) yaşam kalitesini iyileştirebileceğini göstermektedir. Bu çalışmanın amacı, erken uygulanan palyatif bakımın KHOAK hastalarında yaşam kalitesi üzerindeki etkisini araştırmaktır.

Gereç ve Yöntem: Mart 2021’den Mart 2026’a kadar “akciğer kanseri, palyatif bakım, destekleyici bakım, yaşam kalitesi” anahtar kelimeleri kullanılarak PubMed, Web of Science ve Cochrane Library olmak üzere üç ana veri tabanında arama yapıldı. Arama son 5 yılda yayınlanan randomize kontrollü çalışmalar dahil olacak şekilde sınırlandırıldı.

Bulgular: Dahil edilme kriterlerine uyan toplam dört çalışma incelendi. Yaşam kalitesi toplam üç çalışmada, Kanser Tedavisinin Fonksiyonel Değerlendirmesi-Akciğer (FACT-L) ve bir çalışmada, Avrupa Kanser Araştırma ve Tedavi Organizasyonu Yaşam Kalitesi Ölçekleri (EORTC QLQ-C30/LC13) kullanılarak değerlendirildi. Üç çalışmada EPB gruplarına dahil edilen hastalar için yaşam kalitesinin onkolojik bakım alan gruba kıyasla daha yüksek ($p<0,05$) olduğu görüldü.

Sonuç: Sonuçlarımız, erken uygulanan palyatif bakımın KHOAK hastalarının yaşam kalitesini iyileştirdiğini göstermektedir. Palyatif bakımın erken entegrasyonu KHOAK hastaları için klinik olarak anlamlı ve uygulanabilir bir bakım modeli olarak kullanılabilir.

Anahtar Kelimeler: Akciğer kanser, palyatif bakım, yaşam kalitesi.

INTRODUCTION

Lung cancers are clinically divided into two main groups: small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC), which accounts for more than 80% of all cases. NSCLC, which has high morbidity and mortality rates worldwide, is one of the leading causes of death (Wan et al., 2015). The advanced stage of the disease is characterized by significant disease progression, often involving metastasis to other organs beyond the lungs (Zullo et al., 2025). At this stage, treatment options become more limited and less effective, and curative approaches are often not possible (Kratzer et al., 2024). During this process, patients face severe symptoms that significantly reduce their quality of life, such as shortness of breath, persistent cough, pain, and fatigue (Mercadante et al., n.d.).

Lung cancer patients have a much lower quality of life compared to both healthy individuals and patients with other types of cancer. This is directly related to the severity of the disease-specific symptoms. Despite the development of new treatments, symptom burden and associated psychological distress remain quite high in patients with advanced-stage disease (Sung et al., 2017; Wenninger et al., 2013). From the time of diagnosis, patients generally report high levels of distress related to emotional and functional well-being (Kuon et al., 2019).

Palliative care represents a holistic approach aimed at enhancing the quality of life for patients and their families confronting life-threatening illnesses. It focuses on preventing and mitigating suffering through early identification, comprehensive assessment, and the targeted management of pain alongside other physical, psychosocial, and spiritual challenges. (Palliative Care, n.d.). Current data in the literature show that delayed application of palliative care does not provide a complete improvement in the quality of life of patients (Nowicki et al., 2015; Reports & 2016). Therefore, the American Society of Clinical Oncology (ASCO) recommends the integration of palliative care within the first eight weeks following diagnosis in patients with advanced-stage disease (Ferrell et al., 2017). This supportive care, initiated early, aims to alleviate the patient's suffering by preventing symptom worsening (Varma et al., n.d.). Furthermore, this approach has been shown to not only improve the patient's quality of life but also reduce the challenges faced by caregivers and the need for aggressive medical interventions at the end of life (Bakitas et al., 2009; Wright et al., 2008).

One study randomized metastatic lung cancer (MLC) patients to receive either standard care with palliative care or standard care alone, concluding that patients assigned to the intervention had higher quality of life scores, fewer depressive symptoms, and longer survival (Temel et al., 2010). A study examining the impact of palliative care on anxiety and depression levels in lung cancer patients compared outpatients and inpatients in the Palliative Care Unit. The results showed that inpatients had significantly better outcomes and reduced psychological distress compared to outpatients receiving home care (Delibegovic et al., n.d.). However, moving away from the traditional terminally focused approach, initiating palliative care early in the process and in a personalized manner is considered the most effective strategy in lung cancer management (Daveson et al., 2015; Polanski et al., 2016).

While current guidelines recommend early integration of palliative care, its specific effects on quality of life throughout the disease process have not been sufficiently investigated. Therefore, the aim of our study is to comprehensively evaluate the effects of early palliative care (EPC) on quality of life in NSCLC patients.

MATERIAL AND METHODS

This study aimed to review published studies on palliative care practices in patients diagnosed with NSCLC and to examine the effects of intervention program components on quality of life. Ethical committee approval was not required. The ethical aspects and principles of our research were conducted in accordance with the principles of the Declaration of Helsinki.

Databases Used in the Study

Three major databases—PubMed, Web of Science, and the Cochrane Library—were searched over the past five years using the keywords "lung cancer, palliative care, supportive care, and quality of life." Boolean operators (AND/OR) were also used to combine search terms across each database as appropriate. The search examined the title, abstract, and keyword fields. This review examines the findings of the studies included in this compilation.

Inclusion Criteria

- Adult patients with NSCLC aged 18 years and older,
- Randomized controlled trials (RCTs) evaluating the effectiveness of palliative care,
- Studies comparing palliative care with standard care or a control group,
- Studies reporting quality of life outcomes,
- Studies published in English,
- Studies published between March 2021 and March 2026.

Exclusion Criteria

- Studies that do not follow a randomized controlled trial design,
- Published abstracts, articles without full text, and review articles,
- Studies that do not contain sufficient data,
- Studies published in languages other than English.

RESULTS

From a total of n=452 records obtained through database searching, n=232 articles were excluded after removing duplicate articles and reviewing titles/abstracts. Of the n=220 articles reviewed, n=195 did not meet the criteria and n=3 studies were excluded due to unavailable full-text, leaving n=22 articles for full-text review. In this evaluation, n=18 more studies were excluded due to intervention inappropriateness (n=7), invalid outcome criteria (n=6), protocol lacking data (n=2), and population differences (n=3). As a result, n=4 studies meeting the criteria were included in this review.

The scope of interventions presented in the studies included in our review varied according to preferred EPC models and targeted clinical outcomes. In three studies conducted by Chen et al., the Functional Assessment of Cancer Treatment-Lung (FACT-L) scale was used to assess quality of life; while Allende et al. In the study conducted by (2024), the European Organization for Cancer Research and Treatment Quality of Life Scales (EORTC QLQ-C30 and QLQ-LC13) modules were preferred. When the quality of life outcomes were examined, it was observed that in the three studies using the FACT-L scale, EPC significantly increased the quality of life compared to standard oncological care ($p < 0.05$). However, in the study using the EORTC scale group, there was no statistically significant difference in quality of life scores between the groups. The intervention design, purpose, outcome measures, and main findings of the studies included in our review are detailed in Table 1.

DISCUSSION

The positive effects of EPC on quality of life in patients with non-small cell lung cancer are well known (Temel et al., 2010). However, there are significant differences in terms of the measurement tools used and patient populations. The three studies we examined (Chen et al., 2021, 2022, 2023) show that the inclusion of EPC from the diagnosis stage leads to statistically significant improvements in quality of life ($p<0.05$). However, the study by Allende et al. (2024), despite using a similar methodological approach, did not show a significant difference in quality of life ($p>0.05$). The main reason for this may be the sensitivity of different questionnaires measuring quality of life. In fact, the Chen group's studies used the FACT-L scale, which is more sensitive to lung cancer-specific symptoms and functions, while Allende's study preferred the more general scale, the EORTC QLQ-C30 (Allende et al., 2024). FACT-L is a highly validated, multi-lingual questionnaire extensively used in lung cancer clinical trials. It is recognized for its comprehensive scope and strong psychometric properties, including high reliability, internal consistency, and sensitivity (Butt et al., 2005). Looking at the literature, FACT-L stands out as the most promising approach in terms of quality of life when compared to EORTC QLQc30 and QLQ-LC13 (Eser et al., 2016). This suggests that it is an effective tool in demonstrating the success of palliative rehabilitation. Intervention timing is the most critical determinant of sustained recovery. The most recent study we reviewed concluded that the greatest benefit after intervention was achieved in patients with baseline quality of life scores above 70. This also shows that including patients in the palliative process while their functional capacity is high (baseline quality of life > 70) provides the greatest benefit (Allende et al., 2024). Furthermore, proactive support initiated at the beginning of treatment may have preserved the patient's functional independence (Liu et al., 2025a; Temel et al., 2010). Consequently, the role of EPC in preserving quality of life and functional status in NSCLC patients cannot be ignored. However, despite this strong evidence, the fact that palliative referrals are still made "late" in clinical practice (Oswalt et al., 2024) indicates that the importance of palliative rehabilitation within a multidisciplinary team should be emphasized more.

The results of this study also highlight the importance of establishing a multidisciplinary model for early interdisciplinary palliative care. Consequently, we believe that a holistic approach should be taken from the very beginning of the disease process, encompassing symptom control, psychosocial support, and especially the maintenance of basic functional status. All the evidence we have gathered strongly suggests that EPC should be considered as part of the multidisciplinary treatment of NSCLC patients from diagnosis. In future studies, it would be more beneficial to examine the relationship between the improvement in quality of life and the patient's "level of independence" in daily life, rather than solely through a statistical p-value analysis.

CONCLUSION

In patients with non-small cell lung cancer, multidisciplinary and holistic palliative care programs initiated early stand out as an effective approach to improving quality of life and clinical outcomes. Furthermore, findings showing that patient-specific protocols such as E-WARM (Early, Holistic, Assessment, Reassessment, and Multidisciplinary Management) can provide similar and significant benefits in quality of life, regardless of the center's resources, support the applicability of EPC programs even in resource-constrained settings.

The timing, frequency, and content of EPC interventions should be individualized considering patients' clinical characteristics, performance status, and symptom requirements. However, larger-scale randomized controlled trials including standard assessment methods (FACT-L, EORTC QLQc30, QLQ-LC13, etc.) and long-term follow-up data will contribute to determining the most effective palliative care approach.

REFERENCES

Allende, S., Turcott, J. G., Verástegui, E., Rodríguez-Mayoral, O., Flores-Estrada, D., Pérez Camargo, D. A., ... & Arrieta, O. (2024). Early incorporation to palliative care (EPC) in patients with advanced non-small cell lung cancer: the PACO randomized clinical trial. *the oncologist*, *29*(10), e1373-e1385.

Bakitas, M., Lyons, K. D., Hegel, M. T., Balan, S., Barnett, K. N., Brokaw, F. C., ... & Ahles, T. A. (2009). The project ENABLE II randomized controlled trial to improve palliative care for rural patients with advanced cancer: baseline findings, methodological challenges, and solutions. *Palliative & supportive care*, *7*(1), 75-86.

Butt, Z., Webster, K., Eisenstein, A. R., Beaumont, J., Eton, D., Masters, G. A., & Cella, D. (2005). Quality of life in lung cancer: The validity and cross-cultural applicability of the Functional Assessment of Cancer Therapy–Lung Scale. *Hematology/Oncology Clinics*, *19*(2), 389-420.

Chen, M., Yang, L., Yu, H., Yu, H., Wang, S., Tian, L., & Liu, S. (2022). Early palliative care in patients with non–small-cell lung cancer: a randomized controlled trial in Southwest China. *American Journal of Hospice and Palliative Medicine®*, *39*(11), 1304-1311.

Chen, M. T., Yu, H. J., Yang, L. J., Wang, S. X., Tian, L., Liu, S. H., & Yu, H. Q. (2021). Efficacy of early interdisciplinary palliative care based on WARM model in non-small-cell lung cancer. *Zhonghua yi xue za zhi*, *101*(45), 3736-3741.

Chen, M., Yu, H., Yang, L., Yang, H., Cao, H., Lei, L., ... & Wang, S. (2023). Combined early palliative care for non-small-cell lung cancer patients: a randomized controlled trial in Chongqing, China. *Frontiers in Oncology*, *13*, 1184961.

Daveson, B. A., de Wolf-Linder, S., Witt, J., Newson, K., Morris, C., Higginson, I. J., & Evans, C. J. (2015). Results of a transparent expert consultation on patient and public involvement in palliative care research. *Palliative medicine*, *29*(10), 939-949.

Delibegovic, A., & Sinanovic, O. (2013). The Influence of Palliative Care on the Level of Anxiety and Depression in Lung Cacer Patients. *Medical Archives*, *67*(4), 263.

Eser, S., Göksel, T., Erbaycu, A. E., Baydur, H., Başarık, B., Yanık, A. Ö., ... & Eser, E. (2016). Comparison of generic and lung cancer-specific quality of life instruments for predictive ability of survival in patients with advanced lung cancer. *Springerplus*, *5*(1), 1833.

Ferrell, B. R., Temel, J. S., Temin, S., Alesi, E. R., Balboni, T. A., Basch, E. M., ... & Smith, T. J. (2017). Integration of palliative care into standard oncology care: American Society of Clinical Oncology clinical practice guideline update. *Journal of clinical oncology*, *35*(1), 96-112.

Kratzer, T. B., Bandi, P., Freedman, N. D., Smith, R. A., Travis, W. D., Jemal, A., & Siegel, R. L. (2024). Lung cancer statistics, 2023. *Cancer*, *130*(8), 1330-1348.

Kuon, J., Vogt, J., Mehnert, A., Alt-Epping, B., van Oorschot, B., Sistermanns, J., ... & Thomas, M. (2019). Symptoms and needs of patients with advanced lung cancer: early prevalence assessment. *Oncology research and treatment*, *42*(12), 650-659.

Mercadante, S., Grassi, Y., Cascio, A. L., Restivo, V., & Casuccio, A. (2023). Characteristics of untreated cancer patients admitted to an acute supportive/palliative care unit. *Journal of Pain and Symptom Management*, *65*(6), e677-e682.

Krajnik, M. (2016). Dejection and self-assessment of quality of life in patients with lung cancer subjected to palliative care. *Contemporary oncology (Poznań, Poland)*.

World Health Organization: National Cancer Control Programmes: policies and managerial guidelines. http://www.who.int/cancer/palliative/definition/en/

Polanski, J., Jankowska-Polanska, B., Rosinczuk, J., Chabowski, M., & Szymanska-Chabowska, A. (2016). Quality of life of patients with lung cancer. *OncoTargets and therapy*, 1023-1028.

Bilaçeroğlu, S. (2016). Role of palliative care in improving the quality of life in elderly with advanced lung disease. *Current Geriatrics Reports*, *5*(2), 103-109.

Sung, M. R., Patel, M. V., Djalalov, S., Le, L. W., Shepherd, F. A., Burkes, R. L., ... & Leighl, N. B. (2017). Evolution of symptom burden of advanced lung cancer over a decade. *Clinical Lung Cancer*, *18*(3), 274-280.

Temel, J. S., Greer, J. A., Muzikansky, A., Gallagher, E. R., Admane, S., Jackson, V. A., ... & Lynch, T. J. (2010). Early palliative care for patients with metastatic non–small-cell lung cancer. *New England journal of medicine*, *363*(8), 733-742.

Varma, A., Weinstein, J., Seabury, J., Rosero, S., Zizzi, C., Dilek, N., ... & Heatwole, C. (2023). Patient-reported impact of symptoms in lung cancer (PRISM-LC). *Translational Lung Cancer Research*, *12*(7), 1391.

Wan, J. W., Gao, M. Z., Hu, R. J., Huang, H. Y., Wei, Y. Y., Han, Z. J., & Yan, Z. H. (2015). A preliminary study on the relationship between circulating tumor cells count and clinical features in patients with non-small cell lung cancer. *Annals of translational medicine*, *3*(22), 352.

Wenninger, K., Helmes, A., Bengel, J., Lauten, M., Völkel, S., & Niemeyer, C. M. (2013). Coping in long-term survivors of childhood cancer: relations to psychological distress. *Psycho-oncology*, *22*(4), 854-861.

Wright, A. A., Zhang, B., Ray, A., Mack, J. W., Trice, E., Balboni, T., ... & Prigerson, H. G. (2008). Associations between end-of-life discussions, patient mental health, medical care near death, and caregiver bereavement adjustment. *Jama*, *300*(14), 1665-1673.

Yu, Z., Yang, X., Wu, J., Yu, X., Cui, J., Gao, X., ... & Yu, L. (2025). Surgical resection for pulmonary metastases from head and neck adenoid cystic carcinoma: a propensity-matched survival analysis. *Journal of Cancer Research and Clinical Oncology*, *151*(12), 330.

Table 1. Methods and key findings from studies examining the effects of palliative care on quality of life in lung cancer.

Authors (year)	Intervention	Aim	Measurement Method	Results
Chen et al. (2021)	OC, n = 22: Oncology care EPC, n = 23: Understanding and perception of the disease; psychological coping; nutritional guidance for cancer pain; and medical decision-making.	The effects of palliative support therapy on the quality of life of NSCLC patients.	FACT-L for quality of life, measuring the patient's physical, social, emotional, and functional aspects..	The EPC group had significantly higher quality of life compared to the OC group ($p<0.001$).
Chen et al. (2022)	EPC+OC, n =38 OC, n =32	The impact of early integration of interdisciplinary palliative care on the quality of life of NSCLC patients	FACT-L for quality of life, measuring the patient's physical, social, emotional, and functional aspects.	The EPC+OC group had significantly higher quality of life compared to the OC group ($p<0.05$).

Chen et al. (2023)	EPC+OC, n = 102: Quality of life, nutritional status, pain management, and psychological support OC, n = 82: Oncological care	Comparing the effects of early integration of interdisciplinary palliative care on the quality of life of NSCLC patients	FACT-L for quality of life, measuring the patient's physical, social, emotional, and functional aspects.	The EPC+OC group had significantly higher quality of life compared to the OC group ($p<0.05$).
Allende et al. (2024)	EPC Group (n=42): Received patient-centered, coordinated care aimed at alleviating pain, understanding the disease and coping strategies, improving symptoms and functional status, and planning for advanced care. SOC Group (n=34): Received only standard oncological care.	Evaluating the impact of early integration of palliative care compared to standard oncological care (SC) in NSCLC patients in Mexico	EORTC QLQ-C30 and QLQ-LC13 for quality of life assessment.	There was no statistically significant difference in quality of life scores between the groups.

EPC: Early palliative care group; OC/SOC: Standard oncological care group; NSCLC: Non-small cell lung cancer; FACT-L: Functional Assessment of Cancer Treatment-Lung; EORTC QLQ-C30/LC13: European Organization for Cancer Research and Treatment Quality of Life Scales.

DİŞ HEKİMLİĞİ EĞİTMENLERİNİN SOLAK ÖĞRENCİLERE YÖNELİK FARKINDALIKLARININ VE EĞİTİM UYGULAMALARININ DEĞERLENDİRİLMESİ

Bilge MERACI YILDIRAN

Bolu Abant İzzet Baysal Üniversitesi Diş Hekimliği Fakültesi Periodontoloji Anabilim Dalı, Bolu, Türkiye, ORCID: 0000-0001-9848-0927

Nuray ERCAN

Bolu Abant İzzet Baysal Üniversitesi Diş Hekimliği Fakültesi Periodontoloji Anabilim Dalı, Bolu, Türkiye, ORCID: 0000-0002-8161-7269

ÖZET

Amaç: Diş hekimliği eğitimi büyük çoğunlukla standart sağ el kullanımı üzerine tasarlanmış ünit ve ekipmanlarla yürütülmektedir. Bu durum solak öğrenciler için ergonomik zorluklar ve mesleki hastalık riskleri oluşturabilmektedir. Bu çalışmanın amacı, diş hekimliği fakültelerinde görev yapan öğretim elemanlarının solak öğrencilerin eğitimine ilişkin farkındalık ve eğitim uygulamalarını öğretim deneyimi sürelerine göre karşılaştırmalı olarak değerlendirmektir.

Materyal ve Yöntem: Çalışma, farklı akademik unvanlara sahip 176 öğretim elemanının katılımıyla gerçekleştirilen kesitsel bir anket çalışmasıdır. Katılımcılar klinik/preklinik eğitimde görev aldıkları eğitim-öğretim yılı sayısına göre üç gruba (1. grup 5 yıldan az, 2. grup 5–10 yıl, 3. grup 10 yıldan fazla) ayrılmıştır. Verilerin analizinde Pearson Ki-Kare, Fisher's Exact ve Çoklu Ki-Kare testleri kullanılmıştır.

Bulgular: Katılımcıların %50'si araştırma görevlisi, %32.4'ü öğretim üyesi, %11.9'u doçent, %3.4'ü profesör, %2.3'ü ise öğretim görevlisidir. Katılımcıların %57.4'ü 5 yıldan az, 22.7'si 5-10 yıl, 19,9'u 10 yılda fazla süredir preklinik/klinik eğitim deneyimine sahiptir. Analizler sonucunda öğretim deneyimi süresi ile solak öğrenci sayısı ve kurumdaki resmi yönerge eksikliğine dair farkındalığın arttığı gözlemlenmiştir. "*Çalıştığım kurumda eğitim gören solak öğrenci sayısı hakkında fikrim var*" sorusuna "*katılıyorum*" diyenlerin oranı 1. grupta %11.9, 2. grupta %30.0 ve 3. grupta %14.3'tür (p<0.05). "*Çalıştığım kurumda solak öğrencilerin preklinik ve klinik eğitimine yönelik resmi yönerge/rehberler mevcuttur*" sorusu için "*fikrim yok*" diyenlerinin oranının 1. grupta %79.2, 2. grupta %47.5, 3. grupta ise %42.9 olduğu tespit edilmiştir (p<0.05). Katılımcıların %93,1'i solak öğrencilere yönelik özel düzenlemelerin eğitim kalitesini artıracağını ve %87.5'i eğitim materyallerinin solakların ihtiyaçlarına göre farklılaştırılmasının eğitimde eşitliği sağlayacağını düşünmektedir. Ancak, eğitim materyallerinde solak yaklaşımı kullanma (%14.7) ve sol el kullanımına uygun demonstrasyon yapma (%22.7) oranları düşük bulunmuştur.

Sonuç: Diş hekimliği eğitmenleri, solak öğrencilerin özel düzenlemelere ihtiyaç duyduğu konusunda yüksek farkındalığa sahip olmalarına rağmen, klinik uygulamada bu öğrencilere yönelik spesifik demonstrasyon ve materyal kullanımı oldukça kısıtlıdır. Solak öğrencilerin beceri gelişimini desteklemek ve mesleki sağlık risklerini azaltmak için ergonomik düzenlemeler, eğitim rehberleri ve materyalleri geliştirilmesi önerilmektedir.

Anahtar Kelimeler: Diş Hekimliği Eğitimi, Ergonomi, Solaklık

EVALUATION OF AWARENESS AND EDUCATIONAL PRACTICES OF DENTAL EDUCATORS TOWARD LEFT-HANDED STUDENTS

ABSTRACT

Objective: Dental education is predominantly conducted using units and equipment designed for standard right-handed use. This situation can create ergonomic challenges and occupational health risks

for left-handed students. This study aims to evaluate the awareness and educational practices of dental faculty members regarding the education of left-handed students, comparatively analyzing them based on their teaching experience.

Materials and Methods: This cross-sectional survey was conducted with 176 faculty members of various academic ranks. Participants were divided into three groups based on their years of clinical/preclinical teaching experience: Group 1 (<5 years), Group 2 (5–10 years), and Group 3 (>10 years). Data were analyzed using Pearson's Chi-Square, Fisher's Exact, and Multiple Chi-Square tests.

Results: The sample consisted of 50% research assistants, 32.4% assistant professors, 11.9% associate professors, 3.4% professors, and 2.3% lecturers. Regarding experience, 57.4% had <5 years, 22.7% had 5–10 years, and 19.9% had >10 years. Analysis revealed that awareness of the number of left-handed students and the lack of official institutional guidelines increased with teaching experience. In Group 2, 30.0% agreed with having knowledge of the number of left-handed students, compared to 11.9% in Group 1 and 14.3% in Group 3 ($p<0.05$). When asked about official guidelines for left-handed students, the "no idea" response rate was 79.2% in Group 1, significantly higher than Group 2 (47.5%) and Group 3 (42.9%) ($p<0.05$). While 93.1% of participants believed special arrangements would improve education quality and 87.5% felt differentiated materials would ensure equality, the rates of using a left-handed approach in materials (14.7%) or performing left-handed demonstrations (22.7%) remained low.

Conclusion: Although dental educators exhibit high awareness regarding the needs of left-handed students, specific demonstrations and material usage for these students are limited in clinical practice. Developing ergonomic arrangements, educational guidelines, and specialized materials is recommended to support skill development and mitigate occupational health risks for left-handed students.

TEMPOROMANDIBULAR EKLEM OSTEOARTRİTLİ HASTALARDA PETROTIMPANİK FİSSURA TİPİ VE TİMPANİK FORAMEN MEVCUDİYETİNİN BELİRLENEREK OTOLOJİK SEMPTOMLAR VE RADYOLOJİK BULGULAR İLE ARASINDAKİ İLİŞKİNİN RETROSPEKTİF OLARAK DEĞERLENDİRİLMESİ

Ulvi NOVRUZOV

Araş. Gör., Atatürk Üniversitesi, Diş Hekimliği Fakültesi, Ağız, Diş ve Çene Cerrahisi Anabilim Dalı, 25040 Yakutiye, Erzurum. ORCID ID: 0009-0007-5043-8149

Songül CÖMERT KILIÇ

Prof. Dr., Atatürk Üniversitesi, Diş Hekimliği Fakültesi, Ağız, Diş ve Çene Cerrahisi Anabilim Dalı, 25040 Yakutiye, Erzurum. ORCID ID: 0000-0002-3388-3837

Binali ÇAKIR

Prof. Dr., Atatürk Üniversitesi, Diş Hekimliği Fakültesi, Ağız, Diş ve Çene Radyolojisi Anabilim Dalı, 25040 Yakutiye, Erzurum. ORCID ID: 0000-0002-8525-1444

Amaç: Bu retrospektif çalışmanın amacı, temporomandibular eklem osteoartritli (TME-OA) hastalarda petrotimpanik fissür (PTF) tipleri ile Huschke foramenin (HF) otolojik semptomlar ve radyolojik bulgular ile ilişkisini değerlendirmektir.

Materyal ve Yöntem: Çalışmaya 57 hastaya ait 85 TME-OA eklemi dahil edildi. Demografik veriler ve otolojik semptomlar klinik olarak kaydedildi. Dejeneratif eklem değişiklikleri, PTF tipleri ve HF varlığı konik ışınlı bilgisayarlı tomografi (CBCT) ve manyetik rezonans görüntüleme (MRG) ile değerlendirildi. Yaş, cinsiyet, otolojik semptomlar ve radyolojik bulgular arasındaki ilişkiler Spearman rho ve Pearson ki-kare testleri ile analiz edildi. Gözlemciler arası ve gözlemci içi uyum Cohen kappa testi ile değerlendirildi.

Bulgular: Hastaların büyük çoğunluğu kadın (%91.2) olup yaş ortalaması 33.14 ± 13.94 yıldı. En sık görülen otolojik semptom kulak ağrısı (%54.1), ardından vertigo (%42.0) ve tinnitus (%41.0) idi. CBCT'de kondiler erozyon/skleroz %91.8, glenoid fossada skleroz %87.1, kondiler düzleşme/subkortikal kist %83.5 ve eklem aralığında daralma %85.9 oranında kaydedildi. Kondil tipi %49.4 oranında konvex olarak kaydedildi. MRG'de diskte düzleşme %81.2, redüksiyonsuz disk deplasmanı %41.2, efüzyon %35.3 ve disk perforasyonu %34.1 oranında belirlendi. PTF en sık Tip 1 (%43.5) ve Tip 3 (%36.5) olarak sınıflandırılırken, HF varlığı %28.2 oranında belirlendi. Kulak ağrısı ile HF, pneumatizasyon ve kondil tipi; kulakta dolgunluk ile pneumatizasyon; tinnitus ile yaş, HF ve diskte düzleşme; işitme kaybı ile yaş ve disk perforasyonu; vertigo ile kondiler erozyon arasında istatistiksel olarak anlamlı ($p<0.05$) ve orta düzeyli korelasyonlar görüldü. PTF tipi ve HF varlığı ile yaş, cinsiyet veya radyolojik bulgular arasında anlamlı ilişki saptanmadı. Gözlemci uyumu iyi ile mükemmel arasında değişmekteydi.

Sonuç: TME-OA hastalarında otolojik semptomlar sık görülmekte ve belirli radyolojik bulgularla ilişkili bulunmaktadır. PTF tipi otolojik semptomlar veya görüntüleme bulguları ile ilişkili değilken, HF klinik açıdan önemli bir anatomik belirteç olabilir. Anatomik varyasyonların rutin CBCT ile değerlendirilmesi ve multidisipliner tanısal yaklaşım hasta yönetimini iyileştirebilir.

Anahtar kelimeler: Temporomandibular eklem osteoartriti; petrotimpanik fissür; Huschke forameni; konik ışınlı bilgisayarlı tomografi; manyetik rezonans görüntüleme; otolojik semptomlar; anatomik varyasyonlar

RETROSPECTIVE EVALUATION OF THE ASSOCIATION OF PETROTYMPANIC FISSURE TYPE AND PRESENCE OF TYMPANIC FORAMEN WITH OTOLOGIC SYMPTOMS AND RADIOLOGICAL FINDINGS IN PATIENTS WITH TEMPOROMANDIBULAR JOINT OSTEOARTHRITIS

Objective: The aim of this retrospective study was to evaluate the association of petrotympanic fissure (PTF) types and the presence of the Huschke foramen (FH) with otologic symptoms and radiological findings in patients with temporomandibular joint osteoarthritis (TMJ-OA).

Materials and Methods: A total of 85 TMJ-OA joints from 57 patients were included. Demographic data and otologic symptoms were clinically recorded. Degenerative joint changes, PTF types, and the presence of FH were assessed using cone-beam computed tomography (CBCT) and magnetic resonance imaging (MRI). Associations among age, sex, otologic symptoms, and radiological findings were analyzed using Spearman's rho and Pearson's chi-square tests. Inter-observer and intra-observer agreement were evaluated using Cohen's kappa test.

Results: The majority of patients were female (91.2%), with a mean age of 33.14 ± 13.94 years. The most common otologic symptom was otalgia (54.1%), followed by vertigo (42.0%) and tinnitus (41.0%). CBCT findings recorded condylar erosion/sclerosis in 91.8%, glenoid fossa sclerosis in 87.1%, condylar flattening/subcortical cysts in 83.5%, and joint space narrowing in 85.9% of joints. The condylar type was recorded as convex in 49.4% of cases. MRI revealed disc flattening in 81.2%, disc displacement without reduction in 41.2%, effusion in 35.3%, and disc perforation in 34.1% of joints. PTF was most frequently classified as Type 1 (43.5%) and Type 3 (36.5%), whereas FH was present in 28.2% of joints. Statistically significant moderate correlations ($p < 0.05$) were found between otalgia and FH, pneumatization, and condylar type; ear fullness and pneumatization; tinnitus and age, FH, and disc flattening; hearing loss and age and disc perforation; and vertigo and condylar erosion. No significant associations were observed between PTF type or FH presence and age, sex, or radiological findings. Observer agreement ranged from good to excellent.

Conclusion: Otologic symptoms are common in patients with TMJ-OA and are associated with specific radiological findings. Although PTF type was not associated with otologic symptoms or imaging findings, FH may represent a clinically relevant anatomical marker. Routine CBCT evaluation of anatomical variations and a multidisciplinary diagnostic approach may improve patient management.

Keywords: Temporomandibular joint osteoarthritis; petrotympanic fissure; foramen of Huschke; cone-beam computed tomography; magnetic resonance imaging; otologic symptoms; anatomical variations

PRİMER SİLİYER DİSKİNEZİ VE LOB SINIRLI BRONŞEKTAZİ: OLGU SUNUMU

Şeyma ÖZTÜRK

Kırıkkale Üniversitesi Tıp Fakültesi Tıbbi Patoloji Anabilim Dalı/ Doktor Öğretim Üyesi, ORCID:0000-0002-2167-4253

Zeynep KURT

Kırıkkale Üniversitesi Tıp Fakültesi Hastanesi, TIBBI PATOLOJI, ORCID ID: 0009-0001-9381-3881

ÖZET

Amaç: Bronşektazi, bronş duvarının kalıcı ve anormal dilatasyonu ile karakterize kronik bir akciğer hastalığıdır. Primer siliyer diskinezi ise mukosiliyer klirens bozukluğu ile seyreden, otozomal resesif geçişli nadir bir hastalık olup bronşektazi gelişiminde önemli rol oynamaktadır. Bu çalışmada, primer siliyer diskinezi zemininde gelişen ve sağ orta lob ile sınırlı bronşektazi olgusunun klinik, radyolojik ve patolojik bulgularının sunulması amaçlanmıştır.

Materyal ve Yöntem: Yirmi dört yaşında erkek hasta, nefes darlığı ve göğüs ağrısı şikâyetleri ile başvurmuştur. Yapılan toraks bilgisayarlı tomografi incelemesinde sağ orta lob medial segmentte geniş konsolidasyon alanı ve yaklaşık 2 cm çapa ulaşan kistik bronşektazik dilatasyonlar saptanmıştır. Ayrıca her iki akciğerde milimetrik nonspesifik nodüller izlenmiştir. Hastanın sık tekrarlayan enfeksiyon öyküsü ve kötü kokulu balgam şikâyetleri dikkate alınarak cerrahi tedavi planlanmış ve sağ orta lobektomi uygulanmıştır. Elde edilen materyal makroskopik ve mikroskopik olarak incelenmiştir.

Bulgular: Makroskopik incelemede 9×7,5×3 cm boyutlarında lobektomi materyali izlenmiş olup kesit yüzeylerinde çok sayıda dilate bronş ve bronşioller ile lümenlerinde mukoid materyal birikimi gözlenmiştir. Mikroskopik incelemede bronşiyal dilatasyon, mukoid materyal ve eksüda birikimi ile birlikte peribronşiyal ve interstisyel alanlarda mononükleer inflamatuvar hücre infiltrasyonu, lenfoid folikül oluşumları ve fibrozis saptanmıştır. Bulgular bronşektazi ve kronik bronşiolit ile uyumlu bulunmuştur.

Sonuç: Primer siliyer diskinezi olgularında bronşektazi çoğunlukla diffüz ve bilateral yerleşim gösterse de bazı hastalarda lokalize ve medikal tedaviye dirençli lobar tutulum görülebilir. Bu tür olgularda cerrahi rezeksiyon, enfeksiyon odağını ortadan kaldırarak semptomların azaltılmasında ve yaşam kalitesinin artırılmasında etkili bir tedavi seçeneği sunmaktadır. Sunulan olguda bronşektazinin sağ orta lob ile sınırlı olması cerrahi yaklaşımın uygunluğunu desteklemektedir.

Anahtar Kelimeler: Bronşektazi, Siliyopati, Pulmoner cerrahi girişimleri, Cerrahi Tedavi, Histopatoloji

PRIMARY CILIARY DYSKINESIA AND LOBE-LIMITED BRONCHIECTASIS: A CASE REPORT

ABSTRACT

Objective:
Bronchiectasis is a chronic pulmonary disease characterized by permanent and abnormal dilatation of the bronchial walls. Primary ciliary dyskinesia is a rare autosomal recessive disorder associated with impaired mucociliary clearance and plays an important role in the development of bronchiectasis. This study aims to present the clinical, radiological, and pathological findings of a case of bronchiectasis limited to the right middle lobe in the setting of primary ciliary dyskinesia.

Materials and Methods: A 24-year-old male patient presented with complaints of dyspnea and chest pain. Thoracic computed tomography revealed consolidation in the medial segment of the right middle lobe and cystic bronchiectatic dilatations measuring up to 2 cm in diameter. Additionally, millimetric

nonspecific pulmonary nodules were observed in both lungs. Due to recurrent respiratory infections and foul-smelling sputum, surgical treatment was planned and a right middle lobectomy was performed. The resected specimen was examined macroscopically and microscopically.

Results: Macroscopic examination revealed a 9 × 7.5 × 3 cm lobectomy specimen. Multiple dilated bronchi and bronchioles with intraluminal mucoid material were observed. Histopathological examination demonstrated bronchial dilatation, mucous accumulation, and exudate, accompanied by mononuclear inflammatory cell infiltration in peribronchial and interstitial areas, lymphoid follicle formation, and fibrosis. These findings were consistent with bronchiectasis and chronic bronchiolitis.

Conclusion: Although bronchiectasis in primary ciliary dyskinesia is typically diffuse and bilateral, localized lobar disease resistant to medical therapy may also occur. In such cases, surgical resection is an effective treatment option for eliminating the infectious focus, reducing symptom burden, and improving quality of life. In the present case, the localization of bronchiectasis to the right middle lobe supports the appropriateness of the surgical approach.

Keywords: Bronchiectasis, Ciliopathy, Pulmonary Surgical Procedures, Surgical Treatment, Histopathology

OKSİMATRİNİN TESTİS TORSİYON/DETORSİYONUNA BAĞLI İSKEMİ/REPERFÜZYON HASARINDA HİSTOPATOLOJİK ETKİSİNİN ARAŞTIRILMASI

Merve Nur TEPE KOCAMAN

Düzce Üniversitesi Tıp Fakültesi Histoloji ve Embriyoloji Anabilim Dalı, ORCID: 0009-0007-1076-3879

Kayıhan Karaçor

Dr. Öğretim Üyesi, Düzce Üniversitesi Tıp Fakültesi Histoloji ve Embriyoloji Anabilim Dalı, ORCID: 0000-0002-1177-2351

Hakan Soylu

Doç. Dr., Düzce Üniversitesi Tıp Fakültesi Histoloji ve Embriyoloji Anabilim Dalı, ORCID: 0000-0002-5646-2226

ÖZET

Amaç: Testis torsiyonu, spermatik kordonun kendi ekseni etrafında dönmesiyle testis dolaşımının bozulmasına yol açan ve acil müdahale gerektiren önemli bir ürolojik durumdur. Erkek infertilitesinin temel sebeplerinden biri olan bu durumun en yaygın görüldüğü dönem 25 yaş altı erkeklerdir. Torsiyonun meydana getirdiği iskemi, dokuda bulunan reaktif oksijen türlerinin (ROS) artmasına aynı zamanda oksijen miktarının azalmasına neden olarak oksidatif strese yol açar. Ayrıca cerrahi detorsiyon işlemiyle kan akımının yeniden sağlanması reperfüzyon hasarını tetikler ve dokuda ek hücresel hasara sebebiyet verir. Bu süreçte meydana gelen iskemi/reperfüzyon (İ/R) hasarı; germ hücre kaybı, seminifer tübül yapısında hasar ve testiküler fonksiyonlarda işlev kaybı ile sonuçlanabilir. Oksimatrin (OMT), geleneksel Çin tıbbında kullanılan antioksidan ve antiinflamatuar özellikleri ile bilinen doğal bir alkaloiddir. Bu çalışmada, oksimatrinin testis torsiyon/detorsiyonunun neden olduğu İ/R hasarında olası koruyucu etkisinin araştırılması amaçlandı.

Materyal ve Yöntem: Çalışmada toplam 30 adet Wistar albino cinsi erkek sıçan kullanılarak kontrol (n=6), sham (n=6), oksimatrin(OMT) (n=6), torsiyon/detorsiyon (T/D) (n=6) ve T/D+OMT (n=6) olmak üzere beş deney grubu oluşturuldu. OMT uygulanan gruplara 7 gün düzenli olarak intraperitoneal olarak 30mg/kg oksimatrin uygulandı. T/D oluşturulan gruplarda sol testis saat yönünde 720° döndürülerek skrotumda 2 saat süreyle torsiyon uygulandı, ardından detorsiyon yapılıp tekrar skrotumda 3 saatlik reperfüze işlemi gerçekleştirildi. Deney sonunda alınan testis dokuları Hematoksilen-Eozin boyaması ile histopatolojik olarak incelendi ve Cosentino skorlama sistemi ile doku hasarı değerlendirildi.

Bulgular: Yapılan değerlendirmede kontrol, sham ve OMT grupları cosentino skorlaması benzerdi. T/D grubunda Cosentino skorunun anlamlı şekilde arttığı, oksimatrin uygulanan T/D+OMT grubunda belirgin şekilde azaldığı gözlemlendi.

Sonuç: Sonuç olarak, oksimatrinin, testis T/D bağlı oluşan İ/R hasarına karşı testis dokusunda koruyucu etkisi olduğu belirlendi.

Anahtar Kelimeler: Testis, Torsiyon, Detorsiyon, İskemi, Reperfüzyon, Oksimatrin.

RESEARCH OF THE HISTOPATHOLOGICAL EFFECT OF OXIMATRINE IN ISCHEMIA/REPERFUSION INJURY DUE TO TESTICULAR TORSION/DETORSION

ABSTRACT

Purpose: Testicular torsion is a significant urological condition that requires urgent intervention, characterized by the twisting of the spermatic cord around its own axis, leading to impaired testicular circulation. This condition, which is one of the primary causes of male infertility, is most commonly seen in men under the age of 25. The ischemia caused by torsion leads to an increase in reactive oxygen

species (ROS) in the tissue and a decrease in oxygen levels, resulting in oxidative stress. Additionally, restoring blood flow through surgical detorsion triggers reperfusion injury and causes additional cellular damage to the tissue. Ischemia/reperfusion (I/R) damage occurring during this process may result in germ cell loss, damage to the seminiferous tubule structure, and functional impairment of testicular functions. Oxymatrine (OMT) is a natural alkaloid known for its antioxidant and anti-inflammatory properties, used in traditional Chinese medicine. In this study, we aimed to investigate the possible protective effect of oxymatrine against I/R damage caused by testicular torsion/detorsion.

Materials and Methods: In the study, five experimental groups were formed, control (n=6), sham (n=6), oxymatrin(OMT) (n=6), torsion/detorsion (T/D) (n=6) and T/D+OMT (n=6), using a total of 30 Wistar albino male rats.Oxymatrine, 30mg/kg, was administered intraperitoneally to the groups receiving OMT on a daily basis for 7 days. In the T/D groups, the left testis was rotated clockwise 720° within the scrotum for 2 hours, followed by detorsion and a 3-hour reperfusion period within the scrotum. At the end of the experiment, the testis tissues were histopathologically examined using Hematoxylin-Eosin staining, and tissue damage was assessed with the Cosentino scoring system.

Results: In the evaluation, the control, sham, and OMT groups had similar Cosentino scores. It was observed that the Cosentino score increased significantly in the T/D group and decreased significantly in the T/D+OMT group treated with oxymatrine.

Conclusion: In conclusion, it was determined that oxymatrine has a protective effect on testicular tissue against I/R damage caused by testicular T/D.

Keywords: Testis, Torsion, Detorsion, İschemia, Reperfusion, Oxymatrine

1.GİRİŞ

Testis torsiyonu, spermatik kordun uzunlamasına bir eksen boyunca dönmesi ile meydana gelen ve testis perfüzyonunda hasara yol açarak iskemiye neden olan cerrahi bir acil durumdur [1]. Testis torsiyonu her yaş grubunda görülebilmekle birlikte, en sık görülen grup ergen erkeklerdir[2]. Genellikle herhangi bir uyarıcı olmadan meydana gelen testis torsiyonuna; travma, testis tümörü, kriptorşizm, ergenliğe bağlı testis büyümesi, testislerin yatay yerleşimi ve spermatik kordun intraskrotal kısmının uzun olması gibi durumlar neden olabilmektedir [3]. Testis iskemi süresinin uzunluğu ile testistiküler doku kaybı riski doğru orantılıdır. Günümüzde torsiyon tedavisinde, cerrahi detorsiyon işlemi uygulanarak testise kan akımının geri kazandırmak amaçlanır [4]. Torsiyon cerrahi olarak başarılı bir şekilde detorsiyone edilse bile, iskemi-reperfüzyon (I/R) hasarı ile meydana gelen oksidatif stres; spermatogenezde bozulmayı, germ hücre apoptozu [5], sperm sayısında azalma ve sperm hareketliliğinde düşüşe bağlı potansiyel kısırlık gibi uzun vadeli komplikasyon riskini artırır [6].

Oksimatrin (OMT), Geleneksel Çin tıbbı bitkisi olarak bilinen Sophora flavescens'ten izole edilmektedir [7]. Yapılan çalışmalarda antiinflamatuar, antiviral, antikanser, antidiyabetik etkileri ile birlikte çeşitli doku ve organlarınların korunmasına da katkı sağladığı gösterilmiştir [8]. Daha önce yapılan birçok farklı çalışmada oksimatrinin, serebral [9], akciğer [10], böbrek [11], bağırsak [12] ve karaciğer [13] dokularında meydana gelen iskemi/reperfüzyon hasarlarına karşı koruyucu olduğu gösterilmiştir.

Ancak yapılan çalışmalar ayrıntılı şekilde incelendiğinde testis torsiyon ve detorsiyonuna bağlı iskemi reperfüzyon hasarında oksimatrinin etkinliği daha önce değerlendirilmemiştir. Bu çalışmanın amacı; oksimatrinin, sıçan testisinde torsiyon/detorsiyonla oluşturulan iskemi-reperfüzyon hasarına karşı testis de oluşabilecek doku hasarına karşı koruyucu rolünün araştırılmasıdır.

2. YÖNTEM

2.1 Hayvanlar

Çalışmada kullanılan deney hayvanları, Düzce Üniversitesi Deney Hayvanları Araştırma ve Uygulama Merkezi tarafından temin edildi. Çalışmada 2–3 aylık yaş aralığında ve 230 ± 30 gram ağırlığında toplam 30 adet erkek Wistar albino sıçan kullanıldı. Hayvanlar, deney süresince 23 ± 2°C sıcaklıkta, %50–60

nem oranında ve 12 saat aydınlık / 12 saat karanlık döngüsüne sahip ortamda, barındırıldı. Tüm hayvanlar serbest olarak yem ve suya erişim sağlayabilecek şekilde barındırıldı. Çalışma, ilgili etik kurul onayı alınarak gerçekleştirildi.

2.2 Maddeler ve Dozları

Çalışmada deneysel ajan olarak oksimatrin kullanıldı. Oksimatrin salin içerisinde çözülerek hazırlandı ve intraperitoneal (i.p) yolla uygulandı. Kontrol grubuna 7 gün boyunca salin uygulanırken, oksimatrin grubuna 7 gün süreyle 30mg/kg dozunda oksimatrin i.p. olarak verildi. Torsiyon/detorsiyon oluşturulan gruplarda ise oksimatrin cerrahi işlem öncesinde 7 gün süreyle uygulandı.

Tablo: Grupları, verilen madde ve dozu ve hayvan sayılarını özetler.

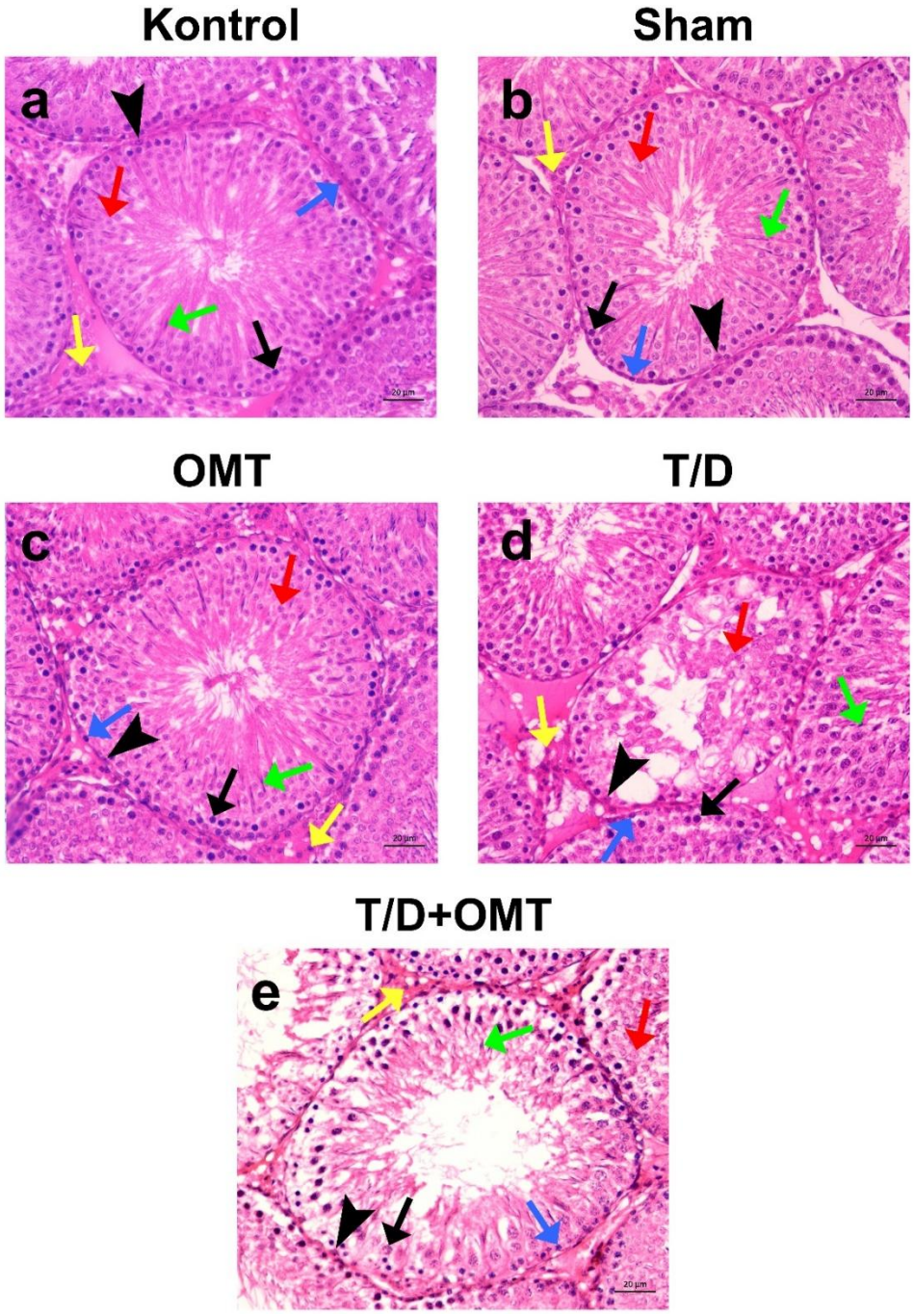
Grup No	Grup Adı	Verilen Madde	Doz	Hayvan Sayısı
1	Kontrol	Salin	-	6
2	Sham	-	-	6
3	Oksimatrin	Oksimatrin	30 mg/kg (7gün)	6
4	T/D	-	-	6
5	Oksimatrin+ T/D	Oksimatrin	30 mg/kg (7gün)	6

Hayvanlar deney gruplarına ayrılarak, deney protokolü doğrultusunda 7 gün süreyle ilgili maddeler uygulandı ve yedinci günün sonunda, hayvanlar 1500mg/kg üretan ile anestezi altına alındı. Anestezi işleminin ardından iskemi/reperfüzyon modelinin oluşturulması için, sol testis skrotal insizyon ile açığa çıkarılarak spermatik kord saat yönünde 720° döndürüldü ve torsiyon oluşturuldu. Testis yaklaşık 2 saat süreyle torsiyone edildi ve skrotuma 4.0 prolen sutur ile sabitlendi. 2 saat sonunda testis detorsiyone edilerek 3 saat reperfüzyona bırakıldı. İşlem sonrasında testis dokuları çıkarıldı ve makroskobik olarak değerlendirildi. Doku örnekleri 24 saat süreyle bouin solüsyonunda fikse edilerek histopatolojik incelemeye hazırlandı. Fiksasyon akabinde rutin histolojik takip işlemlerinden geçirildi ve parafin bloklarına gömüldü. 4 mikrometre kalınlığında kesitler alınarak hematoksilen&eozin ile boyandı. Işık mikroskobu altında kesitler incelendi ve Cosentino skormalası uygulanarak fotoğrafları alındı.

3.BULGULAR

3.1 Histolojik Değerlendirme Bulguları

Histopatolojik değerlendirme sonucu, kontrol, sham ve oksimatrin grupları testis dokularında seminifer tübüller normal yapı ve bütünlüğünü muhafaza ettiği gözlemlendi. Bazal membranının yapısal bütünlüğü ve seminifer tübül duvarı boyunca bazal tabakadan lümene doğru düzenli dizilim gösteren spermatogenik hücrelerin normal spermatogenez süreci geçirdiği görüldü. Seminifer tübül epiteli içerisinde spermatogonyum, primer spermatosit, spermatid ve lümene doğru ilerleyen olgun spermlerin varlığı net şekilde görüldü. Tübül lümenlerinde olgun spermatozoaların belirgin şekilde yerleşim gösterdiği ve yapısal organizasyonun korunduğu izlendi. Seminifer tübüller arası interstisyel alanda normal dağılım gösteren Leydig hücreleri izlendi (Şekil 1a, Şekil 1b, Şekil 1c).



Şekil 1: Hematoksilen&Eozin ile boyanmış farklı grupların boyanmalarını göstermektedir. OMT; oksimatrin, T/D; torsiyon/detorsiyon. Siyah ok başı; sertoli hücrelerini, mavi ok; spermatogonyum, siyah ok; primer spermatosit, kırmızı ok; erken spermatid, yeşil ok; geç spermatid, sarı ok; leydig hücrelerini göstermektedir. Mikroskop büyütmesi 400x ve skala bar 20 µm'dir.

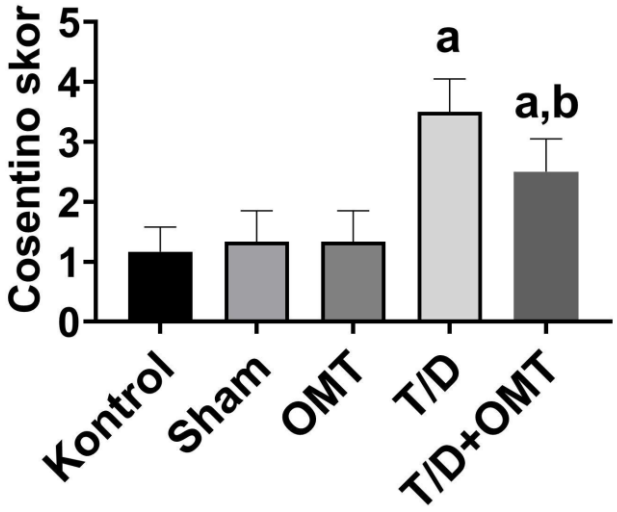
Torsiyon/detorsiyon grubu testis dokularında belirgin histopatolojik değişiklikler dikkat çekiciydi (Şekil 1d). Seminifer tübül duvarı kalınlığının belirgin şekilde azaldığı, germinal epitel tabakasında düzensizlik, hücre kaybı ve hücrelerin lümene dökülmesi gibi yapısal bozukluklar gözlemlendi (Şekil 1d). Tübül lümenlerindeki düzensizlik ile birlikte interstisyel alanlarda genişleme ve yapısal bütünlüğünde bozulmalar meydana geldiği gözlemlendi (Şekil 1d).

Oksimatrin uygulanan torsiyon/detorsiyon grubu testis dokularında, T/D grubuna kıyasla seminfer tübüllerin daha az etkilendiği dikkat çekiciydi (Şekil 1e). Seminifer tübüllerdeki yapısal düzensizliklerin daha az olduğu, lümenine dökülmüş hücre gözlenen seminifer tübül neredeyse yoktu (Şekil 1e). Germinal epitel tabakasının daha düzenli olduğu ve hücresel organizasyonun kısmen korunduğu

belirlendi (Şekil 1e). Spermatogenik seri hücrelerinin hepsi germinal epitelde gözlenmekteydi (Şekil 1e). Özellikle tübül lümeninde azda olsa spermatozoa vardı (Şekil 1e). Interstisyel alanda yapısal bütünlüğün korunduğu gözlemlendi (Şekil 1e).

3.2 Cosentino Skorlama Bulguları

Cosentino skorlamasına göre testis dokusunda histolojik olarak yapılan değerlendirmede, kontrol, sham ve oksimatrin grupları cosentino skorlaması benzerdi (p>0,05)(Şekil 2). Torsiyon/detorsiyon grubunda cosentino skorlaması kontrol, sham ve oksimatrin gruplarına kıyasla anlamlı derecede arttığı belirlendi (p<0,001)(Şekil 2). Oksimatrin uygulanan torsiyon/detorsiyon grubunda cosentino skorunun torsiyon/detorsiyon grubuna kıyasla belirgin seviyede azaldığı gözlendi (p=0,009)(Şekil 2).



Şekil 2. Gruplar arası Cosentino skorlamasının istatitiksel grafiği. GraphPad Prism 9 programı ile One way annova Holm-Šídák's multiple comparisons testi kullanıldı. *P<0,05* anlamlı kabul edildi ve a; kontrol, sham ve oksimatrin gruplarına göre, b; torsiyon/detorsiyon grubuna göre anlamlılığı göstermektedir. OMT; oksimatrin, T/D; torsiyon/detorsiyon.

4. TARTIŞMA ve SONUÇ

Bu çalışmada, testis torsiyonuna bağlı meydana gelen iskemi/reperfüzyon (İ/R) hasarında oksimatrinin histopatolojik etkileri araştırılmıştır. Torsiyon/detorsiyon grubunda seminifer tübüllerin yapısında bozulmalar, germinal epitelde düzensizlik ve hücre kayıpları oluştuğu izlenmiştir. Oksimatrin uygulanan grupta daha az hasar meydana geldiği, seminifer tübül yapısının nispeten daha düzenli olduğu ve spermatogenik hücre serilerinin daha iyi korunduğu gözlenmiştir. Daha önce birçok farklı çalışmada ve farklı organlarda iskemi/ reperfüzyon hasarında oksimatrinin; serebral [9], akciğer [10], böbrek [11], bağırsak [12] ve karaciğer [13] dokularında meydana gelen iskemi/reperfüzyon hasarlarına karşı koruyucu olduğu gösterilmiştir. Bu çalışmada da daha önceki çalışmalarla uyumlu şekilde oksimatrinin testiküler İ/R hasarında koruyucu olduğu ortaya koyulmuştur.

Sonuç olarak, çin tıbbında yaygın olarak kullanılan ve birçok farklı organda meydana gelen İ/R hasarına karşı koruyucu olduğu kanıtlanan oksimatrinin, testis T/D bağlı oluşan İ/R hasarına karşı testis dokusunu da koruduğu bu çalışma ile kanıtlanmıştır. Ancak yapılan çalışma deneysel olduğu ve sadece histopatolojik bir değerlendirme olduğu için, oksimatrinin etki mekanizmasının daha ayrıntılı hücresel düzeyde etki mekanizmasının araştırılması ve klinik olarak kullanılabilmesi için daha yeni çalışmalara ihtiyaç vardır.

KAYNAKLAR

1. Howe, A.S., et al., *Degree of twisting and duration of symptoms are prognostic factors of testis salvage during episodes of testicular torsion.* Transl Androl Urol, 2017. 6(6): p. 1159-1166.

2. Vazquez, J.L., et al., *Testicular torsion and ultrasound-assisted manual detorsion.* Pediatr Radiol, 2025. 55(4): p. 674-681.

3. Ringdahl, E. and L. Teague, *Testicular torsion.* Am Fam Physician, 2006. 74(10): p. 1739-43.

4. Wei, S.M. and Y.M. Huang, *Effect of sulforaphane on testicular ischemia-reperfusion injury induced by testicular torsion-detorsion in rats.* Sci Rep, 2024. 14(1): p. 23420.

5. Karaguzel, E., et al., *Comparison of the protective effect of dipyridamole and acetylsalicylic acid on long-term histologic damage in a rat model of testicular ischemia-reperfusion injury.* J Pediatr Surg, 2012. 47(9): p. 1716-23.

6. Jacobsen, F.M., et al., *The Impact of Testicular Torsion on Testicular Function.* World J Mens Health, 2020. 38(3): p. 298-307.

7. Jiang, G., et al., *Oxymatrine ameliorates renal ischemia-reperfusion injury from oxidative stress through Nrf2/HO-1 pathway.* Acta Cir Bras, 2015. 30(6): p. 422-9.

8. Huan, D.Q., N.Q. Hop, and N.T. Son, *Oxymatrine: A current overview of its health benefits.* Fitoterapia, 2023. 168: p. 105565.

9. Ma, C.S., et al., *Oxymatrine Alleviates Cerebral Ischemia/Reperfusion Injury By Targeting HDAC1 to Regulate Mitochondria-Related Autophagy and Oxidative Stress.* Mol Neurobiol, 2025. 63(1): p. 219.

10.Xiong, Z., J. Xu, and X. Liu, *Oxymatrine exerts a protective effect in myocardial ischemia/reperfusion-induced acute lung injury by inhibiting autophagy in diabetic rats.* Mol Med Rep, 2021. 23(3).

11.Ozturk, H., et al., *Protective effect of oxymatrine against renal ischemia/reperfusion injury in rats.* Bratisl Lek Listy, 2017. 118(4): p. 217-222.

12.Zhao, J., et al., *Oxymatrine attenuates intestinal ischemia/reperfusion injury in rats.* Surg Today, 2008. 38(10): p. 931-7.

13.Jiang, H., et al., *Anti-apoptosis effects of oxymatrine protect the liver from warm ischemia reperfusion injury in rats.* World J Surg, 2005. 29(11): p. 1397-401.

PRENATAL DIAGNOSIS AND POSTNATAL MANAGEMENT OF BOCHDALEK HERNIA IN A FETUS OF A PREGESTATIONAL DIABETIC MOTHER: A CASE REPORT

Mehmet DEMİR

Çiğli Training and Research Hospital, Obstetrics and Gynecology, ORCID :0009-0005-2737-9588

Aim: Bochdalek hernia represents the most common type of congenital diaphragmatic hernia and results from a posterolateral defect of the diaphragm that allows abdominal organs to herniate into the thoracic cavity. The condition may lead to pulmonary hypoplasia and mediastinal shift, significantly affecting neonatal morbidity and mortality. Prenatal identification of this condition is essential for planning perinatal management and improving neonatal outcomes. Congenital diaphragmatic hernia may also coexist with cardiac abnormalities or other developmental anomalies. The aim of this study was to present a prenatally diagnosed case of Bochdalek hernia in a fetus of a mother with pregestational diabetes and to describe the clinical findings, perinatal management, and early neonatal outcome.

Materials and Methods: A 31-year-old pregnant woman, gravida 5 para 2 abortus 2 (G5P2A2), with a history of pregestational type 1 diabetes mellitus was referred to the perinatology clinic after a suspicious thoracic mass was detected during routine obstetric ultrasonography at 17–18 weeks of gestation. Detailed fetal ultrasonography revealed structures consistent with bowel loops and splenic tissue within the thoracic cavity, suggesting congenital diaphragmatic hernia. Polyhydramnios was also detected during antenatal follow-up. Amniocentesis was performed to investigate possible chromosomal abnormalities, and genetic analysis revealed no abnormalities. Prenatal fetal echocardiography demonstrated enlargement of the right cardiac chambers and dilation of the pulmonary artery. Due to the onset of uterine contractions, delivery was performed by cesarean section at 34 weeks and 4 days of gestation.

Results: A live male neonate weighing 2400 g was delivered. Postnatal echocardiography also echocardiography also foramen ovale (PFO) and atrial septal defect (ASD). The newborn was evaluated by the pediatric surgery team and underwent surgical repair during the first week of life. During the operation, an accessory spleen was also identified in addition to the diaphragmatic defect. The herniated small intestine and spleen were lowered into the abdomen from the left side.The neonate was followed in the neonatal intensive care unit for 33 days postoperatively. The clinical course remained stable without major complications.

Conclusion: Congenital diaphragmatic hernia is a serious congenital anomaly that can be diagnosed during the prenatal period through detailed ultrasonographic evaluation. Prenatal diagnosis enables delivery to be planned in tertiary care centers and facilitates timely surgical management after birth. In this case, early prenatal detection allowed appropriate multidisciplinary perinatal management and successful surgical treatment. Associated cardiac findings and the presence of an accessory spleen emphasize the importance of comprehensive prenatal and postnatal evaluation in fetuses suspected of having congenital diaphragmatic hernia.

Keywords: Bochdalek hernia, congenital diaphragmatic hernia, prenatal diagnosis, pregestational diabetes, polyhydramnios

PRENATAL AND POSTNATAL COURSE OF A FETUS WITH MATERNAL HYDATID CYST, INSULIN-TREATED GESTATIONAL DIABETES MELLITUS, AND LEFT PES EQUINOVARUS

Mehmet DEMİR

Çiğli Training and Research Hospital, Obstetrics and Gynecology, ORCID :0009-0005-2737-9588

Aim: Congenital musculoskeletal anomalies identified during prenatal screening require careful evaluation and multidisciplinary management. Pes equinovarus (clubfoot) is one of the most frequently diagnosed congenital orthopedic deformities and may present as an isolated anomaly or as part of a syndromic condition. This report aims to describe the prenatal findings, perinatal management, and early postnatal outcome of a fetus diagnosed with unilateral left pes equinovarus in a pregnancy complicated by maternal hydatid cyst and insulin-treated gestational diabetes mellitus.

Materials and Methods: A 28-year-old pregnant woman (G2P1A1) was referred to our clinic after routine obstetric ultrasonography demonstrated unilateral left pes equinovarus. Detailed fetal anomaly screening was performed to exclude additional structural abnormalities. Genetic evaluation was conducted via amniocentesis, which revealed a normal fetal karyotype. The patient had a history of hepatic hydatid cyst previously treated by interventional radiology. During pregnancy, abdominal ultrasonography demonstrated cystic lesions measuring approximately 10 cm and 5 cm in diameter, compatible with type IV hydatid cyst. The pregnancy was further complicated by gestational diabetes mellitus requiring insulin therapy and close metabolic monitoring.

Results: Serial obstetric ultrasonographic examinations demonstrated persistent isolated left pes equinovarus with normal fetal growth parameters and adequate amniotic fluid volume. Delivery was performed at 38 weeks and 2 days of gestation by cesarean section due to cephalopelvic disproportion. A male neonate weighing 3255 g was delivered. Postnatal physical examination confirmed isolated left pes equinovarus. Neonatal echocardiography revealed an atrial septal defect with left-to-right shunting and mild tricuspid regurgitation. Orthopedic consultation was obtained and treatment with the Ponseti method was initiated. The first casting session was applied on the fifth postnatal day.

Conclusion: Early prenatal detection of pes equinovarus enables appropriate parental counseling and facilitates timely postnatal orthopedic intervention. In the present case, the clinical course was favorable with progressive correction following the Ponseti casting protocol. Comprehensive prenatal assessment and multidisciplinary follow-up remain essential in pregnancies complicated by maternal systemic diseases and fetal musculoskeletal anomalies.

Keywords: Prenatal diagnosis, Pes equinovarus, Hydatid cyst, Gestational diabetes mellitus

MİDE KANSERİNDE İNFLAMATUVAR VE NUTRİSYONEL İNDEKSLERİN LENF NODU METASTAZI İLE İLİŞKİSİ: GASTREKTOMİ UYGULANAN HASTALARDA RETROSPEKTİF BİR ANALİZ

Osman Gökhan GÖKDERE,

Malatya Turgut Özal Üniversitesi, Tıp Fakültesi, Genel Cerrahi A.D., Malatya / Türkiye

ORCID ID: 0000-0003-0161-6600

Amaç: Bu çalışmanın amacı, gastrektomi uygulanan mide kanserli hastalarda inflamatuvar ve nutrisyonel indekslerin lenf nodu metastazı ve metastatik lenf nodu yükü ile ilişkisini değerlendirmek ve bu parametrelerin nodal metastazın öngörülmesindeki potansiyel klinik değerini ortaya koymaktır.

Materyal ve Yöntem: Ocak 2021–Aralık 2025 tarihleri arasında mide tümörü nedeniyle gastrektomi uygulanan 101 hasta retrospektif olarak değerlendirildi. Demografik özellikler, tümör lokalizasyonu, patolojik bulgular ve lenf nodu durumu kaydedildi. Preoperatif laboratuvar verilerinden inflamatuvar ve nutrisyonel indeksler (nötrofil-lenfosit oranı [NLR], platelet-lenfosit oranı [PLR], lenfosit-monosit oranı [LMR], sistemik immün-inflamasyon indeksi [SII], hemoglobin-albümin-lenfosit-platelet [HALP] skoru ve prognostik nutrisyonel indeks [PNI]) hesaplandı. Bu indekslerin metastatik lenf nodu sayısı ile ilişkisi Spearman korelasyon analizi ile değerlendirildi; grup karşılaştırmaları Mann–Whitney U ve Kruskal–Wallis testleri ile yapıldı.

Bulgular: Hastaların yaş ortalaması 65.5±13.5 yıl olup %64.4'ü erkekti. NLR, PLR, LMR ve SII ile metastatik lenf nodu sayısı arasında anlamlı ilişki saptanmadı (tümü için $p>0.05$). HALP skoru ile metastatik lenf nodu sayısı arasında anlamlı olmayan negatif eğilim gözlendi ($\rho=-0.18$, $p=0.075$). Buna karşın PNI skoru ile metastatik lenf nodu sayısı arasında zayıf fakat anlamlı negatif korelasyon mevcuttu ($\rho=-0.26$, $p=0.011$). Lenf nodu pozitif ve negatif gruplar arasında skorlar açısından anlamlı fark izlenmedi. Tümör lokalizasyonu ile anlamlı ilişki saptanmadı.

Sonuç: İnflamatuvar indeksler lenf nodu metastazı ile ilişkili bulunmazken, PNI skorunun metastatik lenf nodu yükü ile ilişkili olduğu saptanmıştır. Bulgular, nodal metastazın öngörülmesinde nutrisyonel ve immün durumun daha belirleyici olabileceğini düşündürmektedir. Daha geniş ve prospektif çalışmalar gereklidir.

Anahtar Kelimeler: Gastrektomi, İnflamatuvar Gastrektomi, Gastrektomi, İnflamatuvar nodu metastazı, Mide metastazı, Mide nutrisyonel indeks

THE RELATIONSHIP BETWEEN INFLAMMATORY AND NUTRITIONAL INDICES AND LYMPH NODE METASTASIS IN GASTRIC CANCER: A RETROSPECTIVE ANALYSIS OF PATIENTS UNDERGOING GASTRECTOMY

Objective: The aim of this study was to evaluate the relationship between inflammatory and nutritional indices and lymph node metastasis as well as metastatic lymph node burden in patients with gastric cancer who underwent gastrectomy, and to determine the potential clinical value of these parameters in predicting nodal metastasis.

Materials and Methods: A total of 101 patients who underwent gastrectomy for gastric tumors between January 2021 and December 2025 were retrospectively analyzed. Demographic characteristics, tumor localization, pathological findings, and lymph node status were recorded. Inflammatory and nutritional indices—including neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), lymphocyte-to-monocyte ratio (LMR), systemic immune-inflammation index (SII), hemoglobin-albumin-lymphocyte-platelet (HALP) score, and prognostic nutritional index (PNI)—were calculated from preoperative laboratory data. The relationship between these indices and the number of metastatic lymph nodes was evaluated using Spearman correlation analysis, while group comparisons were

performed using Mann–Whitney U and Kruskal–Wallis tests.

Results: The mean age of the patients was 65.5±13.5 years, and 64.4% were male. No significant correlation was found between NLR, PLR, LMR, or SII and the number of metastatic lymph nodes (all $p>0.05$). A non-significant negative trend was observed between the HALP score and metastatic lymph node count ($\rho = -0.18$, $p = 0.075$). However, a weak but statistically significant negative correlation was found between PNI score and metastatic lymph node count ($\rho = -0.26$, $p = 0.011$). No significant differences were observed between lymph node-positive and lymph node-negative groups in terms of the scores. No significant association was found with tumor localization.

Conclusion: While inflammatory indices were not associated with lymph node metastasis, the PNI score was found to be related to metastatic lymph node burden. These findings suggest that nutritional and immune status may be more determinant in predicting nodal metastasis. Larger prospective studies are needed.

Keywords: Gastrectomy, Inflammatory scores, Lymph node metastasis, Gastric cancer, Prognostic nutritional index

FERMENTE PANCAR İÇECEĞİNİN TİP 2 DİYABET ÜZERİNE METABOLİK ETKİLERİ

Seda ÖZBEY

Dyt, Fırat Üniversitesi, Sağlık Bilimleri Fakültesi, Beslenme ve Diyetetik, Elazığ, Türkiye.

[1]https://orcid.org/0000-0003-1346-5213

Semra TÜRKOĞLU

Prof. Dr., Fırat Üniversitesi, Sağlık Bilimleri Fakültesi, Beslenme ve Diyetetik, Elazığ, Türkiye.

https://orcid.org/0000-0001-7682-0513

ÖZET

Amaç: Tip 2 diyabetes mellitus (T2DM), küresel ölçekte prevalansı giderek artan ve ciddi metabolik komplikasyonlara yol açan önemli bir halk sağlığı sorunudur. Mevcut farmakolojik tedavilerin uzun süreli kullanımının yan etkileri ve sınırlamaları, doğal ve destekleyici tedavi yaklaşımlarına olan ilgiyi artırmıştır. Bu çalışmanın amacı, streptozotosin (STZ) ile indüklenmiş bir T2DM sıçan modelinde fermente pancar suyunun metabolik etkilerini araştırmak ve bulguları standart bir antidiyabetik ilaç olan metformin ile karşılaştırmaktır.

Materyal ve Yöntem: Çalışmada, 32 adet Sprague-Dawley ırkı erkek sıçan kullanılmış ve rastgele dört gruba ayrılmıştır: Kontrol grubu (DM-), Diyabet grubu (DM+), Diyabet + Metformin grubu (MET, 100 mg/kg) ve Diyabet + Pancar Kvass grubu (PK, 0.5 mL/kg). İki haftalık adaptasyon döneminden sonra, diyabet gruplarına tek doz STZ (45 mg/kg, intraperitoneal) uygulanmış ve dört haftalık müdahale döneminde PK grubuna fermente pancar suyu verilmiştir. Deneyin sonunda serum lipid profili ve karaciğer enzimleri analiz edilmiş, insülin seviyeleri ELISA kullanılarak değerlendirilmiştir.

Bulgular: Pancar kvass uygulamasının serum lipid profili, insülin ve açlık kan şekeri seviyeleri üzerinde metformin grubuna benzer etkiler gösterdiği ortaya konmuştur. Biyokimyasal parametrelerde gruplar arasında istatistiksel olarak anlamlı bir fark bulunmamıştır ($p>0.05$). AST değeri istatistiksel olarak anlamlı olmasa da, PK grubunda diğer gruplara göre daha düşük saptanmıştır ($p>0.05$).

Sonuç: Fermente pancar suyunun serum lipid seviyeleri ve açlık kan şekeri üzerinde metformin benzeri bir etkiye sahip olduğu ve tip 2 diyabet tedavisinde potansiyel bir destekleyici ürün olarak değerlendirilebileceği düşünülmektedir.

Anahtar Kelimeler: Pancar kvass, diyabet, fermente içecek.

METABOLIC EFFECTS OF FERMENTED BEETROOT BEVERAGE ON TYPE 2 DIABETES

ABSTRACT

Aim: Type 2 diabetes mellitus (T2DM) is a significant public health problem with an increasing global prevalence and leads to serious metabolic complications. The side effects and limitations of long-term use of current pharmacological treatments have increased interest in natural and supportive treatment approaches. The aim of this study is to investigate the metabolic effects of fermented beet juice in a streptozotocin (STZ)-induced T2DM rat model and to compare the findings with metformin, a standard antidiabetic drug.

Material and Methods: In this study, 32 male Sprague-Dawley rats were used and randomly divided into four groups: Control group (DM-), Diabetes group (DM+), Diabetes + Metformin group (MET, 100 mg/kg), and Diabetes + Beetroot Kvass group (PK, 0.5 mL/kg). After a two-week adaptation period, the

diabetes groups received a single dose of STZ (45 mg/kg, intraperitoneal) and during the four week intervention period, the PK group was given fermented beet juice. At the end of the experiment serum lipid profile and liver enzymes were analyzed, insülin levels were evaluated using ELISA.

Results: Beetroot kvass administration has been shown to have effects on serum lipid profile, insulin, and fasting blood glucose levels similar to those of the metformin group. No statistically significant differences were found among groups in biochemical parameters ($p>0.05$). Although the AST value was not statistically significant, it was found to be lower in the PK group compared to other groups. ($p>0.05$).

Conclusion: It is thought that fermented beet juice has a metformin-like effect on serum lipid levels and fasting blood glucose and can be considered as a potential supportive product in the treatment of type 2 diabetes.

Keywords: Beetroot kvass, diabetes, fermented beverage.

HEMŞİRELİK ÖĞRENCİLERİNİN CİNSEL SAĞLIK OKURYAZARLIĞI VE CİNSEL MİTLERE İNANMA DURUMLARININ BELİRLENMESİ

Sevgi ARSLAN

Yüksek Lisans Öğrencisi Amasya Üniversitesi, Sağlık Bilimleri Enstitüsü, Doğum ve Kadın Hastalıkları Hemşireliği Programı, Amasya, Türkiye, ORCID: 0009-0007-3020-023X

Elif KETEN EDİS

Doç. Dr., Amasya Üniversitesi, Sağlık Bilimleri Fakültesi, Doğum ve Kadın Hastalıkları Hemşireliği Anabilim Dalı, Amasya, Türkiye, ORCID: 0000-0002-5587-6726

ÖZET

Amaç: Bu araştırmada hemşirelik öğrencilerinin cinsel sağlık okuryazarlığı ile cinsel mitlere inanma durumlarının belirlenmesi amaçlanmıştır.

Yöntem: Bu tanımlayıcı-kesitsel araştırma Ocak-Mart 2026 tarihleri arasında bir devlet üniversitesinde öğrenim gören 286 hemşirelik öğrencisi ile gerçekleştirilmiştir. Araştırma verileri Tanıtıcı Bilgi Formu, Cinsel Sağlık Okuryazarlığı Ölçeği ve Cinsel Mitler Ölçeği kullanılarak toplanmıştır. Verilerin analizinde bağımsız örneklem t test, tek yönlü varyans analizi, Kruskall Wallis-H testi ve Pearson korelasyon analizi kullanılmıştır. Araştırmaya başlamadan önce etik kurul onayı ve kurum izni alınmıştır.

Bulgular: Öğrencilerin yaş ortalaması 20,96±2.02yıl olup; %40,9'u 3. sınıf, %30,8'i 4. sınıfta öğrenim görmektedir. Doğum ve kadın hastalıkları dersi alan öğrenci oranı %70,6, üreme/cinsel sağlık hakkında eğitim/bilgi alanların oranı %75,2'dir. Öğrencilerin %59,4'ü cinsel sağlık okuryazarlığı kavramını bilmektedir. Cinsel sağlık okuryazarlığı toplam puan ortalaması 52,48±10,09, cinsel mitler toplam puan ortalaması ise 62,83±19,10 olarak bulunmuştur. Cinsel sağlık okuryazarlığı ile cinsel mitler arasında negatif yönlü düşük düzeyde anlamlı bir ilişki saptanmıştır. Cinsel Sağlık Okuryazarlığı Ölçeği ve Cinsel Mitler Ölçeği toplam puan ortalamaları ile sınıf, ikamet yeri, doğum ve kadın hastalıkları dersi alma, üreme/cinsel sağlık hakkında eğitim/bilgi alma, cinsel sağlık okuryazarlığı kavramını bilme ve cinsel sağlık ile ilgili bilgisini yeterli düzeyde bulma durumları arasında anlamlı fark saptanmıştır. Ayrıca geliri giderine eşit olan ve aile içinde cinsel sağlık ile ilgili konuları rahat konuşabilen öğrencilerde cinsel sağlık okuryazarlığı puan ortalaması daha yüksek bulunmuştur ($p<0,05$). **Sonuç:** Öğrencilerin cinsel sağlık okuryazarlığının ortalamanın üzerinde olduğu, cinsel mitlere inanma durumlarının ise düşük-orta seviyede olduğu belirlenmiştir. Eğitim programlarında cinsel sağlık eğitimine daha fazla yer verilmesi önerilmektedir.

Anahtar Kelime: Cinsel mitler, Cinsel sağlık, Hemşirelik öğrencileri, Sağlık okuryazarlığı

DETERMINATION OF NURSING STUDENTS' SEXUAL HEALTH LITERACY AND THEIR BELIEFS IN SEXUAL MYTHS

ABSTRACT

Aim: This study aimed to determine nursing students' sexual health literacy and their beliefs in sexual myths.

Methods: This descriptive-cross-sectional study was conducted with 286 nursing students studying at a state university between January and March 2026. Data were collected using an Introductory Information Form, the Sexual Health Literacy Scale, and the Sexual Myths Scale. Independent samples t-test, one-way analysis of variance, Kruskal-Wallis H test, and Pearson correlation analysis were used to analyze the data. Ethical committee approval and institutional permission were obtained before the research began.

Results: The average age of the students was 20.96±2.02 years; 40.9% were in the 3rd year, and 30.8% were in the 4th year. 70.6% of students had taken a course in obstetrics and gynecology, and 75.2% had received education/information on reproductive/sexual health. 59.4% of the students were aware of the concept of sexual health literacy. The average total score for sexual health literacy was 52.48±10.09, and for sexual myths, 62.83±19.10. A low-level, statistically significant negative correlation was found between sexual health literacy and sexual myths. A significant difference was found between the mean total scores of the Sexual Health Literacy Scale and the Sexual Myths Scale, and factors such as class level, place of residence, taking courses on obstetrics and gynecology, receiving education/information about reproductive/sexual health, knowledge of the concept of sexual health literacy, and perceiving one's knowledge of sexual health as sufficient. Additionally, the average sexual health literacy score was found to be higher among students whose income equals their expenses and among those who can comfortably discuss sexual health topics within the family ($p<0.05$).

Conclusion: The study found that students had above-average sexual health literacy and low-to-moderate belief in sexual myths. It is recommended that sexual health education be given more prominence in educational programs.

Keywords: Sexual myths, Sexual health, Nursing students, Health literacy

ONKOLOJİK VERİ ANALİZİNDE MODEL ROBUSTNESS: 30 DEĞİŞKENLİ BİR SİMÜLASYON SENARYOSUNDA GLMM VE ANOVA KARŞILAŞTIRMASI

Fırat DEMİR

Van YYU, Faculty of Medicine, Biostatistics Department, PhD Student, Türkiye

ORCID: 0009-0008-6815-2488

Sıddık KESKİN

Head of Department of Biostatistics, Faculty of Medicine, Van Yüzüncü Yıl University, Türkiye

Zeve Campus, ORCID: 0000-0001-9355-6558

Özet

Giriş ve Amaç: Klinik onkoloji araştırmaları, çok sayıda bağımsız değişkenin etkileşim içinde olduğu ve genellikle hastaların farklı merkezlerde tedavi görmesinden kaynaklanan hiyerarşik yapılar barındırır. Bu çalışmanın amacı, 30 farklı açıklayıcı değişken içeren tipik bir onkoloji veri yapısında; geleneksel ANOVA ile Genelleştirilmiş Doğrusal Karma Modellerin (GLMM) tahmin doğruluğunu, varyans açıklama kapasitesini ve Tip I hata oranlarını Monte Carlo simülasyonu üzerinden karşılaştırmaktır.

Materyal ve Yöntem: Çalışma, 500 sanal hastadan oluşan bir kohort üzerinde 1.000 yinelemeli Monte Carlo simülasyonu yürütülmüştür. Veri seti toplam 30 bağımsız değişken içerecek şekilde kurgulandı. Hiyerarşik yapıyı temsilen veri setine 10 farklı klinik merkez dahil edilmiş ve merkezler arası varyans oranı (ICC) %15 olarak belirlendi. Veriler, sabit etkili ANOVA ve rastgele kesim noktalı GLMM yaklaşımlarıyla analiz edildi ve Akaike Bilgi Kriteri (AIC), istatistiksel güç ve düzeltilmiş R^2 ölçütleri üzerinden kıyaslandı.

Bulgular: Simülasyon sonuçları, 30 değişkenli bu yapıda GLMM'nin klasik yöntemlere göre daha muhafazakar ve hassas sonuçlar ürettiğini ortaya koydu. Bulgulara göre; GLMM, ANOVA'ya kıyasla daha yüksek bir açıklanmış varyans (R^2_{adj})=0.74 vs 0.62) ve daha düşük bir bilgi kriteri (AIC=1.912,4 vs 2.145,8) sergileyerek model uyumunda üstünlük sağladığı görüldü. ANOVA modelinin hiyerarşik varyansı göz ardı etmesi, Tip I hata oranının %9'a yükselmesine neden olur iken GLMM, merkez etkisini rastgele bileşen olarak tanımlayarak bu oranı %5 eşik değerinde tutuğu saptandı. Ayrıca, ANOVA tarafından anlamsız olarak değerlendirilen 4 parametre, GLMM'nin varyans ayrıştırma yeteneği sayesinde istatistiksel olarak anlamlı bulunduğu tespit edildi.

Sonuç: 500 hasta ve 30 değişkenli bu simülasyon çalışması, çok merkezli onkoloji verilerinde hiyerarşik yapının modele dahil edilmemesinin, yanıltıcı p-değerlerine ve klinik çıkarım hatalarına yol açabileceğini kanıtlamaktadır. GLMM, varyansın kaynağını doğru dekompoze ederek hem hatalı anlamlılık riskini minimize etmekte hem de modelin açıklayıcılığını artırmaktadır. Sonuç olarak, yüksek boyutlu ve katmanlı klinik verilerin analizinde GLMM'nin ANOVA'ya kıyasla daha robust ve güvenilir bir metodolojik çerçeve sunduğu saptandı.

Anahtar Kelimeler: GLMM, ANOVA, Simülasyon, Onkoloji.

OSTEOSARCOMA OF THE ANTERIOR MANDIBLE: A CASE REPORT

Rabia Duman Tepe

Specialist Dentist, Istanbul University Faculty of Dentistry, Department of Oral and Maxillofacial Radiology, 0000-0001-9496-5441

Buğra Doğan

Specialist Dentist, Istanbul University Faculty of Dentistry, Department of Oral and Maxillofacial Radiology, 0009-0005-3982-1994

Nihan Aksakallı

Associate Professor, Istanbul University Faculty of Dentistry, Department of Oral Pathology, 0000-0002-2380-1148

ABSTRACT

Objective: Osteosarcoma is a rare but aggressive malignant bone tumor in the jaws. This study aims to present the clinical, radiological, and histopathological findings of an osteosarcoma located in the anterior mandible.

Materials and Methods: A 16-year-old male patient presented with swelling in the anterior region of the mandible. Clinical examination and cone-beam computed tomography (CBCT) imaging were performed. Magnetic resonance imaging (MRI) and positron emission tomography/computed tomography (PET/CT) findings were included in the evaluation. The radiological findings were correlated with histopathological evaluation.

Results: CBCT images revealed an ill-defined, mixed-density lesion in the anterior mandible, characterized by cortical destruction, expansion, and extension into adjacent soft tissues. MRI demonstrated bone marrow signal alteration, heterogeneous internal structure, and invasion into surrounding soft tissues. Contrast-enhanced images showed heterogeneous enhancement. PET/CT revealed increased FDG uptake in the same region, indicating high metabolic activity. Histopathological examination demonstrated a highly cellular tumor. In the superficial areas, a thick layer of atypical young mesenchymal cells was observed. Tumor cells were arranged around osteoid in a lace-like pattern. Areas containing atypical tumor cells embedded within a chondroid matrix were also observed. In deeper regions, trabecular bone and intervening fatty bone marrow were identified. Based on these findings, the lesion was diagnosed as osteosarcoma.

Conclusion: Osteosarcoma of the mandible is a rare entity with aggressive characteristics. Radiological evaluation plays a crucial role in determining lesion extent and guiding diagnosis. This case highlights the importance of comprehensive clinical, radiological, and histopathological assessment in the diagnosis of osteosarcoma.

Keywords: Osteosarcoma, mandible, CBCT, MRI, PET/CT

THE GUT-BRAIN-SKIN AXIS IN ACNE: IMPACT OF POLENODERM

Major Gheorghe Giurgiu

Deniplant-Aide Sante Medical Center, Biomedicine, Bucharest, Romania

https://orcid.org/0000-0002-5449-2712

Prof. dr. Manole Cojocaru

Titu Maiorescu University, Faculty of Medicine, Bucharest, Romania
https://orcid.org/0000-0002-6871-577X

ABSTRACT

Background It is increasingly believed that the interaction between skin microbes and host immunity plays an important role in acne. Acne also has close connections with the gastrointestinal tract, and many argue that the gut microbiota could be involved in the pathogenic process of acne. The emotions of stress, have been hypothesized to aggravate acne by altering the gut microbiota. The presence of a gut-brain-skin axis that connects gut microbes, oral probiotics, and diet, currently an area of intense scrutiny, to acne severity. This study concentrates on the skin and gut microbes in acne, the role that the gut-brain-skin axis plays in the immunobiology of acne, and newly emerging microbiome-based therapies that can be applied to treat acne.

Obiective The purpose of this study was to compare the diversity of the skin microbiota in acne patients before and after taking Polenoderm.

Materials and methods A longitudinal cohort study was performed on 20 participants with moderate to severe facial acne with no recent use of oral and topical antibiotics/retinoids.

Results Hence, it is crucial to understand Polenoderm impact on the acne skin microbiota which is thought to be perturbed, our study provides insight into the skin microbiota in acne and how it is modulated by Polenoderm and diet.

Conclusion Acne also has close connections with the gastrointestinal tract, and many argue that the gut microbiota could be involved in the pathogenic process of acne. As understanding of the microbiome in healthy skin and the pathophysiology of acne continues to develop, new therapeutic targets are arising.

Keywords: acne, gut-brain-skin axis microbiota, Polenoderm, diet

PROGNOSTIC AND PHARMACOGENOMIC RELEVANCE OF SLC7A11 IN HEPATOCELLULAR CARCINOMA

Hasti Balali

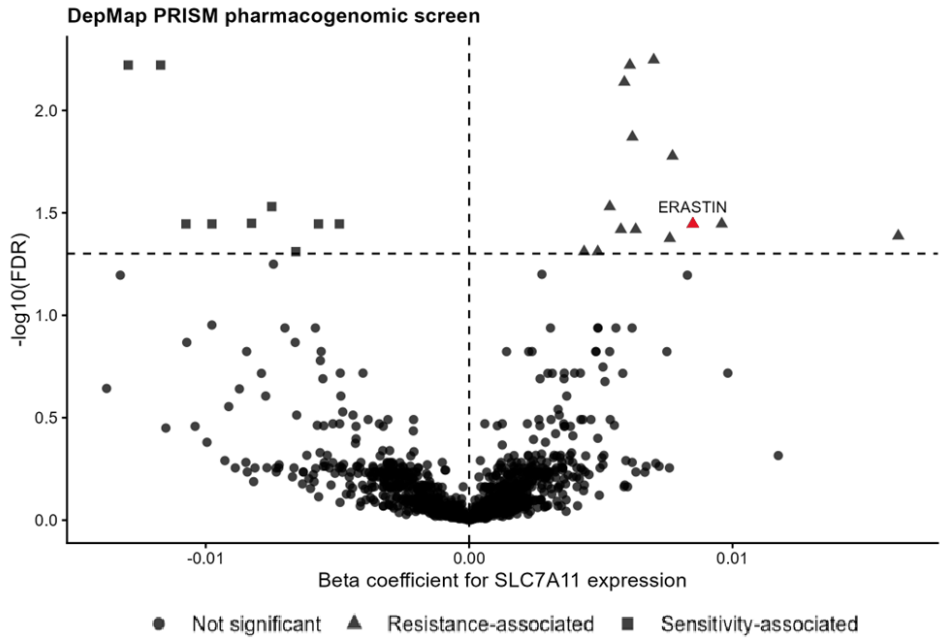
Department of Biosciences, University of Milan, Milan, Italy

Ali Morabbi

Department of Pharmaceutical Sciences, University of Milan, Milan, Italy

Background: SLC7A11 encodes xCT, the light-chain subunit of the cystine/glutamate antiporter system Xc^-, and has a central role in cystine uptake, redox balance, and ferroptosis regulation. The clinical and pharmacogenomic relevance of SLC7A11 in liver hepatocellular carcinoma (LIHC) remains incompletely defined. **Methods:** SLC7A11 expression and survival associations were evaluated in TCGA-LIHC. Tumor and normal liver tissues were compared using normalized logCPM values and Wilcoxon testing. Overall survival was assessed by median-based expression stratification, Kaplan–Meier analysis, and Cox proportional hazards models, including stage-adjusted multivariable analysis. Pharmacogenomic relevance was examined using a lineage-adjusted DepMap PRISM screen across 1,482 compounds, with drug AUC modeled as a function of SLC7A11 expression and cancer lineage. Multiple testing correction was performed using the Benjamini–Hochberg method. **Results:** SLC7A11 was markedly overexpressed in LIHC tumors relative to normal liver tissue (median logCPM 1.05 vs −1.94; $p < 2.2 \times 10^{-16}$). High SLC7A11 expression was associated with inferior overall survival (log-rank p = 0.00044) and remained an independent adverse prognostic factor after adjustment for stage (HR = 1.87, 95% CI 1.27–2.76; p = 0.00148). In the DepMap PRISM analysis, SLC7A11 expression was significantly associated with AUC for 23 compounds after false discovery rate correction, including 9 sensitivity-associated and 14 resistance-associated hits. Among pathway-relevant compounds, Erastin showed a significant positive association with SLC7A11 expression (n = 388, β = 0.0085, FDR = 0.0358), indicating higher AUC values in models with higher SLC7A11 expression rather than increased sensitivity. **Conclusion:** SLC7A11 is strongly upregulated in hepatocellular carcinoma and represents an independent marker of poor prognosis. Pharmacogenomic screening indicates that SLC7A11 expression is associated with broader drug-response patterns; however, transcript-level SLC7A11 alone does not indicate increased sensitivity to Erastin.

Keywords: SLC7A11; Ferroptosis; Hepatocellular carcinoma; Pharmacogenomics; DepMap PRISM



PAGET'S DISEASE OR BONE METASTASIS? THE PIVOTAL ROLE OF ADVANCED IMAGING IN PROSTATE CANCER DIAGNOSIS

Fatjona Kraja

Surgery Department, Faculty of Medicine, University of Medicine Tirana

Oncology Clinic, University Hospital Center Mother Teresa, Tirana, Albania

Background: Differentiating benign skeletal conditions from malignant involvement is essential in prostate cancer (PCa) management. Paget's disease of bone (PDB) can closely mimic PCa bone metastases, with overlapping symptoms such as bone pain, imaging abnormalities, and elevated bone turnover markers, potentially leading to misdiagnosis and inappropriate treatment.

Methods: A comparative review evaluated clinical features, multimodality imaging (X-ray, bone scintigraphy, CT, MRI, and PSMA PET/CT), and biochemical markers including alkaline phosphatase (ALP) and prostate-specific antigen (PSA).

Findings: PDB is often asymptomatic but may present with localized pain, deformities, and fracture risk, whereas PCa bone metastases typically cause diffuse pain and complications such as pathological fractures and spinal cord compression. Imaging is central to differentiation: PDB demonstrates cortical thickening, bone expansion, and "cotton wool" changes, with intense, well-demarcated uptake on bone scans. In contrast, PCa metastases appear as multiple irregular sclerotic lesions with diffuse uptake. CT/MRI show preserved cortex in PDB versus cortical destruction and marrow infiltration in metastases. Although ALP may be elevated in both, PSA remains a key discriminator. Serum calcium is usually normal in PDB but may increase in advanced metastatic disease. Importantly, PSMA PET/CT has emerged as a highly sensitive modality for detecting PCa metastases, however, uptake may also occur in PDB, representing a potential diagnostic pitfall that necessitates correlation with morphology and clinical context.

Conclusion: Accurate distinction between PDB and PCa bone metastases requires integrated clinical, biochemical, and imaging assessment. Recognition of characteristic radiologic patterns and appropriate interpretation of PSMA PET findings are essential to avoid misclassification and ensure optimal management.

Keywords: Prostate cancer, Paget's disease of bone, bone metastases, PSMA PET/CT.

References:

1. Stuart H Ralston, et al.Diagnosis and Management of Paget's Disease of Bone in Adults: A Clinical Guideline, Journal of Bone and Mineral Research, 2019.
2. Nasibeh Mohseninia, et al.Bone Metastasis in Prostate Cancer: Bone Scan Versus PET Imaging,Seminars in Nuclear Medicine, 2024.
3. Rendina D, et al. Diagnosis and treatment of Paget's disease of bone: position paper from the Italian Society of Osteoporosis, Mineral Metabolism and Skeletal Diseases (SIOMMMS). J Endocrinol Invest. 2024.
4. Oflas M, et al. Paget's Disease Mimicking Prostate Cancer Metastasis with ^{68}Ga-PSMA PET/CT. Mol Imaging Radionucl Ther. 2024

DETERMINANTS OF QUALITY OF LIFE AFTER CANCER DIAGNOSIS IN ALBANIA: A PROSPECTIVE COHORT STUDY

Fatjona Kraja

Faculty of Medicine, University of Medicine Tirana

Bledar Kraja

University Hospital Center "Mother Teresa", Tirana, Albania

Background

A cancer diagnosis represents a critical and often distressing period, characterized by significant psychological burden and symptom distress, with early impacts on patients' quality of life (QoL). Understanding short-term QoL trajectories and their determinants is essential for informing supportive care strategies and optimizing early oncologic management.

Methods

This prospective cohort study included 300 adult patients with newly diagnosed malignancies at the national oncology center. QoL was assessed using the EORTC QLQ-C30 questionnaire at diagnosis and at three months. Changes in global health status, functional domains, and symptom scales were evaluated. Within-patient differences were analyzed using paired statistical tests, and associations between QoL changes and sociodemographic and clinical variables were explored across subgroups.

Results

At three months, patients demonstrated a significant improvement in overall perceived health compared with baseline. Emotional functioning showed the most pronounced recovery, while changes in physical, role, cognitive, and social functioning were more modest and did not reach statistical significance. Symptom burden declined consistently, with notable reductions in pain, insomnia, dyspnea, and financial difficulties related to cancer. QoL improvements were not uniform across the cohort. Greater gains were observed among patients aged 61–70 years, those who were employed, individuals residing in urban areas, and patients with higher educational levels. From a clinical perspective, improvements in global health status were particularly evident among patients with gastrointestinal, genitourinary, gynecological, and skin cancers. Favorable QoL trajectories were also associated with localized disease, absence of metastases, and treatment with curative intent, especially surgical management.

Conclusions

The first three months after cancer diagnosis show improved emotional well-being and overall quality of life, with reduced symptoms, highlighting early patient adaptation and the need for integrated psychosocial and supportive care.

Keywords

quality of life, oncology, early outcomes, symptom burden

PROSTATE CANCER IN A REAL-WORLD COHORT: CLINICAL CHARACTERISTICS AND PROGNOSTIC DETERMINANTS

Fatjona Kraja

Faculty of Medicine, University of Medicine Tirana, Surgery Department, Tirana, Albania

University Hospital Center "Mother Teresa", Oncology Service, , Tirana, Albania

Aurel Janko

Faculty of Medicine, University of Medicine Tirana, Surgery Department, Tirana, Albania

University Hospital Center "Mother Teresa", Urology Service, Tirana, Albania

Erald Karaull

University Hospital Center "Mother Teresa", Oncology Service, , Tirana, Albania

Rezart Xhani

Faculty of Medicine, University of Medicine Tirana, Surgery Department, Tirana, Albania

University Hospital Center "Mother Teresa", Urology Service, Tirana, Albania

Introduction

Data on prostate cancer in Albania remain scarce. This study aimed to evaluate the demographic and clinical characteristics of patients with prostate cancer and to identify prognostic factors associated with disease progression and progression-free survival (PFS).

Materials and Methods

This retrospective study included 600 patients with histologically confirmed prostate adenocarcinoma. Progression-free survival was estimated using the Kaplan–Meier method, and potential prognostic factors were analyzed using Cox proportional hazards regression models.

Results

The mean age at diagnosis was 72.1 ± 7.1 years, with the majority of patients (85.3%) aged over 65 years. Most cases were diagnosed de novo (86%) and at advanced clinical stages (stage III–IV in 87.5% of patients). High-grade disease was prevalent, with ISUP grade 4–5 tumors observed in 49.6% of cases, and bone metastases present in 51%. A significant association was identified between higher ISUP grade and advanced TNM stage ($r = 0.279$, $p < 0.001$). The median progression-free survival was 3.0 years. On multivariate analysis, advanced clinical stage (HR = 2.052, $p < 0.001$) and absence of surgical treatment (HR = 2.549, $p = 0.001$) were independently associated with an increased risk of disease progression.

Conclusions

Prostate cancer in Albania is frequently diagnosed at advanced stages and with high-grade histology. Clinical stage and surgical management emerged as the most significant independent predictors of progression-free survival. These findings underscore the need for improved early detection strategies and optimized multidisciplinary management to enhance patient outcomes.

Key words: Prostate cancer, progression-free survival, prognostic determinants.

DIETARY GUANOSINE MONOPHOSPHATE SUPPLEMENTATION EFFECTS ON GROWTH, BLOOD CHEMISTRY, STRESS TOLERANCE, AND DISEASE RESISTANCE OF STINGING CATFISH *Heteropneustes fossilis*

Shahir Chowdhury

Department of Aquaculture, Faculty of Fisheries, Sylhet Agricultural University, Sylhet-3100, Bangladesh

Tanwi Dey

Department of Aquaculture, Faculty of Fisheries, Sylhet Agricultural University, Sylhet-3100, Bangladesh

Md. Sakhawat Hossain

Department of Aquaculture, Faculty of Fisheries, Sylhet Agricultural University, Sylhet-3100, Bangladesh

ABSTRACT

Functional supplement guanosine monophosphate (GMP) dietary inclusion effects have been evaluated in stinging catfish *Heteropneustes fossilis* through a 90-day feeding trial. Experimental fish (35/tank) with an initial weight of 5.0 g were fed with graded levels of GMP 0, 0.05, 0.1, 0.2, and 0.4% for diet groups D1 (control), D2, D3, D4, and D5, respectively, in triplicate. Fish fed a D3 diet showed significantly higher final body weight compared to D1 and D5; however, growth performances of fish on the D3 diet didn't differ significantly from D2 and D4 diets. Fish fed D2 to D4 diets showed significantly improved feed utilization performances. Plasma glucose and BUN levels significantly reduced in the D3 group. No influence of diet was observed on cholesterol and AST levels in fish; however, these values increased in treatment diets with higher inclusion levels. Triglyceride levels in fish were significantly higher in D4 and D5 diets compared to control. Higher supplementation at the 0.4% level has negatively influenced ALT in fish. Fish fed D5 diets had significantly higher protein and ALT content than the control, with other groups showing intermediate values. After 15 days of *Aeromonas hydrophila* challenge, fish fed GMP-supplemented D3 to D5 diets had significantly higher survival, while the control group had the lowest. In the salinity stress test, D4-fed fish had a significantly longer lethal time 50 (LT50) than the control, with other groups showing intermediate values. In conclusion, 0.1–0.2% dietary GMP is optimal for enhancing stinging catfish growth and health.

Keywords: guanosine monophosphate, stinging catfish, salinity stress, infection, blood chemistry

STRESS AND ACADEMIC PRESSURE ON STUDENT MENTAL HEALTH

Munevver Pazharbek

Saken seifullin kazakh agro-technical university, ORCID ID: 0009-0002-5356-7302

ABSTRACT

Academic stress and pressure have become increasingly important concerns in modern education systems, significantly affecting student mental health, motivation, and overall well-being. Students are often exposed to high expectations from schools, families, and society, including performance-based evaluations, competitive examinations, and heavy workloads. While moderate stress can sometimes improve motivation and focus, chronic academic pressure may lead to anxiety, depression, burnout, sleep disturbances, and reduced academic performance. Contributing factors include intensive grading systems, comparison-based learning environments, limited emotional support, and insufficient coping strategies among students. In many cases, students struggle to balance academic demands with rest, leisure, and social life, which further intensifies psychological strain. Digital technologies and constant connectivity may also increase pressure through social comparison and reduced recovery time. Educational systems are increasingly recognizing the importance of mental health support through counseling services, stress management programs, curriculum flexibility, and positive learning environments. Mindfulness training, time management education, and supportive teacher-student relationships can help reduce stress levels and improve resilience. However, challenges remain, including stigma around mental health, lack of access to psychological support, and deeply rooted academic competition cultures. Addressing academic stress requires a balanced approach that values both academic achievement and student well-being. Overall, reducing excessive academic pressure can improve mental health outcomes, enhance learning efficiency, and promote healthier development in students. Continued research and policy reform are essential for creating supportive and sustainable educational environments.

Keywords: academic stress, student mental health, anxiety, burnout, education pressure, well-being

POLYCYSTIC OVARY SYNDROME (PCOS) IN YOUNG WOMEN: AWARENESS AND MANAGEMENT

Munevver Pazharbek

Saken seifullin kazakh agro-technical university, ORCID ID: 0009-0002-5356-7302

ABSTRACT

Polycystic Ovary Syndrome (PCOS) is one of the most common hormonal disorders affecting young women, with significant implications for reproductive health, metabolic function, and emotional well-being. It often develops during adolescence or early adulthood and may present with irregular menstrual cycles, acne, excessive hair growth, weight changes, and difficulties related to ovulation. Despite its high prevalence, PCOS is frequently underdiagnosed or diagnosed late due to variable symptoms, limited awareness, and misconceptions that menstrual irregularities are always a normal part of youth. Early recognition and appropriate management are essential for improving long-term health outcomes and quality of life. Contemporary approaches to PCOS management emphasize individualized care that combines medical treatment, lifestyle interventions, and psychological support. Healthy nutrition, regular physical activity, adequate sleep, and stress reduction can improve insulin sensitivity, hormonal balance, and symptom control. Medical treatments may include hormonal therapy to regulate menstrual cycles, medications to improve insulin resistance, and targeted therapies for acne or excessive hair growth, depending on patient needs and physician guidance. Regular monitoring is important because PCOS is associated with increased risks of type 2 diabetes, cardiovascular complications, infertility, and mental health challenges such as anxiety and depression. Education and awareness programs can help young women recognize symptoms earlier, seek medical advice promptly, and reduce stigma surrounding reproductive and hormonal health. Schools, universities, and healthcare systems can play an important role by promoting accessible health information and supportive care services. Despite progress, challenges remain, including inconsistent diagnostic criteria, unequal access to specialists, social stigma, and lack of awareness in many communities. Overall, improving awareness and management of PCOS can enhance physical health, emotional well-being, and future reproductive outcomes. Continued research, early screening, and patient-centered healthcare strategies are essential for better support of young women living with PCOS. Greater understanding of PCOS represents an important step toward more equitable and effective women's healthcare worldwide.

Keywords: PCOS, young women, hormonal health, menstrual irregularity, insulin resistance, women's health

SLEEP DEPRIVATION AND ITS EFFECTS ON ADOLESCENT HEALTH

Munevver Pazharbek

Saken seifullin kazakh agro-technical university, ORCID ID: 0009-0002-5356-7302

ABSTRACT

Sleep deprivation is a growing public health issue among adolescents, with significant effects on physical health, cognitive performance, emotional stability, and academic achievement. Adolescence is a critical developmental period requiring sufficient sleep for brain maturation, memory consolidation, and hormonal regulation. However, modern lifestyles, increased academic workload, excessive screen time, early school start times, and social media use have contributed to widespread sleep insufficiency in this age group. Chronic lack of sleep can lead to reduced concentration, impaired learning, mood disturbances, irritability, weakened immune function, and increased risk of anxiety and depression. It may also negatively affect metabolic health, increasing the risk of obesity and long-term cardiovascular problems. Sleep deprivation further impacts decision-making abilities and reaction times, raising safety concerns in daily activities. Educational and healthcare systems are increasingly addressing this issue through awareness programs, sleep hygiene education, and discussions about school schedule adjustments. Encouraging consistent sleep routines, limiting nighttime screen exposure, and promoting healthy lifestyle habits are important preventive strategies. Despite growing awareness, challenges remain, including academic pressure, cultural undervaluing of sleep, and technology dependence among adolescents. Overall, adequate sleep is essential for healthy adolescent development, and addressing sleep deprivation can significantly improve mental health, academic success, and long-term well-being. Continued research and public health interventions are necessary to promote healthier sleep behaviors in young populations.

Keywords: sleep deprivation, adolescents, mental health, academic performance, circadian rhythm, sleep hygiene

VACCINE HESITANCY AND ITS IMPACT ON PUBLIC HEALTH

Munevver Pazharbek

Saken seifullin kazakh agro-technical university, ORCID ID: 0009-0002-5356-7302

ABSTRACT

Vaccination is one of the most effective public health interventions in modern history, essential for preventing infectious diseases, reducing mortality, and protecting communities worldwide. However, vaccine hesitancy—the delay in acceptance or refusal of vaccines despite availability—has become a growing challenge for healthcare systems. This issue is influenced by multiple factors, including misinformation, distrust in institutions, cultural beliefs, fear of side effects, limited health literacy, and unequal access to medical services. Traditionally, immunization programs achieved high coverage through public campaigns, school requirements, and trust in healthcare professionals. In recent years, however, the rapid spread of false information through digital media has significantly increased uncertainty and skepticism regarding vaccine safety and effectiveness. Vaccine hesitancy can lead to declining immunization rates, resulting in outbreaks of preventable diseases such as measles, pertussis, and influenza. Reduced vaccine uptake also weakens herd immunity, placing vulnerable populations—including infants, elderly individuals, and immunocompromised patients—at greater risk. In addition, outbreaks create economic burdens through increased healthcare costs, hospitalization, workforce disruption, and emergency response measures. Public health systems increasingly address hesitancy through evidence-based communication, community engagement, transparent safety monitoring, and partnerships with trusted healthcare providers. Educational campaigns tailored to cultural and social contexts can improve understanding and confidence in vaccination. Healthcare professionals play a particularly important role, as recommendations from trusted clinicians strongly influence vaccine acceptance. Digital strategies, including monitoring misinformation trends and promoting reliable health information online, are also becoming essential. Despite these efforts, challenges remain, including political polarization, historical mistrust, unequal healthcare access, and rapidly changing information environments. Overall, vaccine hesitancy threatens disease prevention efforts, increases public health risks, and undermines progress made through immunization programs. Continued research, effective communication, and equitable healthcare policies are crucial for strengthening vaccine confidence and protecting population health. Addressing vaccine hesitancy responsibly and compassionately is essential for resilient healthcare systems and healthier societies worldwide.

Keywords: vaccine hesitancy, public health, immunization, misinformation, herd immunity, disease prevention

VITAMIN D DEFICIENCY AS A PUBLIC HEALTH ISSUE

Munevver Pazharbek

Saken seifullin kazakh agro-technical university, ORCID ID: 0009-0002-5356-7302

Abstract

Vitamin D deficiency has emerged as a significant public health concern worldwide, affecting individuals of all ages and contributing to a wide range of health problems. Vitamin D plays a crucial role in calcium absorption, bone mineralization, immune function, and overall metabolic health. Traditionally, it has been obtained through sunlight exposure, certain foods, and dietary supplements. However, modern lifestyles characterized by increased indoor activity, urbanization, limited sun exposure, air pollution, and inadequate dietary intake have contributed to rising deficiency rates in many populations. Certain groups, including children, adolescents, older adults, pregnant women, and individuals living in regions with limited sunlight, may be at higher risk. Inadequate vitamin D levels can lead to weakened bones, rickets in children, osteomalacia in adults, increased fracture risk, muscle weakness, and impaired immune responses. Emerging research also suggests associations between vitamin D deficiency and chronic diseases, although these relationships continue to be studied. Public health systems increasingly address this issue through nutritional education, food fortification programs, screening of high-risk groups, and evidence-based supplementation strategies. Encouraging safe sun exposure, balanced diets including vitamin D–rich foods, and regular health assessments can improve prevention and early management. Healthcare professionals play an important role in identifying symptoms, recommending testing when appropriate, and guiding individualized treatment. Despite these efforts, challenges remain, including lack of awareness, unequal healthcare access, socioeconomic disparities, and inconsistent supplementation practices. Misuse of supplements without medical guidance may also create health risks. Overall, vitamin D deficiency can reduce quality of life, increase disease burden, and place pressure on healthcare systems if left unaddressed. Continued research, preventive policies, and accessible health education are essential for improving population vitamin D status and long-term well-being. Addressing vitamin D deficiency responsibly represents an important step toward stronger bones, healthier communities, and more effective preventive healthcare worldwide.

Keywords: vitamin D deficiency, public health, bone health, nutrition, supplementation, preventive medicine

LONG-TERM SURVİVAL İN A 47-YEAR-OLD GLİOBLASTOMA PATİENT WİTH MULTİPLE RECURRENCES: A CASE REPORT

Oumaima Bouchra

Laboratory of Cellular and Molecular Pathology, Faculty of Medicine and Pharmacy, Hassan II University of Casablanca, Casablanca, Morocco

Pathology Department, University Hospital Ibn Rochd, Casablanca, Morocco

Amina Essalihi

Laboratory of Cellular and Molecular Pathology, Faculty of Medicine and Pharmacy, Hassan II University of Casablanca, Casablanca, Morocco

Pathology Department, University Hospital Ibn Rochd, Casablanca, Morocco

Soukaina Barigou

Pathology Department, University Hospital Ibn Rochd, Casablanca, Morocco

Zineb Khadrouf

Laboratory of Immunology and Biodiversity, Faculty of Sciences, Ain Chock, Hassan II University of Casablanca, Casablanca, Morocco

Khadija Khadiri

Laboratory of Immunology and Biodiversity, Faculty of Sciences, Ain Chock, Hassan II University of Casablanca, Casablanca, Morocco

Mehdi Karkouri

Laboratory of Cellular and Molecular Pathology, Faculty of Medicine and Pharmacy, Hassan II University of Casablanca, Casablanca, Morocco

Pathology Department, University Hospital Ibn Rochd, Casablanca, Morocco

ABSTRACT

Background: Glioblastoma (GBM), IDH-wildtype, is the most aggressive primary brain malignancy in adults, with a median overall survival of 12–15 months. Despite maximal safe resection and the Stupp protocol, recurrence is nearly inevitable within the first year, and reports of long-term survivors experiencing multiple recurrences remain rare. The objective of this study is to describe a glioblastoma case with three recurrences, multi-compartmental tumor spread, and survival exceeding 30 months, illustrating the histopathological evolution and the individualized multimodal therapeutic approach.

Methods: Clinical, histopathological, and follow-up data were retrospectively collected from medical records at the Oncology and anatomic pathology Departments of Ibn Rochd University Hospital, Casablanca. Tumor specimens from the initial diagnosis and successive recurrences were analyzed using hematoxylin–eosin staining and immunohistochemistry (GFAP, Olig2, IDH1 R132H, ATRX, p53). Tumor classification followed the 2021 WHO Classification of CNS Tumors.

Case presentation: A 47-year-old male with a family history of cancer presented with a right frontal cystic lesion and signs of intracranial hypertension. Histopathology and immunohistochemistry confirmed glioblastoma. Following gross total resection and the Stupp protocol, three recurrences occurred at <3 weeks, 2 months, and 27 months, involving both cerebral hemispheres and the posterior fossa. Pathology revealed progressive pseudopalisading necrosis, microvascular proliferation, and hemorrhagic remodeling, while the GBM phenotype remained stable. Salvage therapy with bevacizumab–irinotecan was well tolerated. At last follow-up (>30 months post-diagnosis), the patient remained alive with preserved functional status.

Conclusion: This case illustrates the biological heterogeneity of glioblastoma and supports individualized multimodal management as a contributor to extended survival in patients.

ALTERED LUNG MYCOBIOME REFLECTS A TUMOR-ASSOCIATED MICROENVIRONMENT REMODELING IN LUNG CANCER

Muchamad Dafip

Study Program of Doctor in Biotechnology, Postgraduate School, Universitas Gadjah Mada, Yogyakarta, 55284, Indonesia.

Ali Zainal Abidin

Department of Molecular Medicine, Master's Program in Biomedical Sciences, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada, Yogyakarta, Indonesia.
Division of Surgical Oncology, Department of Surgery, Faculty of Medicine, Public Health, and Nursing, Universitas Gadjah Mada/ Dr Sardjito General Hospital, Yogyakarta, Indonesia.

Nina Sakina Lessy

Department of Molecular Medicine, Master's Program in Biomedical Sciences, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada, Yogyakarta, Indonesia.

Alik Sander

Department of Molecular Medicine, Master's Program in Biomedical Sciences, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada, Yogyakarta, Indonesia.

Aprilia Indra Kartika

Study Program of Doctor in Biotechnology, Postgraduate School, Universitas Gadjah Mada, Yogyakarta, 55284, Indonesia

Didik Setyo Hariyanto

Department of Anatomical Pathology, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada/Dr. Sardjito General Hospital, Yogyakarta, Indonesia

Suci Widhianti

Department of Dermatology and Venereology, Faculty of Medicine, Universitas Sebelas Maret/Dr. Moewardi General Hospital, Surakarta, Indonesia

Dewi Kartikawati Paramita

Department of Histology and Cell Biology, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada, Yogyakarta, Indonesia

Sofia Mubarika Haryana

Department of Histology and Cell Biology, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada, Yogyakarta, Indonesia.
Precision Oncology-Based Omics Research Collaboration Center (PKR-PrOmics), Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada, Yogyakarta, Indonesia.

Tri Wibawa

Department of Microbiology, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada, Yogyakarta, Indonesia.

ABSTRACT

In lung cancer, the immunosuppressive and inflammatory tumor microenvironment may induce dysbiosis of the pulmonary mycobiome, including the expansion of opportunistic fungi. However, bronchoalveolar lavage fluid (BALF)-based studies comparing mycobiome profiles between lung cancer types and chronic pulmonary inflammation remain limited. This study aimed to characterize fungal community composition, ecological interactions, and candidate discriminatory taxa in patients with lung cancer. This study included 15 BALF samples from five patients with non-small cell lung cancer (NSCLC), five with small-cell lung cancer (SCLC), and five with non-infectious interstitial lung

disease (ILD) as clinical controls. BALF samples were collected during standard diagnostic procedures and centrifuged at 8,000 × g for 15 min at 4 °C. The resulting pellets were used for DNA isolation. Fungal communities were profiled using full internal transcribed spacer (ITS) region-based amplicon sequencing on the Illumina MiSeq 300PE platform, followed by QIIME2-based bioinformatics and ecological statistical analyses. Alpha diversity indices were comparable among groups and showed no significant differences ($p \geq 0.050$). In contrast, Bray–Curtis beta diversity revealed significant compositional separation between lung cancer and ILD groups ($p \leq 0.050$). The fungal community was dominated by Ascomycota, followed by Basidiomycota and Mucoromycota. At the species level, NSCLC was characterized by Phialophora geniculata, Sterigmatomyces halophilus, and Candida blankii; SCLC by Kluyveromyces marxianus, Acremonium charticola, and C. albicans; and ILD by Syncephalastrum monosporum, Remersonia thermophila, and Xeromyces bisporus. Co-occurrence analysis showed group-specific interaction patterns, with Rhizopus microsporus, C. albicans, and Chaetomiaceae sp. emerging as central nodes in NSCLC, SCLC, and ILD, respectively. These findings suggest that lung cancer may drive local fungal microecological remodeling, potentially influencing the homeostasis of inflammation and immunosuppression. Further longitudinal studies are needed to validate these key fungal taxa as BALF-based signatures for distinguishing malignancy from chronic pulmonary inflammation and supporting precision oncology.

Keywords: bronchoalveolar lavage fluid; lung cancer; mycobiome; fungal dysbiosis; tumor microenvironment.

INCLUSION EFFECTS OF GUANOSINE MONOPHOSPHATE IN FISHMEAL-REPLACED ALTERNATIVE PROTEIN DIETS ON THE GROWTH AND HEALTH OF CLIMBING PERCH (*Anabas testudineus*)

Habiba Khan Ilham

Department of Aquaculture, Faculty of Fisheries, Sylhet Agricultural University, Sylhet-3100, Bangladesh

Tanwi Dey

Department of Aquaculture, Faculty of Fisheries, Sylhet Agricultural University, Sylhet-3100, Bangladesh

MD. Sakhawat Hossain

Department of Aquaculture, Faculty of Fisheries, Sylhet Agricultural University, Sylhet-3100, Bangladesh

ABSTRACT

The application of dietary functional supplements in high alternative protein-based diets has received great attention to eliminate or reduce the negative effects of high alternative protein in aquafeed. Recently, guanosine monophosphate (GMP), a purine nucleotide, received great attention as a functional supplement in aquafeed. No studies have examined GMP supplementation in high alternative protein diets for climbing perch (*Anabas testudineus*). This 60-day trial assessed the effects of fully replacing fishmeal (FM) with soybean meal (SBM) plus GMP supplementation, on growth, blood chemistry, immunity, and stress resistance in climbing perch. FM protein in the control diet (D1) was replaced with 33.3% (D2), 66.7% (D3), and 100% (D4) SBM protein, with 0.2% GMP added to each replacement group. Four iso-nitrogenous diets were randomly assigned to triplicate fish groups (3.7 g). Significantly higher growth and feed utilization performance was observed in D2 while other diets showed comparable growth. Plasma Cholesterol content was significantly higher and lower in D1 and D4 diet group respectively. Total protein content showed the opposite trend. D2 and D3 diet had favorable biochemical responses. Whole body composition and amino acid retention improved at moderate FM replacement levels (D2 and D3). Fish fed D2 diet exhibited significantly higher peroxidase activity than the control and diet D3 also showed improved activity. Salinity stress tolerance improved across the diets with significantly higher LT50 values in diet D2 fed group. In conclusion, FM protein could be replaced ≤66.7% by SBM protein with GMP supplementation in diets for climbing perch.

Keywords: Guanosine monophosphate, Climbing perch, Salinity stress, Growth, Blood chemistry

THE ROLE OF MODERN BIOMETRY IN IOL CALCULATOON ON PATOENTS WOTH DOWN SYNDROME

Cușnir Magdalena

Moldovan State University of Medicine and Pharmacy „N. Testemițanu" Republic of Moldova

Şcerbatiuc Cristina

Moldovan State University of Medicine and Pharmacy „N. Testemițanu" Republic of Moldova, Republican Clinical Hospital „Timofei Moșneaga" Republic of Moldova

ABSTRACT

Introduction: Patients with Down syndrome have ocular characteristics relevant to cataract surgery, including short axial length, shallow anterior chambers, and a high prevalence of hyperopia. These characteristics affect the accuracy of intraocular lens (IOL) power calculations and increase the risk of postoperative refractive errors. Modern optical biometry and new generation formulae, have been developed to improve the predictability of refractive outcomes.

Materials and methods: The analysis was supported by data from studies published in the last 5 years, identified in medical databases: PubMed, ScienceDirect and SpringerLink. Comparative studies on the performance of IOL calculation formulas and the accuracy of optical biometry versus ultrasound were included.

Results: Biometric measurements obtained by optical interferometry (swept-source OCT) and A-scan ultrasound were analyzed. IOL power was calculated using the Barrett Universal II, SRK/T and Hoffer Q formulas. Refractive accuracy was assessed by the prediction error (the difference between the postoperative and the estimated refraction), expressed as mean error and mean absolute error at 1 and 3 months postoperatively. Optical biometry demonstrated superior reproducibility compared with ultrasound, but was limited by patient cooperation in some cases. The Barrett Universal II formula showed the lowest mean absolute error, especially in eyes with axial length <22 mm, followed by the Hoffer Q. The SRK/T formula showed greater variation in prediction error in short eyes.

Conclusions: Modern optical biometry significantly improves the accuracy of IOL calculation in patients with Down syndrome, but does not completely eliminate the risk of refractive errors. The Barrett Universal II formula offers the best predictability in most cases, especially in hyperopic eyes and eyes with short axial length. The choice of formula should be individualized, and the combined use of biometric methods remains essential in cases with limited cooperation.

Keywords: Down syndrome, cataract, ocular biometry

DOPPLER ULTRASONOGRAPHY AND MULTI-OMICS PROFILING REVEAL THE THERAPEUTIC RESPONSE OF QICHUAN JINGNAONING FORMULA IN RATS WITH VERTEBRAL ARTERY-TYPE CERVICAL SPONDYLOSIS

Qinfeng Zhou

Science and Technology Experimental Center, Shanghai University of Traditional Chinese Medicine, Shanghai 201203, China

ABSTRACT

Introduction: Vertebral artery-type cervical spondylosis (CSA) is associated with vertebrobasilar hemodynamic disturbance and local cervical inflammatory injury. Qichuan Jingnaoning Formula (QCJNN) is a traditional herbal formula used for CSA; however, its pharmacological basis and therapeutic monitoring indicators remain insufficiently understood.

Methods: A rat model of CSA was established by combining dynamic imbalance induction with local sclerosing-agent injection. Doppler ultrasonography was used to assess vertebral artery blood flow, while histopathological examination and behavioral tests were performed to evaluate tissue injury and functional impairment. To identify mechanism-related indicators, RNA sequencing, targeted neurotransmitter metabolomics, and bicuculline, a GABA_A receptor antagonist, were applied.

Results: CSA rats showed reduced blood flow velocity in the compressed vertebral artery and disrupted left–right vertebral artery perfusion balance. QCJNN improved vertebral artery hemodynamics, particularly left vertebral artery blood flow, without inducing obvious abnormal changes in right vertebral artery perfusion. Histopathological analysis further showed that QCJNN attenuated cervical inflammatory infiltration, vascular wall injury, and local tissue damage, accompanied by improvement in selected behavioral parameters. Transcriptomic analysis indicated that the GABAergic synapse pathway was associated with QCJNN treatment. Targeted metabolomics suggested QCJNN-related recovery of local GABA levels. Bicuculline partially weakened QCJNN-associated changes in local GABA, selected working-memory-related parameters, and NO/eNOS-related vascular indices, supporting the potential involvement of GABA_A receptor-related signaling.

Conclusions: QCJNN alleviated vertebral artery hemodynamic impairment and cervical inflammatory injury in CSA rats. Doppler ultrasonography combined with transcriptomic and metabolomic profiling may provide useful multimodal indicators for evaluating QCJNN response and its potential GABAergic–endothelial mechanism.

Keywords: cervical spondylosis; Doppler ultrasonography, vertebral artery hemodynamics; Qichuan Jingnaoning Formula, RNA sequencing, metabolomics; GABA_A receptor

IDLE THOUGHTS MANAGEMENT SCALE

Muhammad Safi Aslam
Department of Applied Psychology, School of Professional Psychology, University of Management and Technology, Lahore, Pakistan, ORCID: 0009-0003-9697-3340
Dr. Shahnila Tariq
Department of Applied Psychology, School of Professional Psychology, University of Management and Technology, Lahore
Anum Arif Butt
Fatima Jinnah Graduate College (W), Chuna Mandi, Lahore

ABSTRACT
The term “idle thoughts” refers to those recurring thoughts that often arise when a person is usually doing nothing, such as waiting for something etc. These thoughts have been reported to often adopt the shape of a stream, one thought often leading to another, and a person finds himself detracted and lost in a pool of random thoughts within no time. Moreover, these thoughts may also become disturbing some of the times, causing stress, panic, anxiety and even depression. The current research endeavored at constructing a scale which could measure how these idle thoughts are managed by the thinker. Idle Thoughts Management Scale comprises of twenty-one items and five subscales: Engaging Thoughts, Strategize and Plan, Diverting through social media, Diverting through book reading and Prayers for fulfillment of thoughts. The tool has well established psychometric properties, a considerable internal consistency reliability and a significant construct validity. It can be utilized for further research especially in Cognitive Psychology.
Keywords: Idle thoughts, recurring thoughts, random thoughts

AUTOMATED KIDNEY TUMOR CLASSIFICATION FROM CT IMAGES WITH GRAD-CAM VISUALIZATION AND DEEP LEARNING NEURAL NETWORKS

E. Mukesh

Student, EEE Dept, Dr. M.G.R. Educational and Research Institute, Chennai, India

S. Tharun Krishnan

Student, EEE Dept, Dr. M.G.R. Educational and Research Institute, Chennai, India

K. Sujatha

Professor, EEE Dept, Dr. M.G.R. Educational and Research Institute, Chennai, India.

N.P.G. Bhavani

Professor, ECE Department, Saveetha Institute of Medical and Technical Sciences, India.

Tatireddy Omsai Reddy

Student, ECE Department, Saveetha Institute of Medical and Technical Sciences, India

ABSTRACT

Kidney tumors pose significant diagnostic challenges due to their heterogeneous appearances in CT imaging, often leading to subjective interpretations and delayed interventions. This study introduces an automated deep learning framework for classifying kidney tumors from CT images, leveraging convolutional neural networks (CNNs) enhanced with Grad-CAM visualization for interpretable predictions. We utilize a dataset of 1,200 annotated CT slices, preprocessed via histogram equalization and data augmentation to address class imbalance. A ResNet-50 backbone, fine-tuned with transfer learning, achieves 94.2% accuracy, 92.5% sensitivity, and 95.8% specificity in distinguishing benign, malignant, and cystic tumors, outperforming baseline models like VGG-16 by 8%. Grad-CAM heatmaps provide pixel-level explanations, highlighting tumor boundaries and enhancing clinical trust. Our approach demonstrates robust generalization on an external validation set (AUC: 0.97), paving the way for AI-assisted radiology workflows in oncology.

Keywords: Kidney tumor, Deep learning, CT images, Grad-CAM visualization, VGG-16

TOPOGRAPHICAL AND MORPHOMETRIC EVALUATION OF THE FEMORAL NERVE AND ITS ANATOMICAL ASSOCIATION WITH THE FEMORAL VESSELS

Zdravka Harizanova

Department of Anatomy, Histology and Embryology, Faculty of Medicine, Medical University of Plovdiv, 15A Vassil Aprilov Blvd., 4002, Bulgaria

Ferihan Popova

Department of Anatomy, Histology and Embryology, Faculty of Medicine, Medical University of Plovdiv, 15A Vassil Aprilov Blvd., 4002, Bulgaria

Sabri Sabri

Department of Anatomy, Histology and Embryology, Faculty of Medicine, Medical University of Plovdiv, 15A Vassil Aprilov Blvd., 4002, Bulgaria

Fanka Gerginska

Department of Anatomy, Histology and Embryology, Faculty of Medicine, Medical University of Plovdiv, 15A Vassil Aprilov Blvd., 4002, Bulgaria

Lilia Grozlekova

Department of Anatomy, Histology and Embryology, Faculty of Medicine, Medical University of Plovdiv, 15A Vassil Aprilov Blvd., 4002, Bulgaria

Zlatizara Todorova

Department of Anatomy, Histology and Embryology, Faculty of Medicine, Medical University of Plovdiv, 15A Vassil Aprilov Blvd., 4002, Bulgaria

Vyara Zaykova

Department of Anatomy, Histology and Embryology, Faculty of Medicine, Medical University of Plovdiv, 15A Vassil Aprilov Blvd., 4002, Bulgaria

Polina Ivanova

Department of Anatomy, Histology and Embryology, Faculty of Medicine, Medical University of Plovdiv, 15A Vassil Aprilov Blvd., 4002, Bulgaria

Atanas Baltadjiev

Department of Anatomy, Histology and Embryology, Faculty of Medicine, Medical University of Plovdiv, 15A Vassil Aprilov Blvd., 4002, Bulgaria

ABSTRACT

Introduction: The femoral triangle represents a region of considerable anatomical and clinical relevance because it contains essential neurovascular components, including the femoral nerve, femoral artery, and femoral vein. Variations in the anatomical arrangement and morphometric features of these structures may increase the likelihood of iatrogenic damage during clinical and surgical procedures.

Aim: This study aimed to perform a comprehensive topographical and morphometric assessment of the femoral nerve within the femoral triangle.

Materials and Methods: Anatomical dissection was carried out on a lower extremity specimen preserved in 10% formalin. The trajectory of the femoral nerve, its morphometric characteristics, and its anatomical relations to the femoral vessels were analyzed. Measurements were obtained using the anterior superior iliac spine and the pubic tubercle as osseous reference landmarks.

Results: The femoral nerve was identified at an average distance of 5.3 cm from the anterior superior iliac spine and 5.5 cm from the pubic tubercle. The mean extent of the femoral nerve trunk within the

femoral triangle before branching was measured at 2.3 cm. Anatomically, the femoral nerve was positioned lateral to the femoral artery, whereas the femoral vein was located medially.

Conclusion: The findings of this investigation expand current understanding of the topographical anatomy and morphometric parameters of the femoral nerve in the femoral triangle. Furthermore, they underline the clinical significance of anatomical variability in the femoral neurovascular region. Such data may be valuable in minimizing the risk of iatrogenic injury during invasive and surgical interventions.

Keywords: femoral triangle, femoral nerve, femoral artery, femoral vein, morphometric analysis

ENTREPRENEURSHIP EDUCATION AS A DRIVER OF VENTURE CREATION INTENTIONS: EVIDENCE FROM OMAN

Dr. Padmalosani Dayalan

Faculty, Department of Economics and Business Administration University of Technology and Applied Sciences, Ibra Sultanate of Oman

Dr. Edukondala Rao Jetti

Faculty, Department of Economics and Business Administration University of Technology and Applied Sciences, Ibra Sultanate of Oman

ABSTRACT

In both developed and developing economies, entrepreneurship has become one of the key pillars for economic growth, innovation and job generation. Over the years, Oman has increased its focus on entrepreneurship and small business development in its economic diversification strategies under the national development plans. Within this framework, higher educational institutions can be seen to play a key role in developing the competences necessary for entrepreneurship and in motivating students towards entrepreneurial pathways. Thus, entrepreneurship education is becoming a significant focus in universities as a means of cultivating entrepreneurial attitudes, improving business skills and cognitive abilities, and reinforcing students' intention to form ventures.

This research explores entrepreneurship education as a factor of venture creation intentions among university students in Oman. This paper uses a multidimensional lens considering various educational, personal and environmental factors that may affect entrepreneurial intentions. The study focuses on the role of entrepreneurial knowledge, entrepreneurial self-efficacy, innovation orientation, risk-taking propensity and perceived institutional support on students' willingness to start new businesses. It will also be explored how entrepreneurship educational input variables influence students to increase their confidence, opportunity recognition abilities and creativity entrepreneurial readiness components.

This study uses a descriptive-survey approach with the questionnaire, as the method of data collection and participants include undergraduate and postgraduate students from various higher education institutions in Oman. Descriptive statistics, correlation analysis and regression methods will be used to examine the data over how much entrepreneurship education predict venture creation intentions. The framework proposed in this research is based on the theories of entrepreneurial intention and seeks to deliver empirical evidence for the effectiveness of entrepreneurship education programmes in regard with the Omani higher education ecosystem.

The study anticipates that: An entrepreneurship education positively influences the student’s entrepreneurial attitude and thus creates a strong influence towards their intent to start a new venture. The result will show entrepreneurship education students more entrepreneurial confidence creativity and self-employment motivation than an education that is little exposure in opportunity based educational learning.

It will add to the existing knowledge on entrepreneurship education and entrepreneurial intentions especially in context of the Gulf and Middle East which have limited empirical studies. Results will have important implications for connecting stakeholders together (policymakers, university administrators and educators) for effective entrepreneurship curricula development, experiential learning opportunities to serve as a national incubation model, and innovation–driven education. Finally, this study seeks to support development of sustainable entrepreneurial ecosystem by engaging youth in formulating effective actionable strategies for business creation that leads towards achieving the long-term economic development objectives of Oman.

EMERGING ROLES OF BIOACTIVE COMPOUNDS IN THE PREVENTION AND MANAGEMENT OF NEUROPATHY

Pooja Rasal

Department of Pharmacology, JES's SND College of Pharmacy, Babhulgaon, Dist. Nashik, India.

Gaurav Kasar

Department of Pharmacology, Divine College of Pharmacy, Satana, Dist. Nashik, India.

ABSTRACT

Neuropathy is a progressive neurological disorder characterized by nerve damage, sensory dysfunction, pain, and impaired motor activity, commonly associated with diabetes, chemotherapy, infections, and neurodegenerative diseases. Conventional therapies mainly provide symptomatic relief and often fail to prevent neuronal degeneration. In recent years, bioactive compounds derived from plants, marine organisms, and functional foods have gained considerable attention for their neuroprotective potential. These compounds, including polyphenols, flavonoids, alkaloids, terpenoids, omega-3 fatty acids, and curcumin, exhibit antioxidant, anti-inflammatory, anti-apoptotic, and neuroregenerative properties. Emerging evidence suggests that bioactive molecules can modulate multiple molecular pathways involved in oxidative stress, mitochondrial dysfunction, neuroinflammation, and axonal degeneration, thereby improving neuronal survival and nerve conduction. Furthermore, advances in nanotechnology and targeted drug delivery systems have enhanced the bioavailability and therapeutic efficacy of several natural compounds in neuropathic conditions. This review highlights the recent advances in the therapeutic applications of bioactive compounds in neuropathy, focusing on their mechanisms of action, preclinical and clinical evidence, and future prospects for developing safer and more effective neuroprotective strategies.

Keywords: Neuropathy, Bioactive Compounds, Neuroprotection, Oxidative Stress, Neuroinflammation

Assessing the Biological Efficiency, Vitamin Profile, and Antioxidant Properties of Summer Mushroom Species

S. M. Rejbanul Islam

Department of Horticulture, Sylhet Agricultural University, Sylhet-3100, Bangladesh.

Jannatul Ferdousi

Department of Horticulture, Sylhet Agricultural University, Sylhet-3100, Bangladesh.

ABSTRACT

Mushrooms are popular edible fungi and functional foods rich in protein, vitamins, and antioxidants. This study aimed to characterize collected germplasm, preserve mycelium, and evaluate growth, yield, nutritional composition, and antioxidant activities of selected mushroom species during the summer season in Sylhet, Bangladesh. Six strains-POP, PO2, and PO10 (*Pleurotus ostreatus*), CO (*Pleurotus citrinopileatus*), CID (*Calocybe indica*), and Reishi (*Ganoderma lucidum*) were collected from the Mushroom Development Institute (MDI). The experiment was conducted from June to October 2025 at Sylhet Agricultural University using a Completely Randomized Design with three replications. Mycelial growth on Potato Dextrose Agar (PDA) showed significant variation: CID had the fastest rate (0.91 cm/day, 100% efficiency), while Reishi was slowest (0.47 cm/day). In substrate cultivation, POP, PO2, PO10, and CO completed spawn run in 16–20 days; CID and Reishi took 20–25 days. CID peaked in biological efficiency (16.89% in first flush). Morphologically, Reishi had longest stipes (up to 23.75 cm) and thickest caps (up to 18.01 mm); PO10 had smallest dimensions. Maximum fruiting bodies occurred in PO2 (13 in first flush). Nutritional compositions: POP richest in B1 (1.41 mg/100g DW), B3 (3.62 mg/100g), B5 (5.46 mg/100g); Reishi in B2 (2.40 mg/100g) and beta-carotene (104.68 mg/100g); PO2 in vitamin C (33.03 mg/100g). Reishi overcome in antioxidants: total phenolic content (2.40 mg GAE/g), flavonoid content (2.50 mg QE/g), DPPH (83.91%), and Fe^{2+} chelating (85.83). Correlation analyses revealed strong positive associations between yield parameters and morphological traits like cap diameter and stipe thickness. While antioxidant capacity was closely linked to phenolic and flavonoid contents. The finding suggested that CID, POP, and PO2 are promising germplasm for summer cultivation due to rapid growth, high yield, nutrition while Reishi is for its higher antioxidant properties. The successful preservation of mycelial cultures at 3°C provides a basis for local spawn production. It is recommended to optimize cultivation protocols for these strains and promote their adoption to support sustainable mushroom farming and improve livelihoods for summer season.

Keywords: Mushroom germplasm, MDI, Biological efficiency, Vitamin B, Yield.

THYROID HORMONE LEVELS AND THEIR ASSOCIATION WITH PLASMA ZINC LEVELS AMONG ADOLESCENT AFGHAN REFUGEES; A CROSS-SECTIONAL STUDY

Dr Saima Shaheen

Demonstrator, Department of Biochemistry, Khyber Girls Medical College, Hayatabad, Peshawar.

Dr Nabila Sher

Professor, Khyber Girls Medical College, Hayatabad, Peshawar

Dr. Kalsoom Tariq

Associate Professor Department of Biochemistry, Khyber Girls Medical College, Hayatabad, Peshawar.

ABSTRACT

Introduction: Thyroid hormones play an important role in the development and maintenance of nearly all tissues. In Pakistan, hypothyroidism and hyperthyroidism prevalence are 4.1% and 5.1%, respectively, and with increasing age, prevalence increases approximately to 10% in adults over 65 years of age. Malnutrition or nutritional deficiencies in the body can be the cause of thyroid disorders. Zinc (Zn) and copper (Cu), have important roles in regulating biological processes, maintaining normal thyroid function, and preventing thyroid diseases.

Objective: The objective of study was to find out levels of the thyroid hormones (TSH, T3 and T4) and its association with plasma zinc levels among adolescents Afghan refugees living in Peshawar, Pakistan.

Methodology:

Study design: Cross-sectional study

Study setting; It was conducted in the experimental Laboratory of Hayatabad Medical Complex, Hayatabad, Peshawar, Khyber Pakhtunkhwa (Pakistan) and University of Nottingham, England.

Subjects: A total of 206 adults from Khazana Afghan Refugee Camp, Peshawar were recruited and demographic details were done using a standard questionnaire.

Methods: We measured the patient's weight and height to calculate body mass index (BMI). Each participant blood sample was taken, so that many indicators could be measured. The concentrations of plasma zinc were measured by Inductively coupled plasma mass spectrometry (ICPMS) ,and TSH, T3, and T4 were done by using cobas e 601 which is a completely automated analyzer that performs immunoassay analysis using electrochemiluminescence (ECL) technology.

Results: Gender was equally divided into 103 females and 103 males with age group of 10-14 was (65.5%) and 15-19 was (34.5%). According to results (99.0%) participants had normal TSH levels, (79.1%) of participants had normal T3 levels, while (78.6%) of participants had normal T4 levels. T3 and T4 was low in (10.7 and 18.4 %) respectively. Serum Zinc levels in majority (65%) of participants had normal zinc levels while 35% of the participants were found to be deficient in zinc. There was significant association between gender and age group p value 0.02. A significant association was found between the gender and T3 levels. Females had more ratio of increased T3 levels. There was significant association between gender and T4 levels. However there was no significant association between thyroid hormones Zinc and other parameters.

Conclusion: This non-significant study did not find a direct relationship between thyroid hormones and zinc levels, there is still evidence to suggest that maintaining adequate zinc levels may be important for proper thyroid function. Further research is needed to fully understand the relationship between these two factors. Keywords; malnutrition, hyperthyroidism, hypothyroidism

Keywords; malnutrition, hyperthyroidism, hypothyroidism

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EFFECTS OF SOIL PHYSICOCHEMICAL PROPERTIES ON DISTRIBUTION AND COMPOSITION OF FUNGAL SPECIES ISOLATED FROM DIFFERENT ECOSYSTEMS OF AMHARA REGION, NORTH WEST ETHIOPIA

Fasika Melese

Department of Biology College of Sciences, Bahir Dar University, P. O. Box: 79, Bahir Dar, Ethiopia

Department of Biology College of Natural and Computational Science Debark University, P. O. Box 90, Debark, Ethiopia

Destaw Damtie

Department of Biology College of Sciences, Bahir Dar University, P. O. Box: 79, Bahir Dar, Ethiopia

Sissay Menkir

Department of Biology College of Sciences, Bahir Dar University, P. O. Box: 79, Bahir Dar, Ethiopia

Mulugeta Kibret

Department of Biology College of Sciences, Bahir Dar University, P. O. Box: 79, Bahir Dar, Ethiopia

ABSTRACT

Background: The aboveground fungal community and its capacity to recycle nutrients can be positively or negatively affected by the soil' s physicochemical characteristics. However, little is known about how soil cover type, soil physical and chemical properties, and soil culturable fungi affect the diversity and composition of soil microbial communities.

Methods: To investigate this, soil samples were collected from eight locations, each with at least 14 subsamples. The researcher' s initial evaluation was used to select locations to capture a range of fungal species. Soil culturable fungi were isolated using the serial dilution method with sterile distilled water, followed by inoculation and incubation at 25-28 ° C for 5- 14 days. Fungi were identified based on macro- and microscopic structures. Soil samples were analyzed for their physical and chemical properties at the Bahir Dar University Laboratory and the Competence Design and Supervision Laboratory Center in Bahir Dar, Ethiopia. The results showed that the soil samples appeared black, red, or light red. The measured soil property ranges were pH from 6. 37 to 7. 7.7; available phosphorus from 9. 17 ppm to 36. 98 ppm; available nitrogen from 18% to 66%; organic carbon from 1. 54% to 7. 09%; water content from 6. 75% to 19. 78%; bulk density from 1 to 1. 57 g/cm ^{3}; and pore space from 6. 47% to 16. 86%. The structural requisition model indicated that organic carbon (3. 68), species richness (0. 097), pH (0. 66), and water content (0. 08) positively influenced the Shannon- Wiener diversity index of soil fungi, while total nitrogen (- 45. 45. 08), available phosphorus (- 0. 05), bulk density (- 1. 04), and soil porosity (- 0. 17) had a negative effect. In conclusion, the physical and chemical properties of soil significantly impact soil microfungi diversity and the composition of microbial communities across different soil ecosystems. Our findings suggest that soils with higher levels of available phosphorus, total nitrogen, water content, and pH tend to harbor fewer fungal species.

Keywords: fungi, composition, ecosystem, soil properties, distribution

ADOPTION OF IMPROVED POSTHARVEST MANAGEMENT PRACTICES DEVELOPED BY THE NIGERIAN STORED PRODUCTS RESEARCH INSTITUTE (NSPRI) AMONG TOMATO MARKETERS IN KWARA STATE, NIGERIA

LIJOKA, Kehinde Osemawe

Department of Agricultural Extension and Rural Development; Federal University of Technology, Minna, Niger State, Nigeria

Y. Muhammed

Department of Agricultural Extension and Rural Development; Federal University of Technology, Minna, Niger State, Nigeria

S. Jibrin

Department of Agricultural Extension and Rural Development; Federal University of Technology, Minna, Niger State, Nigeria

ABSTRACT

This study examined the adoption of improved postharvest management practices developed by the Nigerian Stored Products Research Institute (NSPRI) among tomato marketers in Kwara State, Nigeria. The study specifically assessed respondents' awareness, availability of NSPRI technologies, access to information sources, effectiveness of information dissemination channels, and extent of adoption of improved postharvest practices. A multistage sampling procedure was used to select 229 tomato marketers for the study, while data were collected using structured questionnaires and analysed using descriptive statistics such as frequency counts, percentages, weighted sums, weighted means, and ranking techniques. The findings revealed that 66.8% of the respondents were aware of improved postharvest management practices, with extension agents (53.6%) and market associations (44.4%) serving as the major sources of awareness. Ventilated plastic crates were the most available technology (97.8%), whereas cold chain systems had the least availability (6.1%). About 65.1% of the respondents had access to information on improved postharvest practices, mainly through research institutes, extension agents, fellow marketers, and mass media channels. Extension agents were ranked as the most effective source of information dissemination with a weighted mean score of 2.86. Despite the relatively high awareness and access to information, the overall adoption of NSPRI improved postharvest technologies remained low, as all the technologies recorded weighted mean scores below the adoption benchmark of 3.0. Cold chain systems ranked highest in adoption (WM = 2.75), while ventilated plastic crates ranked least (WM = 1.88). The study concluded that inadequate availability, limited technical support, and poor access to modern storage facilities constrained adoption. The study recommends strengthening extension services, improving access to postharvest technologies, and enhancing training programmes for tomato marketers to reduce postharvest losses and improve marketing efficiency.

Keywords: Adoption; Postharvest, Management; Stored, Tomatoes

NEUROPROTECTIVE EFFECTS OF GREEN TEA EXTRACT ON AGE-RELATED COGNITIVE DECLINE IN A RAT MODEL

Huma Ikram

Neurochemistry and Biochemical Neuropharmacology Research Unit, Department of Biochemistry, University of Karachi, Karachi-75270, Pakistan.

Rumaisa Zakir

Neurochemistry and Biochemical Neuropharmacology Research Unit, Department of Biochemistry, University of Karachi, Karachi-75270, Pakistan.

Darakhshan J. Haleem

Neurochemistry and Biochemical Neuropharmacology Research Unit, Department of Biochemistry, University of Karachi, Karachi-75270, Pakistan.

ABSTRACT

The present study investigated the neuroprotective effects of standardized green tea extract (GTE) against age-related cognitive decline in a rat model. Twenty-four male Albino Wistar rats were divided into young (4 months) and aged (24 months) groups, receiving either water or GTE (30 mg/kg) daily for five weeks. Spatial learning and memory were assessed weekly using Morris water maze (MWM) and novel object recognition (NOR) tests. Hippocampal tissues were analyzed for antioxidant enzymes (superoxide dismutase, catalase, glutathione peroxidase), inflammatory markers (interleukin-6, interleukin-1β), brain-derived neurotrophic factor (BDNF), and monoamine neurotransmitters (serotonin, 5-HIAA). Aged rats exhibited significant cognitive impairments in MWM and NOR tests compared to young controls. Chronic GTE administration significantly improved spatial learning and recognition memory in aged rats from week three onwards. This was accompanied by enhanced antioxidant enzyme activities, reduced pro-inflammatory cytokine levels, increased BDNF expression, and restoration of hippocampal monoamine levels. Our findings demonstrate that GTE exerts multi-target neuroprotective effects, attenuating age-related cognitive decline through antioxidant, anti-inflammatory, and neurochemical mechanisms.

Keywords: green tea, neuroprotection, cognitive decline, aging, rat model, oxidative stress, Morris water maze test, novel object recognition test

WORK CLIMATE AND OCCUPATIONAL FATIGUE IN FURNITURE WORKERS

Ranti Ekasari
Department of Public Health, Universitas Islam Negeri Alauddin Makassar, Sultan Alauddin Street, 92113, Indonesia

Maghfirah Insan Sakinah
Department of Public Health, Universitas Islam Negeri Alauddin Makassar, Sultan Alauddin Street, 92113, Indonesia

Suci Rahmi
Department of Public Health, Universitas Islam Negeri Alauddin Makassar, Sultan Alauddin Street, 92113, Indonesia

Nur Sasmita
Department of Public Health, Universitas Islam Negeri Alauddin Makassar, Sultan Alauddin Street, 92113, Indonesia

Muh. Abdul Wahab
Department of Public Health, Universitas Islam Negeri Alauddin Makassar, Sultan Alauddin Street, 92113, Indonesia

ABSTRACT

One element of the work environment that can impact worker productivity and health is workplace heat, which can cause fatigue. Due to the production process and workplace environmental conditions, the furniture industry is one industry likely exposed to heat. Using an analytical cross-sectional design and a quantitative approach, this study aimed to examine the correlation between work climate and job fatigue among furniture workers in Hertasning, Makassar. Primary data from the Heat Stress Monitor questionnaire and the Job Fatigue Measurement Questionnaire were used for univariate and bivariate analyses. A sample of 30 employees was selected purposively. This analysis was conducted using the chi-square test in SPSS. Most respondents were male (100 percent), adults or adolescents (96 percent), with more than five years of work experience (90 percent), and work durations of eight hours (90 percent). Most respondents experienced work climates above the Threshold Limit Value (WBGT 29.1–30.1°C, TLV 18–28°C). This study concluded that a hot work climate significantly influences work fatigue in furniture workers, with significant correlations between age (p=0.770), length of service (p=0.543), and work duration (p=0.894). However, there was a significant correlation between work climate and work fatigue (p=0.028; OR=4.800). To reduce heat exposure and the risk of fatigue, improvements to the work environment are needed, such as fans, comfortable rest areas, and job rotation.

Keywords: Fatigue, Work Climate, Workers

SMART GRID-BASED HYBRID WIND AND PHOTOVOLTAIC ENERGY MODELING FOR SUSTAINABLE POWER SUPPLY IN HEALTHCARE FACILITIES

Zouhir Boumous
Laboratory of Electrical Engineering, Electronic and Renewable Energy, University of Souk Ahras, Route Annaba B.P. 1553, Souk Ahras, Algeria, LAS Laboratory, University of Setif1, Setif, Algeria
Samira Boumous
Laboratory of Electrical Engineering, Electronic and Renewable Energy, University of Souk Ahras, Route Annaba B.P. 1553, Souk Ahras, Algeria, LAS Laboratory, University of Setif1, Setif, Algeria
Hamou Nouri
Laboratory of Electrical Engineering, Electronic and Renewable Energy, University of Souk Ahras, Route Annaba B.P. 1553, Souk Ahras, Algeria, LAS Laboratory, University of Setif1, Setif, Algeria

ABSTRACT

The healthcare sector increasingly depends on reliable, sustainable, and uninterrupted electrical energy to ensure the continuous operation of critical medical equipment, diagnostic systems, intensive care units, and digital healthcare infrastructures. Conventional power systems are often associated with high operational costs, greenhouse gas emissions, and vulnerability to grid failures, particularly in remote and underserved regions. In this context, renewable energy technologies integrated with smart grid systems offer a promising solution for improving energy reliability and sustainability in healthcare environments. This study presents an advanced modeling framework for hybrid wind and photovoltaic (PV) energy systems integrated into a smart grid architecture dedicated to healthcare facilities and medical infrastructures. The proposed system combines photovoltaic arrays, wind turbines, battery energy storage systems, and intelligent energy management strategies to provide stable and efficient electricity for hospitals and healthcare centers. Detailed mathematical models of wind and PV generation are developed considering environmental conditions such as solar irradiance, wind speed, and temperature variations. Maximum power point tracking (MPPT) techniques and smart control algorithms are implemented to maximize renewable energy harvesting and optimize power distribution. The smart grid model incorporates real-time monitoring, adaptive load management, and predictive control strategies to ensure continuous power supply during peak demand periods and emergency situations. The study also evaluates the system performance under variable climatic conditions, equipment failures, and fluctuating healthcare energy demands. Key parameters including energy efficiency, voltage stability, operational reliability, and reduction of carbon emissions are analyzed through simulation scenarios. Results demonstrate that the integration of hybrid renewable energy systems within smart healthcare infrastructures significantly enhances energy resilience, minimizes power interruptions, and reduces dependence on conventional fossil-fuel-based electricity generation.

HEALTH SCIENCES

Aishwarya S

Department of EEE, R.M.K. Engineering College, India

ABSTRACT

Health sciences encompass a broad and deeply human field dedicated to understanding, preserving, and restoring well-being across individuals and communities. At its core, this discipline bridges the gap between scientific discovery and compassionate care, reminding us that behind every diagnosis, treatment, and research breakthrough is a real person whose life stands to be transformed. Over the decades, health sciences have evolved far beyond the traditional boundaries of medicine. Today, they embrace nutrition, mental health, public health policy, genetics, and technology. From the quiet corridors of rural clinics to the bustling laboratories of urban research centers, health professionals carry the shared mission of reducing suffering and extending quality of life. What makes this field particularly compelling is its constant evolution. Emerging challenges such as antimicrobial resistance, chronic lifestyle diseases, and growing mental health crises demand innovative thinking, interdisciplinary collaboration, and above all, empathy. At the same time, advances in artificial intelligence, genomics, and preventive care are opening doors once thought firmly closed. Ultimately, health sciences are not merely about treating illness. They are about honoring human dignity, championing equity, and nurturing a world where every person has the opportunity to live fully and healthily.

Keywords: Compassionate Care, Public Health, Interdisciplinary Collaboration, Preventive Care, Mental Health, Chronic Disease.

ULTRASONIC DETECTION OF WATER ADULTERATION IN MILK FOR FOOD QUALITY AND CONSUMER HEALTH PROTECTION

Derra Mourad

Associate Professor Dr., Faculty of Applied Sciences, Ibn Zohr University, Agadir, Morroco.

ORCID ID: 0000-0003-2395-2859

ABSTRACT

Food adulteration remains a significant public health concern, particularly in dairy products where the addition of unauthorized substances can compromise both nutritional quality and consumer safety. Among the most common forms of adulteration, the dilution of milk with water affects its physicochemical composition and alters key quality parameters, including fat, protein, lactose, conductivity, viscosity, and thermal properties. Such modifications may negatively influence shelf life, storage stability, and technological performance during processing. This study investigates the detection of water adulteration in milk using an ultrasonic backscattering pulse–echo approach. Different proportions of water were added to raw milk samples, which were then analyzed over a temperature range of 20 °C to 40 °C. The proposed ultrasonic technique demonstrated strong potential for rapid and reliable evaluation of milk quality. The findings indicate that the method is non-destructive, hygienic, cost-effective, and suitable for real-time quality assessment. Furthermore, the use of a single ultrasonic transducer simplifies the experimental setup while maintaining measurement efficiency. The study highlights the relevance of ultrasonic inspection techniques in medical and health-related food safety applications, offering a promising tool for monitoring dairy product authenticity and protecting consumer health.

Keywords: Milk adulteration; Food safety; Ultrasonic testing; Pulse–echo technique; Dairy quality control; Water detection; Non-destructive evaluation; Consumer health; Milk quality assessment; Food authenticity

SAĞLIK YÖNETİMİNDE ENDÜSTRİ 5.0: YAPAY ZEKÂ VE İŞBİRLİKÇİ ROBOTLARIN (COBOT) SAĞLIK HİZMETLERİ ENTEGRASYONUNA YÖNELİK BİR SİSTEMATİK DERLEME

Cafer BARAN

Yüksek Lisans Öğrencisi, Dicle Üniversitesi, İktisadi ve İdari Bilimler Fakültesi, Sağlık Yönetimi, Diyarbakır, Türkiye, https://orcid.org/0009-0008-7347-9899

Merve ÖTER

Yüksek Lisans Öğrencisi, Dicle Üniversitesi, İktisadi ve İdari Bilimler Fakültesi, Sağlık Yönetimi, Diyarbakır, Türkiye, https://orcid.org/0009-0005-5041-6914

ÖZET

Amaç: Bu çalışmanın amacı, Endüstri 5.0 prensiplerinin sağlık yönetimine entegrasyonunu mevcut literatür ışığında incelemek; özellikle yapay zekâ (YZ) ve iş birlikçi robot (cobot) teknolojilerinin potansiyel etkilerini değerlendirmek ve söz konusu teknolojilerin sağlık hizmet sunumunu insan merkezli hale getiren Healthcare 5.0 yaklaşımına dönüştürmedeki rolünü ortaya koymaktır.

Materyal ve Yöntem: Bu çalışma, web of science veri tabanı üzerinden "healthcare industry" OR "healthcare sector" OR "health management" AND "industry 5.0" OR "cobot" anahtar kelimeleriyle 2022-2026 yılları arasında yayınlanan erişime açık 23 makaleyi inceleyen PRISMA'ya uygun olarak bir sistematik inceleme türünde yürütülmüştür.

Bulgular: Elde edilen bulgular, Endüstri 5.0'ın sağlık alanındaki idari, klinik ve operasyonel süreçleri önemli ölçüde geliştirdiği, insan döngülü yapay zekâ (HITL-AI) uygulamalarının, tanı doğruluğunu artırdığı, tıbbi hataları, idari iş yükünü ve sağlık profesyonellerinin tükenmişlik oranlarını düşürdüğü tespit edilmiştir. İnsan Kaynakları Yönetimi (İKY) açısından yapay zekâ destekli analitiklerin, işe alım, yetenek yönetimi ve personel planlamasını optimize ederek çalışan memnuniyetini ve operasyonel verimliliğini artırdığı, IoT, bulut bilişim, 6G ve akıllı giyilebilir cihazların hastaların eş zamanlı ve uzaktan izlenmesini sağlayarak reaktif (hastalık odaklı) bir sağlık modelinden proaktif (önleyici) bir modele geçişi hızlandırdığı, otonom mobil robotlar ve işbirlikçi robotların (cobot) hastane lojistiği ve hasta bakımına destek sağlayarak personel eksikliklerinin telafisine katkı sunduğu rapor edilmiştir.

Sonuç: Bu çalışma, Endüstri 5.0'ın sağlık yönetiminde yapay zekâ ve cobot teknolojileri aracılığıyla insan merkezli, verimlilik odaklı ve daha dayanıklı bir yapı oluşturma potansiyeline sahip olduğunu göstermektedir. Bu teknolojiler operasyonel süreçleri iyileştirirken sağlık çalışanlarının iş yükünü azaltmakta ve karar destek süreçlerini güçlendirmektedir. Buna karşılık dijital altyapı eksiklikleri, birlikte çalışabilirlik sorunları ve etik riskler önemli sınırlılıklar olarak öne çıkmaktadır. Bu nedenle sağlık sistemlerinde güçlü dijital altyapıların kurulması, dijital yetkinliklerin artırılması ve etik-yasal çerçevelerin geliştirilmesi gerekmektedir.

Anahtar Kelimeler: Endüstri 5.0, Sağlık Yönetimi, Yapay Zekâ, Cobot

INDUSTRY 5.0 IN HEALTHCARE MANAGEMENT: A SYSTEMATIC REVIEW ON THE INTEGRATION OF ARTIFICIAL INTELLIGENCE AND COLLABORATIVE ROBOTS (COBOTS) INTO HEALTHCARE SERVICES

ABSTRACT

Objective: The objective of this study is to examine the integration of Industry 5.0 principles into healthcare management in light of the current literature; specifically, to assess the potential impacts of artificial intelligence (AI) and collaborative robot (cobot) technologies, and to highlight the role of these technologies in transforming healthcare delivery into a human-centered approach known as Healthcare 5.0.

Materials and Methods: This study was conducted as a systematic review in accordance with PRISMA guidelines, analyzing 23 open-access articles published between 2022 and 2026 using the keywords “healthcare industry” OR “healthcare sector” OR “health management” AND “Industry 5.0” OR “cobot” in the Web of Science database.

Findings: The findings indicate that Industry 5.0 significantly improves administrative, clinical, and operational processes in the healthcare sector; human-in-the-loop artificial intelligence (HITL-AI) applications increase diagnostic accuracy and reduce medical errors, administrative workload, and burnout rates among healthcare professionals. From a Human Resources Management (HRM) perspective, AI-powered analytics optimize recruitment, talent management, and workforce planning, thereby increasing employee satisfaction and operational efficiency. IoT, cloud computing, 6G, and smart wearable devices enable real-time and remote patient monitoring, accelerating the transition from a reactive (disease-focused) healthcare model to a proactive (preventive) one, and that autonomous mobile robots and collaborative robots (cobots) contribute to addressing staff shortages by supporting hospital logistics and patient care.

Conclusion: This study demonstrates that Industry 5.0 has the potential to create a human-centered, efficiency-focused, and more resilient structure in healthcare management through the use of artificial intelligence and cobot technologies. These technologies improve operational processes while reducing the workload of healthcare workers and strengthening decision-support processes. Conversely, deficiencies in digital infrastructure, interoperability issues, and ethical risks emerge as significant limitations. Therefore, it is essential to establish robust digital infrastructure, enhance digital competencies, and develop ethical and legal frameworks within healthcare systems.

Keywords: Industry 5.0, Healthcare Management, Artificial Intelligence, Cobot

COMPARISON OF METHICILLIN-SUSCEPTIBLE AND METHICILLIN-RESISTANT *Staphylococcus aureus* BACTEREMIA IN A TERTIARY CARE HOSPITAL: DISTRIBUTION ACROSS HOSPITAL UNITS

Melike Nur Özçelik

Department of Infectious Diseases and Clinical Microbiology, Tekirdağ Namık Kemal University, Faculty of Medicine, Tekirdağ, Türkiye, ORCID: 0000-0003-3208-6331

Merve Kılıç Tekin

Department of Infectious Diseases and Clinical Microbiology, University of Health Sciences Haseki Training and Research Hospital, ORCID: 0000-0001-8590-230X

ABSTRACT

Aim: *Staphylococcus aureus* is a leading cause of both community-acquired and healthcare-associated bacteremia. Methicillin resistance limits therapeutic options and is associated with adverse clinical outcomes. This study aimed to evaluate the distribution of methicillin resistance in hospital-acquired *S. aureus* bacteremia and to assess differences across hospital units.

Materials and Methods: This retrospective study included patients with at least one positive blood culture bottle yielding methicillin-susceptible (MSSA) or methicillin-resistant (MRSA) *S. aureus* between January 2022 and January 2024. A total of 188 patients were analyzed. Patients were grouped according to methicillin susceptibility, and their distribution across hospital units was compared. Categorical variables were analyzed using appropriate statistical tests, and a *p-value* <0.05 was considered statistically significant.

Results: Of the 188 patients, 100 (53.2%) had MSSA and 88 (46.8%) had MRSA bacteremia. MRSA cases were predominantly observed in intensive care units (79.5%), significantly higher than MSSA cases (56%) (p = 0.001). No statistically significant differences were observed between MSSA and MRSA groups in hematology-oncology units (13% vs. 4.5%, p = 0.08), internal medicine units (17% vs. 11.4%, p = 0.29), or surgical units (14% vs. 4.5%, p = 0.06) (Table 1).

Conclusion: MRSA bacteremia was significantly more frequent in intensive care units. These findings highlight the importance of strengthening infection control measures and antimicrobial stewardship practices, particularly in critical care settings.

Table 1. Distribution of Methicillin-Susceptible and Methicillin-Resistant *Staphylococcus aureus* Bacteremia Across Hospital Units

Hospital Units	**MSSA** (n=100) %	**MRSA** (n=88) %	***p-value***
Hematology-Oncology	13 (13)	4 (4.5)	0.08
Internal Medicine Units	17 (17)	10 (11.4)	0.29
Surgical Units	14 (14)	4 (4.5)	0.06
Intensive Care Units	56 (56)	70 (79.5)	**0.001**
Total	100 (100)	88 (100)	-

Keywords: Intensive Care Units, Methicillin Resistance, *Staphylococcus aureus*

Presentation Language: Turkish

ASSESSMENT OF THE BINDING INTERACTION BETWEEN HONOKIOL AND MDM2

İhsan NALKIRAN

Department of Medical Biology, Faculty of Medicine, Recep Tayyip Erdoğan University, Rize, Türkiye,
ORCID: 0000-0002-7246-2592

ABSTRACT

Objective: Honokiol is a natural bioactive compound found in Magnolia species and is known for its remarkable anticancer properties. It has been reported to exhibit antiproliferative and proapoptotic effects in various cancer cell types. Murine double minute 2 (MDM2) is a major negative regulator of the tumor suppressor protein p53 and is considered an important therapeutic target. This study aimed to evaluate the interaction potential of honokiol with the MDM2 protein through molecular docking analysis.

Materials and Methods: The crystal structure of MDM2 was obtained from the Protein Data Bank database. Protein preparation was performed using Discovery Studio and AutoDock Tools by removing water molecules and the co-crystal ligand, followed by the addition of polar hydrogens and Kollman charges. Honokiol and the positive control Nutlin-3a were downloaded from PubChem and subjected to energy minimization before docking analysis. Grid box parameters were set at X: -25.987, Y: 8.802, Z: -9.948 with dimensions of 30 Å × 30 Å × 30 Å. Molecular docking analyses were performed using AutoDock Vina.

Results: The binding energy of the Honokiol–MDM2 complex was calculated as -7.7 kcal/mol, while Nutlin-3a showed a binding energy of -7.9 kcal/mol. Honokiol formed two conventional hydrogen bonds with TYR100 and HIS96 and also showed hydrophobic interactions with LYS51, LEU54, LEU57, LEU61, ILE99, and VAL93. Nutlin-3a formed one conventional hydrogen bond with GLN59. These findings indicated stable binding of honokiol within the active pocket of MDM2.

Conclusion: Honokiol demonstrated strong binding potential toward MDM2 with a docking score close to that of Nutlin-3a. Its interactions with key active site residues suggest that honokiol may serve as a promising natural MDM2-targeting inhibitor. Further experimental validation is required to support these findings.

Keywords: Honokiol, MDM2, Molecular Docking, Nutlin-3a

INVESTIGATION OF CELASTROL-MMP14 BINDING INTERACTION

Ihsan NALKIRAN

Department of Medical Biology, Faculty of Medicine, Recep Tayyip Erdogan University, Rize, Türkiye,
ORCID: 0000-0002-7246-2592

ABSTRACT

Objective: Celastrol is a pentacyclic triterpene compound derived from *Tripterygium wilfordii* Hook F. and is known for its anti-inflammatory, antitumor, and neuroprotective effects. Due to its low toxicity and multi-target activity, it is considered an important anticancer agent. Matrix metalloproteinase 14 (MMP14) is the first membrane-type matrix metalloproteinase involved in angiogenesis, invasion, and basement membrane remodeling and is an important target in tumor progression. This study aimed to investigate the interaction potential of celastrol with the MMP14 protein through molecular docking analysis.

Materials and Methods: The crystal structure of MMP14 was obtained from the Protein Data Bank. The protein structure was prepared using Discovery Studio and AutoDock Tools by removing water molecules and the co-crystal ligand, followed by the addition of polar hydrogens and Kollman charges. Celastrol and Marimastat, used as the positive control, were downloaded from PubChem and energy minimized before docking. Grid box parameters were set at X: 4.3, Y: -8.4, Z: 8.7 with dimensions of 30 Å × 30 Å × 30 Å. Molecular docking analyses were performed using AutoDock Vina.

Results: The binding energy of the Celastrol–MMP14 complex was -7.2 kcal/mol, while Marimastat showed -7.0 kcal/mol. Celastrol formed one conventional hydrogen bond with ASP212 at 2.05 Å and showed a hydrophobic interaction with ILE209. Marimastat formed multiple hydrogen bonds with TYR335, TYR362, and LE396. The binding energy close to the positive control indicated successful binding within the active site.

Conclusion: The findings demonstrated that celastrol has strong binding potential toward MMP14. Its docking score being similar to Marimastat suggests that celastrol may serve as a potential natural MMP14 inhibitor. Further experimental studies are required to validate these findings.

Keywords: Celastrol, MMP14, Molecular Docking, Marimastat

THE RETROSPECTIVE EVALUATION OF THERAPY REGİMENS AND CLINICAL OUTCOMES OF PATIENTS WİTH MYASTHENIA GRAVIS IN AN INTENSIVE CARE UNIT

Mefküre Durmuş

Karadeniz Technical University, Faculty of Pharmacy, Department of Clinical Pharmacy, Trabzon, Türkiye, Orcid: 0000-0001-9745-4196

Davut Aydın

Karadeniz Technical University, Faculty of Medicine, Department of Chest Diseases, Division of Intensive Care, Trabzon, Türkiye, Orcid: 0000-0002-8983-644X

Introduction

Myasthenia gravis (MG) is a chronic autoimmune neuromuscular disorder that may progress to respiratory failure and require intensive care unit (ICU) admission. Management in the ICU often necessitates treatment escalation with immunosuppressive therapies, which may increase the risk of infectious complications and affect clinical outcomes.

Aim

This study aimed to evaluate MG-related treatments administered before and during ICU hospitalization and to assess clinical outcomes, with a particular focus on infectious complications and discharge disposition.

Materials and Methods

This retrospective observational study included MG patients admitted to the ICU of a tertiary care hospital between February 2023 and June 2025. Ethical permission was obtained.

Results

Five MG patients were included; 80% were male, mean age was 54.6±20 years. Dyspnea was present in all patients at ICU admission, while dysphagia and bradyphasia were observed in 60% and 20%, respectively. ICU admission was mainly due to deterioration in general condition (60%), sepsis (20%), and myasthenic crisis (20%). The median ICU length of stay was 17 days (IQR:13.5-46). During ICU hospitalization, 3 patient received pulse-dose methylprednisolon. Two of these patients additionally underwent intavenous immunoglobulin therapy and plasmapheresis. Respiratory bacterial growths (one gram-positive bacteria, two gram-negative bacteria) were developed in all patients receiving pulse-dose corticosteroids at a median of 8 days after treatment initiation. One patient exposed to higher immunosuppression developed both respiratory (gram-negative bacteria) and bloodstream (gram-positive bacteria) infections, resulting in prolonged ICU stay. Following ICU discharge, 80% of patients were transferred to other hospital wards, whereas 20% were referred to a lower-level ICU.

Conclusion

In MG patients requiring ICU care, escalation of immunossuppressive therapy was frequently associated with early infectious complications and prolonged hospitalization. Careful monitoring, timely infection surveillance, and appropriate step-down strategies may improve clinical outcomes in this high-risk population.

Key words: Myasthenia gravis, Immunosuppressive therapy, treatment escalation, infectious complications

Table 1: The descriptive data of myasthenia gravis patients who were in the ICU

Variables	Results

Number of patients, n	5
Sex (Male), n (%)	80%
Median age (years)	57 (IQR: 34.5-73.5)
Median ICU length of stay (days) median (IQR)	17 (IQR: 13.5-46)
Clinical feature	**n (%)**
Dyspnea	5 (100)
Dysphagia	3 (60)
Bradyphasia	1 (20)
Admission cause	**n (%)**
General condition decline	60
Sepsis	20
Myasthenic crisis	20
Home medication for MG	**n (%)**
Pyridostigmine	20
Pyridostigmine-corticosteroid	20
Pyridostigmine-rituximab	20
Eculizumab	20

Immunosuppressive regimen groups	**Microbiologic findings (culture/bacteria)**
Pulse dose corticosteroid-immunoglobulin-plasmapheresis	Respiratory/gram-negative bacteria
Pulse dose corticosteroid-immunoglobulin-plasmapheresis	Respiratory/gram-positive bacteria
Pulse dose corticosteroid	Respiratory/gram-negative bacteria
Non-pulse dose corticosteroid-immunoglobulin-mycophenolate	Respiratory/gram-negative bacteria and Blood/gram-negative bacteria
Non-pulse dose corticosteroid-azathiopurine	No bacterial growth
Used antibacterial drug groups in ICU	**Agents**

Carbapenem	Meropenem, imipenem/cilastatin
Polymyxins	Polymyxin B, colisthimethate
Glycopeptides	Vancomycin
Oxazolidinone	Linezolid
Cephalosporin	Ceftriaxone
Quinolone	Ciprofloxacin
Sulfonamide	Trimethoprim-sulfamethoxazole
Antifungal	Fluconazol
Antiviral	Tenofovir disoproxil

MASKE ARKASINDAKİ ÖLÜMCÜL TABLO: FARKLI KLİNİK SEYİRLİ İKİ MENİNGOKOKSEMİ OLGUSU

İlknur Kaba

Dr. Öğr. Üyesi, Hitit Üniversitesi Tıp Fakültesi Erol Olçok Eğitim Araştırma Hastanesi Çocuk Sağlığı ve Hastalıkları Anabilim Dalı, Çorum, Türkiye, ORCID: 0000-0003-0969-7548

Amaç: Meningokoksemi pediatrik yaş grubunda hızlı progresyon ve yüksek mortalite ile seyreden invaziv bir enfeksiyondur. Ancak erken dönemde nonspesifik bulgularla başlayarak tanıda gecikmeye neden olabilmektedir. Bu çalışmada, klinik ve mikrobiyolojik olarak doğrulanmış iki farklı meningokoksemi olgusunun sunulması ve hastalığın değişken klinik seyir özelliklerinin vurgulanması amaçlandı.

Materyal ve Yöntem: Çocuk yoğun bakım ünitesinde izlenen iki olgu retrospektif olarak değerlendirildi. Hastaların demografik özellikleri, klinik bulguları, laboratuvar sonuçları, uygulanan tedaviler ve mikrobiyolojik inceleme sonuçları ayrıntılı olarak incelendi.
Bulgular: Dört aylık kız hasta yaygın purpurik döküntü ile başvurmuş, kısa sürede septik şok, ciddi metabolik asidoz, hipoglisemi ve dolaşım yetmezliği gelişmiştir. Yoğun bakım tedavisine rağmen fulminan seyirle kaybedilmiş olup mikrobiyolojik etken saptanamamıştır.

Dört yaş erkek hasta ise ateş ve peteşiyal döküntü ile başvurmuş, erken dönemde meningokoksemi ön tanısı ile ampirik antibiyotik tedavisi başlanmıştır. Takibinde koagülopati gelişmiş, ancak yoğun bakım desteği ile klinik düzelme sağlanmıştır. BOS incelemesinde Neisseria meningitidis DNA'sı saptanmış ve serogrup Y ile uyumlu bulunmuştur.

Sonuç: Meningokoksemi erken dönemde benign bulgularla başlayabilmekte ve kısa sürede fulminan, hayatı tehdit eden bir tabloya dönüşebilmektedir. Mikrobiyolojik doğrulama her zaman mümkün olmayabilir. Klinik şüphe varlığında erken ve agresif tedavi yaklaşımı prognoz açısından hayati öneme sahiptir. Bu iki olgu, hastalığın geniş klinik spektrumunu ve erken müdahalenin önemini açıkça göstermektedir.

Anahtar Kelimeler: meningokoksemi, septik şok, purpura fulminans, Neisseria meningitidis

THE FATAL CONDITION BEHIND THE MASK: TWO CASES OF MENINGOCOCCEMIA WITH DISTINCT CLINICAL COURSES

Objective: Meningococcemia is an invasive infection characterized by rapid progression and high mortality in the pediatric population. However, it may initially present with nonspecific symptoms, leading to delays in diagnosis. This study aimed to present two cases of meningococcemia, one clinically and one microbiologically confirmed, and to emphasize the variability in clinical presentation.

Materials and Methods: Two patients followed in the pediatric intensive care unit were retrospectively evaluated. Demographic characteristics, clinical findings, laboratory results, treatment approaches, and microbiological data were analyzed in detail.

Results: A 4-month-old female patient presented with widespread purpuric rash and rapidly developed septic shock, severe metabolic acidosis, hypoglycemia, and circulatory failure. Despite intensive care management, the patient died due to a fulminant course, and no microbiological pathogen was identified. A 4-year-old male patient presented with fever and petechial rash, and empirical antibiotic therapy was initiated with a preliminary diagnosis of meningococcemia. During follow-up, coagulopathy developed; however, clinical improvement was achieved with intensive care support. Cerebrospinal fluid analysis revealed the presence of *Neisseria meningitidis* DNA, consistent with serogroup Y.

Conclusion: Meningococcemia may begin with seemingly benign symptoms but can rapidly progress to a fulminant and life-threatening condition. Microbiological confirmation may not always be possible.

In the presence of clinical suspicion, early and aggressive treatment is crucial for improving prognosis. These two cases highlight the broad clinical spectrum of the disease and the critical importance of early intervention.

Keywords: Meningococcemia, Septic shock, Purpura fulminans, Neisseria meningitidis

EFFECT OF PHYSICAL ACTIVITY ON CARDIOVASCULAR HEALTH: A CRITICAL REVIEW OF CURRENT EVIDENCE

Faria Nawab

State Unani Medical College, Prayagraj, India

Mohammad Ahsan

Imam Abdulrahman Bin Faisal University, Dammam, Saudi Arabia

ABSTRACT

Background: Cardiovascular diseases (CVDs) remain the leading cause of morbidity and mortality worldwide. Physical activity is widely recognized as a key modifiable lifestyle factor that significantly influences cardiovascular health.

Objective: This critical review aims to synthesize current evidence on the effects of physical activity on cardiovascular health, evaluate the strengths and limitations of existing research, identify gaps in the literature, and propose future research directions.

Methods: Relevant literature was searched using databases including PubMed, Google Scholar, and Scopus, focusing on studies published between 2014 and 2024. Keywords such as physical activity, cardiovascular health, exercise, sedentary behavior, and cardiac rehabilitation were used.

Key Findings: Evidence consistently demonstrates that regular physical activity improves cardiovascular function, reduces risk factors such as hypertension, obesity, and dyslipidemia, and enhances overall cardiac outcomes. However, several limitations exist, including variability in exercise protocols, limited long-term follow-up studies, and underrepresentation of certain populations. Furthermore, inconsistencies in physical activity measurement tools and insufficient research in developing regions remain significant gaps.

Conclusion: Physical activity plays a crucial role in maintaining cardiovascular health, yet further research is required to optimize exercise recommendations and improve patient-specific interventions. Future studies should focus on standardized methodologies, long-term randomized controlled trials, and the integration of wearable technologies for accurate monitoring.

Keywords: Physical Activity, Cardiovascular Health, Exercise, Sedentary Behavior, Cardiac Rehabilitation

THE ROLE OF MANAGEMENT ACCOUNTING IN ENHANCING DECISION-MAKING IN NIGERIAN PUBLIC SECTOR ORGANIZATIONS

Umar Baba Shaaba
Head of Department, Accounting Ahman Pategi University, Kwara State, Nigeria
ORCID: 0009-0007-5789-8690

ABSTRACT

This study examines the role of management accounting in enhancing decision-making processes within Nigerian public sector organizations. In the face of increasing demand for transparency, accountability, and efficiency in public financial management, management accounting has emerged as a critical tool for improving governance outcomes. The study specifically evaluates the effectiveness of budgeting, variance analysis, cost control techniques, and performance evaluation systems in facilitating informed decision-making. A descriptive survey research design was adopted, with primary data collected through structured questionnaires administered to 120 respondents across selected ministries and government agencies. Secondary data were sourced from relevant academic literature, policy documents, and financial reports. The findings reveal that management accounting significantly contributes to improved planning, monitoring, and control of public resources. Budgetary systems and variance analysis were identified as the most influential tools in guiding managerial decisions. However, the effectiveness of these tools is constrained by challenges such as inadequate professional capacity, weak institutional frameworks, lack of technological integration, and political interference. The study concludes that strengthening management accounting practices is essential for achieving efficient public sector performance and sustainable development. It recommends capacity building, adoption of digital accounting systems, and reinforcement of regulatory frameworks to enhance accountability and decision-making efficiency.

Keywords:

Management Accounting, Decision-Making, Public Sector, Budgetary Control, Nigeria

ANN-DRIVEN OPTIMIZATION OF ZINC OXIDE NANOPARTICLES (ZNO-NPS) FOR ANTI-DIABETIC DRUG DELIVERY

Sumayya Akram

Government College University, Faisalabad, ORCID ID: 0009-0008-7648-954X

Muhammad Nouman Majeed

Government College University, Faisalabad

ABSTRACT

Background: Metformin, a first-line anti-diabetic agent, exhibits suboptimal bioavailability and off-target limitations that constrain its therapeutic efficacy. Zinc oxide nanoparticles offer a promising nanocarrier platform; however, systematic computational optimization of ZnO NP–drug complexes against key diabetic targets remains underexplored.

Methods: Molecular docking was performed using AutoDock Vina against AMPK (PDB: 4CFE), DPP-4 (PDB: 2QT9), and PPARγ (PDB: 2PRG). Molecular dynamics (MD) simulations were conducted over 50 ns using GROMACS. ADMET profiling was carried out *via* SwissADME and pkCSM. An artificial neural network (ANN) feedforward regression model (architecture: 12–8–4–1) was trained on a dataset of 320 optimized nanoformulation descriptors to predict bioavailability indices.

Results: Free metformin exhibited docking scores of −5.2, −4.8, and −5.6 kcal/mol against AMPK, DPP-4, and PPARγ, respectively. ZnO NP-conjugated metformin yielded improved scores of −7.9, −8.3, and −7.4 kcal/mol, reflecting binding energy improvements of 34.1%, 42.2%, and 24.4% per target. MD simulations demonstrated stable complex trajectories with RMSD values converging between 0.18–0.31 nm and a sustained hydrogen bond count of 4–6 across all target systems. ADMET profiling predicted high gastrointestinal absorption (probability: 0.84) and low hepatotoxicity risk (toxicity probability: 0.17). The ANN model achieved R^2 = 0.962 and RMSE = 0.038 on the test set, with optimized nanoformulation parameters yielding a predicted 41.3% improvement in bioavailability relative to the free drug.

Conclusion: This integrated *in silico* framework demonstrates that ANN-guided ZnO NP optimization substantially enhances the binding affinity, stability, and predicted bioavailability of metformin, supporting its advancement as a computationally validated nanocarrier candidate for anti-diabetic therapy.

SEMAGLUTIDE: TRANSFORMING METABOLIC HEALTH IN DIABETES AND OBESITY MANAGEMENT

Kiran Kulkarni

Doctor of Pharmacy, JES's SND College of Pharmacy, Yeola, Dist. Nashik, India

ABSTRACT

Semaglutide is a glucagon-like peptide-1 (GLP-1) receptor agonist that has emerged as a significant therapeutic agent in the management of type 2 diabetes mellitus and obesity. Since its development and subsequent approvals for clinical use, semaglutide has demonstrated remarkable efficacy across multiple health parameters, extending beyond glycemic control to include substantial weight reduction, cardiovascular risk improvement, and potential benefits in other metabolic conditions. This review aims to provide a comprehensive evaluation of semaglutide's pharmacological properties, clinical applications, safety profile, and future therapeutic potential.This review synthesizes evidence from pivotal clinical trials including the SUSTAIN and PIONEER programs for diabetes management, the STEP program for weight management, and cardiovascular outcome trials. We examined pharmacological studies detailing semaglutide's mechanism of action, comparative analyses with other antidiabetic medications, and emerging research on novel applications. Additionally, we assessed current clinical guidelines, patient selection criteria, and real-world data on administration, adherence, and safety profiles across different patient populations.

Keywords: Semaglutide, GLP-1 receptor agonist, type 2 diabetes mellitus, obesity, weight management, STEP program.

ADMET, MOLECULAR DOCKING, AND MOLECULAR DYNAMICS ANALYSIS OF FLAVONE DERIVATIVES AS SARS-COV-2 RDRP INHIBITORS

Mohammed MERZOUKI

Laboratory of Applied Chemistry and Environment (LCAE), Faculty of Sciences, University Mohamed Premier, PB 60000, Oujda, Morocco

Ahmed CHETOUANI

Regional center for education and training professions in the eastern region (CRMEF), Morocco,

ORCID ID: 0000-0003-1132-4468

ABSTRACT

The aim of this study was to identify potential targets for the SARS-CoV-2 RdRp protein for the development of new therapeutic drugs based on natural substances derived from aromatic and medicinal plants. In this research work, a library of five flavone-derived natural compounds (4a, 4b, 4c, 4d, and 4e) was established, while the standard favipiravir-RTP was investigated using an in silico approach involving several important steps: (a) application of Lipinski's rule of five and ADMET parameters, (b) molecular docking analysis, and (c) molecular dynamics simulation over a period of 100 ns.

The obtained results demonstrated that the five compounds exhibited better pharmacological responses than the standard compound, showing promising outcomes without significant limitations. Consequently, two flavone derivatives (4d and 4e) were selected due to their higher binding energies compared with the reference molecule, with binding affinities of −7.036 kcal/mol and −7.141 kcal/mol, respectively. Furthermore, the stability of the two best compounds bound to the SARS-CoV-2 RdRp protein was confirmed through molecular dynamics (MD) simulations, revealing stable trajectories (RMSD and RMSF), consistent interaction profiles, and desirable molecular properties.

This in silico analysis demonstrated the potential of several compounds derived from aromatic and medicinal plants to inhibit the SARS-CoV-2 RdRp protein, making them promising candidates for further in vitro and in vivo investigations for the treatment of COVID-19 patients.

EVALUATION OF THE *IN VITRO* ANTIOXIDANT AND ANTIDIABETIC ACTIVITIES OF QUINOA (*CHENOPODIUM QUINOA* WILLD.) SEED EXTRACTS AND THE QUANTIFICATION OF THEIR BIOACTIVE COMPOUNDS

Zaina Idir

Laboratory of Bioressources, Boitechnology, Ethnopharmacology and Health, Faculty of Sciences, Mohammed First University, Oujda 60000, Morocco

Rhizlane Abdnim

Laboratory of Bioressources, Boitechnology, Ethnopharmacology and Health, Faculty of Sciences, Mohammed First University, Oujda 60000, Morocco

Soukaina Terroufi

Laboratory of Bioressources, Boitechnology, Ethnopharmacology and Health, Faculty of Sciences, Mohammed First University, Oujda 60000, Morocco

Ilham Abidi

Hassan II Institute of Agronomy and Veterinary sciences, Rabat 10112, Morocco

Fatima Aouinti

Laboratory of Bioressources, Boitechnology, Ethnopharmacology and Health, Faculty of Sciences, Mohammed First University, Oujda 60000, Morocco

Nadia Gseyra

Laboratory of Bioressources, Boitechnology, Ethnopharmacology and Health, Faculty of Sciences, Mohammed First University, Oujda 60000, Morocco

ABSTRACT

Oxidative stress plays a major role in diabetic physiopathology; hence, the interest of using natural antioxidants as therapeutic tools exists. Quinoa (*Chenopodium quinoa* Willd.), native to South America and belonging to the family Chenopodiaceae, is a seed crop that exhibits broad genetic diversity, enabling it to adapt to various tough environments, including highlands, salinity, drought, and frost.

This study aimed to assess the *in vitro* antioxidant activity and the inhibitory effects of quinoa seed extracts on key enzymes associated with hyperglycemia. Additionally, it sought to quantify the bioactive compounds present in these extracts.

Antioxidant activity was performed using 2,2′-diphenyl-1-picrylhydrazyl (DPPH) and ferric reducing antioxidant power (FRAP) methods. The α-glucosidase and α-amylase inhibitory activities were investigated using an *in vitro* model.

The hydroethanolic extract of quinoa exhibited the highest antioxidant activity in both DPPH and FRAP methods. This extract also demonstrated the strongest inhibitory effect against α-glucosidase. However, the aqueous extract showed the highest inhibitory effect against α-amylase. Furthermore, the results indicated high levels of phenolic content. The findings suggest that this plant could be a significant source of medically important natural compounds.

Keywords: Chenopodium quinoa Willd.; Antioxidant Activity; Antidiabetic Activity; Bioactive Compounds

EMERGING NON- INVASIVE BIOMARKERS FOR PSORIASIS SEVERITY ASSESSMENT: A REVIEW OF CURRENT EVIDENCE

Yousra Anwar

David Tvildiani Medical University

INTRODUCTION

Psoriasis is a chronic, immune mediated skin disorder affecting 2-4% of the general population [1]. It presents equally in males and females and exhibits a bimodal age distribution, most commonly appearing between 20-30 years and 60-70 years.

The disease is characterized by keratinocyte hyperproliferation, immune dysregulation and systemic inflammation. Accurate assessment of disease severity is critical for treatment and monitoring [2]. Currently used scoring systems, such as the Psoriasis Area and Severity Index (PASI), rely on clinical evaluation and can be subjective [3]. Recent research has focused on non-invasive biomarkers, including cytokines, antimicrobial peptides and microRNAs which may reflect disease severity and correlate with severity scores.

METHODS

A narrative review of the literature was conducted using PubMed and Google Scholar focusing on articles published between 2018 to 2025. Keywords included psoriasis, non-invasive biomarkers, cytokines, severity assessment and microRNAs. Studies were included if they reported correlation between non-invasive biomarkers and psoriasis severity.

RESULTS

Emerging evidence indicates that pro-inflammatory cytokines (IL-17, IL-23, TNF-α) detectable in saliva or serum strongly correlate with PASI scores [4]. Skin surface markers including antimicrobial peptides (hBD-1, hBD-2) and chemokines (CXCL-8), obtained via tape strips have demonstrated consistent associations with disease severity [4].

Circulating microRNAs (miR-21, miR-31, miR-146a) also show potential as molecular indicators of severity [5]. Proteomic and metabolomic markers such as oxidative stress indicators and metabolic profiles, could further enhance clinical evaluation [6].

DISCUSSION

Non-invasive biomarkers offer a practical approach for evaluating psoriasis in a patient friendly manner. Cytokines, antimicrobial peptides and microRNAs correlate with standard clinical scores and could aid in monitoring treatment response [4-6].

While current evidence is promising, large prospective studies are needed to validate these biomarkers and establish their role in clinical practice. This would reduce reliance on invasive sampling and improve quality of life for patients with psoriasis.

Keywords

Psoriasis, Biomarkers, Severity Index, Inflammation

References

Parisi, R., Symmons, D. P., Griffiths, C. E., Ashcroft, D. M., & Identification and Management of Psoriasis and Associated ComorbidiTy (IMPACT) project team (2013). Global epidemiology of psoriasis: a systematic review of incidence and prevalence. The Journal of investigative dermatology, 133(2), 377–385. https://doi.org/10.1038/jid.2012.339

Greb, J., Goldminz, A., Elder, J. et al. Psoriasis. Nat Rev Dis Primers 2, 16082 (2016). https://doi.org/10.1038/nrdp.2016.82

Lebwohl, M., Gooderham, M. J., Warren, R. B., Thaçi, D., Foley, P., Gottlieb, A. B., Torres, T., Popmihajlov, Z., Jou, Y. M., Linaberry, M., Daamen, C., & Griffiths, C. E. M. (2025). Outcomes of Psoriasis Area and Severity Index (PASI) and PASI components in two phase III trials of deucravacitinib in patients with moderate to severe plaque psoriasis. Clinical and experimental dermatology, 50(10), 2030–2036. https://doi.org/10.1093/ced/llaf215

Orro, K., Salk, K., Merkulova, A., Abram, K., Karelson, M., Traks, T., Neuman, T., Spee, P., & Kingo, K. (2023). Non-Invasive Assessment of Skin Surface Proteins of Psoriasis Vulgaris Patients in Response to Biological Therapy. International journal of molecular sciences, 24(22), 16248. https://doi.org/10.3390/ijms242216248

Singh, S., & Rajappa, M. (2026). MicroRNA biomarkers in psoriasis. Clinica chimica acta; international journal of clinical chemistry, 579, 120633. https://doi.org/10.1016/j.cca.2025.120633

Ramessur, R., Corbett, M., Marshall, D., Acencio, M. L., Barbosa, I. A., Dand, N., Di Meglio, P., Haddad, S., Jensen, A. H. M., Koopmann, W., Mahil, S. K., Ostaszewski, M., Rahmatulla, S., Rastrick, J., Saklatvala, J., Weidinger, S., Wright, K., Eyerich, K., Ndlovu, M., Barker, J. N., … BIOMAP consortium (2022). Biomarkers of disease progression in people with psoriasis: a scoping review. The British journal of dermatology, 187(4), 481–493. https://doi.org/10.1111/bjd.21627

STUDYING THE PREVALENCE OF MUSCULOSKELETAL DISORDERS AND MENTAL HEALTH AMONG DENTISTS IN THE WEST OF THE COUNTRY

Vahid Molabashi

Ebrahim Yar Mohammadi

Nazli Rabinejad

Saeed Bashirian

Elaheh Ezzati

ABSTRACT

Introduction: Considering that reducing and preventing musculoskeletal disorders and health problems is a priority for the dental profession and considering the importance of early treatment of skeletal disorders among dentists and providing appropriate solutions to prevent them, this study was conducted among dentists.

Methods: In this cross-sectional study, 100dentists with an average age of 36.9years participated. The Nordic Musculoskeletal Questionnaire was used to assess work-related musculoskeletal disorders and the Kaldbrank Mental Health Survey Questionnaire.

Findings: The results show that there is a significant relationship between neck pain, wrist pain, and back pain and age. On the other hand, there is a direct and significant correlation with work experience and neck pain (r=0.275), shoulder pain (r=0.201), knee pain (r=0.243), and wrist pain (r=0.312). Increasing the average working hours has a direct effect on the prevalence of musculoskeletal disorders (P-VALUE<.(0.05

Conclusion: Design and innovation are needed to implement interventions that lead to a decrease in the prevalence of musculoskeletal disorders and improve mental health, which can be implemented in the dental sector with its distinctive organizational and service characteristics.

Keywords: Musculoskeletal disorders, mental health, dentists

QUANTITATIVE ETHNOBIOLOGICAL ANALYSIS OF LKHEL SAHRAOUI: STRUCTURAL CORE AND BIOCULTURAL RESILIENCE OF A SAHARAN POLYHERBAL FORMULATION FOR DIGESTIVE DISORDERS IN SOUTHERN MOROCCO

Khalid TALEBALI

Biotechnology and Biomolecular Engineering Research Team, Abdelmalek Essaadi University, FST Tangier, Morocco.

Ahmed AARAB

Biotechnology and Biomolecular Engineering Research Team, Abdelmalek Essaadi University, FST Tangier, Morocco.

ABSTRACT

This study analyzes the internal composition and biocultural resilience of Lkhel sahraoui, a complex polyherbal formulation used in southern Morocco to treat digestive disorders such as abdominal pain, bloating, and indigestion. Through a quantitative ethnobotanical approach conducted in 2025 with 34 healers and herbalists, the inventory revealed a diversity of 103 species, dominated by the Lamiaceae, Apiaceae, and Zingiberaceae families. The application of Citation Frequency (CF) and Relative Citation Frequency (RCF) indices statistically identified a core group of 23 species (22.3% of the flora), including primarily Alpinia officinarum, Ammodaucus leucotrichus, and Curcuma longa, which ensure the therapeutic consistency of the recipe. The preparation is distinguished by rigorous empirical knowledge, including fumigation with benzoin (Styrax spp.) and a prolonged maceration lasting one year, aimed at optimizing the extraction of active compounds and the preservation of the remedy in the arid Saharan climate. By combining local, Mediterranean, and exotic species, Saharan Lkhel exemplifies a structured medical system capable of maintaining cultural stability while incorporating adaptive variability to address gastrointestinal health challenges.

Keywords: *Lkhel sahraoui*, digestive disorders, Ethnopharmacologie quantitative, Southern Morocco

EXTREME SLEEP SPINDLES IN A CHILD WITH PSYCHOMOTOR RETARDATION: CLINICAL: A CASE REPORT

SIBARI. BOUTAINA

Department of Neurology, Hassan II University Hospital Center, Fez, Morocco.
Laboratory of Epidemiology and Clinical Research, Faculty of Medicine and Pharmacy, Sidi Mohammed Ben Abdallah University, Fez, Morocco.

SOUIRTI. ZOUHAYR

Department of Neurology, Hassan II University Hospital Center, Fez, Morocco.
Laboratory of Clinical Neuroscience, Faculty of Medicine and Pharmacy, Sidi Mohammed Ben Abdallah University, Fez, Morocco.

ABSTRACT

The study of extreme sleep spindles on Electroencephalogram (EEG) has enabled us to explore the limits of brain activity during slow wave sleep. Whether manifested by abnormally high frequency, prolonged duration or exceptional amplitude, these unusual spindles raise fascinating questions about their neural origins and their impact on cognition and health. They are key markers of thalamocortical function and brain development. In children with autism spectrum disorder (ASD), comorbidities like sleep disturbances and epilepsy are common, often linked to shared genetic and neurodevelopmental pathways. Unlike typical spindles, extreme sleep spindles show high amplitude and fast frequency**,** suggesting deeper neurological disruption. We report the case of a child with psychomotor delay and a single convulsive seizure, where extreme sleep spindles were detected during sleep EEG, underscoring the need to better understand and classify these atypical patterns. They are not just a scientific curiosity: they open up new perspectives for clinical and therapeutic research, while reminding us that normal sleep still conceals many enigmas.

ASSOCIATION OF RS8052394 POLYMORPHISM WITH INCREASED RISK OF PREECLAMPSIA

Mohammad Amin Rostamian

Department of Molecular and Cell Biology, Faculty of Basic Sciences, University of Mazandaran, Babolsar, 47416-95447, Iran

Mohammad Karimian

Department of Molecular and Cell Biology, Faculty of Basic Sciences, University of Mazandaran, Babolsar, 47416-95447, Iran

ABSTRACT

Background: Preeclampsia is one of the most important complications of pregnancy, characterized by hypertension and organ dysfunction, which can threaten both maternal and fetal health. Genetic factors play a significant role in the development of this disorder. Due to its important cellular and molecular functions, the MT1A gene has been considered one of the genes associated with preeclampsia. The present study aimed to investigate the association between the rs8052394 polymorphism in the MT1A gene and the risk of preeclampsia.

Methods: In this case-control study, 50 women diagnosed with preeclampsia were enrolled as the case group and 50 healthy pregnant women were included as the control group. Samples were collected from Shahid Beheshti Hospital (Kashan, Iran). Genomic DNA was extracted from peripheral blood samples, and the rs8052394 polymorphism genotype was determined using the PCR-RFLP method. Statistical analyses were performed using appropriate tests.

Results: The results demonstrated a significant association between the rs8052394 polymorphism in the MT1A gene and an increased risk of preeclampsia ($P<0.05$). The frequency of the risk allele and genotype was higher in patients compared to the control group.

Conclusion: The findings of this study suggest that the rs8052394 polymorphism in the MT1A gene may be considered an important genetic factor contributing to susceptibility to preeclampsia and may play a role in the pathogenesis of this disorder.

Keywords: Preeclampsia, MT1A gene, rs8052394 polymorphism, genetic polymorphism, oxidative stress

ECOLOGY OF CEPS: A MINI-REVIEW

FELLAKI Anas

Laboratory of Natural Resources and Sustainable Development, Faculty of Sciences, Ibn Tofail University, Kenitra, Morocco

ABOUROUH Mohamed

Laboratory of Natural Resources and Sustainable Development, Faculty of Sciences, Ibn Tofail University, Kenitra, Morocco

ELYACOUBI Houda

Laboratory of Natural Resources and Sustainable Development, Faculty of Sciences, Ibn Tofail University, Kenitra, Morocco

ELYAMANI Asmaa

Laboratory of Natural Resources and Sustainable Development, Faculty of Sciences, Ibn Tofail University, Kenitra, Morocco

Aboukhalaf Abdelghani

Laboratory of Natural Resources and Sustainable Development, Faculty of Sciences, Ibn Tofail University, Kenitra, Morocco

ROCHDI Atmane

Laboratory of Natural Resources and Sustainable Development, Faculty of Sciences, Ibn Tofail University, Kenitra, Morocco

ABSTRACT

Ceps are epigeous ectomycorrhizal fungi adapted mainly to temperate and Mediterranean forest ecosystems.
They mainly belong to the genus *Boletus*, especially species such as *Boletus edulis* and *Boletus aereus*. Their ecology is closely linked to the climatic conditions of forests, particularly in humid, sub-humid, and Mediterranean environments. They usually grow in well-drained forest soils, often sandy, loamy, or slightly acidic, rich in organic matter and covered by leaf litter. Soil texture plays an important role in aeration, water retention, and root development.

These fungi live in ectomycorrhizal association with host trees, especially species of *Quercus*, *Fagus*, *Castanea*, *Pinus*, and other forest trees.

This symbiosis allows a beneficial exchange between the fungus and the plant. The tree provides organic nutrients produced by photosynthesis, while the fungus improves water and mineral uptake, especially phosphorus and nitrogen.

Seasonal rainfall is a key factor for the appearance of fruiting bodies. Adequate rain in late summer or autumn generally promotes the development of ceps. Soil temperature also influences mycelial growth and the formation of basidiomata. *Ceps often prefer mature forest habitats with a relatively stable microclimate, moderate shade, and sufficient soil moisture.*

Their distribution also depends on soil pH, organic matter availability, litter thickness, humidity, and the presence of suitable host trees. Year-to-year climate variability explains the strong fluctuations in production.

Some years are highly productive, while others yield little or no harvest.

Human activities such as overharvesting, forest degradation, soil compaction, fires, and changes in forest management may threaten their natural habitats.

Climate change may also affect their distribution, abundance, and fruiting period by modifying rainfall patterns and increasing drought stress.

Studying their ecology is therefore essential for understanding their life cycle and conservation. It also helps improve sustainable harvesting practices and supports attempts to manage or conserve productive forest habitats.

Keywords: *Boletus edulis*, *Boletus aereus*, ecology, climate change, soil textur

GOLD NANOPARTICLE–BASED LATERAL FLOW IMMUNOASSAYS FOR TUBERCULOSIS DIAGNOSIS: MECHANISTIC INSIGHTS, OPTIMIZATION STRATEGIES, AND TRANSLATIONAL PROSPECTS

Emmanuel Tomisin Bello

Department of Science Laboratory Technology, Newland Polytechnic and College of Health Technology, Ilorin.

Majekodunmi Rachael Adedayo

Department of Microbiology, Kwara State University, Malete.

ABSTRACT

Tuberculosis (TB), caused by Mycobacterium tuberculosis, remains one of the leading causes of infectious mortality worldwide, with the greatest burden in low- and middle-income countries where access to centralized molecular diagnostics is limited. Although nucleic acid amplification platforms such as GeneXpert have improved case detection, their infrastructure requirements and cost restrict widespread deployment. Lateral flow immunoassays (LFIAs) offer a rapid, low-cost, and field-deployable alternative; however, conventional antibody-based TB serological tests have demonstrated inconsistent diagnostic performance, resulting in limited clinical acceptance. Gold nanoparticles (AuNPs), owing to their localized surface plasmon resonance properties, tunable size-dependent optical behavior, and ease of surface functionalization, have emerged as promising signal reporters for next-generation TB LFIAs. This review critically synthesizes current advances in AuNP-based LFIA development for TB diagnosis, with emphasis on the mechanistic determinants of assay performance. We examine how nanoparticle synthesis methods, size control, surface charge modulation, conjugation chemistry, and antibody orientation influence immunorecognition kinetics, signal amplification, and analytical sensitivity. The role of antigen selection, including ESAT-6, CFP-10, Ag85 complex proteins, and lipoarabinomannan (LAM), is evaluated in the context of TB immunopathology and HIV co-infection. Additionally, we analyze membrane flow dynamics, hook effects, and stability challenges that contribute to historical limitations of TB serology. Translational considerations such as cross-reactivity, differentiation of active versus latent TB, clinical validation in high-burden settings, and regulatory pathways are also discussed. By integrating insights from nanotechnology, immunodiagnostics, and clinical microbiology, this review proposes a rational engineering framework for optimizing AuNP-based TB LFIAs. We highlight emerging strategies, including signal amplification approaches, multiplex detection architectures, and digital readout integration, that may overcome prior performance barriers. This synthesis offers a path forward for the set up of clinically sound, cost-effective, and robust point-of-care TB diagnostics that are suited for environments with limited resources.
Keywords: Tuberculosis (TB); Mycobacterium tuberculosis; Gold nanoparticles (AuNPs); Lateral flow immunoassay (LFIA); Point-of-care diagnostics.

CHRONIC ARTIFICIAL LIGHT AT NIGHT EXPOSURE DISRUPTS CIRCADIAN RHYTHMS AND MODULATES *P*53 GENE EXPRESSION IN A RAT MODEL OF COLORECTAL CANCER

Rabiu Musa Isah

Department of Human Physiology, Faculty of Basic Medical Sciences, College of Medical Sciences, Federal University of Health Sciences, Azare, Bauchi State, Nigeria

Mahdi Gambo Dissi

Department of Human Physiology, Faculty of Basic Medical Sciences, College of Health Sciences, Bayero University, Kano, Nigeria

Muhammad Ali Salim

Department of Human Physiology, Faculty of Basic Medical Sciences, College of Health Sciences, Bayero University, Kano, Nigeria

ABSTRACT

Background: Artificial light at night (ALAN) is an increasingly prevalent environmental exposure that disrupts circadian organization and is classified as a probable human carcinogen. Circadian disruption alters physiological rhythms and molecular pathways involved in tumor suppression, oxidative balance, which is associated with various health risks, including cancer. Colorectal cancer (CRC) remains a leading cause of cancer-related mortality worldwide, yet the role of ALAN in modulating CRC progression is not fully understood.

Methods: Male Wistar rats were assigned to control (12 hrs light/12 hrs dark), carcinogen-exposed (1,2-dimethylhydrazine + dextran sulfate sodium; DMH/DSS), or carcinogen plus ALAN exposure (18 hrs light/6 hrs dark; 430 lux) groups for 12 weeks, six rats per group. Circadian rhythmicity was assessed using core body temperature and Cosinor analysis. Oxidative stress markers (malondialdehyde [MDA], total antioxidant capacity [TAC]), plasma carcinoembryonic antigen (CEA), colonic *P*53 gene expression, and histopathological changes were evaluated.

Results: ALAN exposure significantly attenuated nocturnal core body temperature, delayed the acrophase and reduced the amplitude of the temperature rhythm. Carcinogen exposure increased MDA, reduced TAC, elevated CEA, downregulated *P*53 expression, and induced colitis-like histological alterations. Combined exposure to carcinogens and ALAN resulted in a further increase in CEA, altered oxidative stress dynamics, significant upregulation of *P*53 gene expression relative to carcinogen-only animals, and progression from inflammatory pathology to dysplastic glandular changes in the colon.

Conclusion: Chronic ALAN exposure disrupts circadian organization and potentiates colorectal cancer progression in the presence of carcinogenic insult. These findings provide experimental evidence that environmental light exposure acts as a disease modifier in colorectal carcinogenesis, highlighting circadian health as a potential target for cancer prevention in modern light-polluted societies.

Keywords: artificial light at night, circadian disruption, colorectal cancer, *P*53, oxidative stress, carcinoembryonic antigen, Wistar rats

DETECTION OF FACE-SWAP DEEPFAKE VIDEOS USING DEEP LEARNING AND MACHINE LEARNING MODELS

Jogendra Kumar

Department of Computer Science and Engineering GBPIET Ghurdauri Pauri Garhwal Uttarakhand, India

Harshit Bhandari

Department of Computer Science and Engineering GBPIET Ghurdauri Pauri Garhwal Uttarakhand, India

Harshdeep Gaur

Department of Computer Science and Engineering GBPIET Ghurdauri Pauri Garhwal Uttarakhand, India

Anuj Chamoli

Department of Computer Science and Engineering GBPIET Ghurdauri Pauri Garhwal Uttarakhand, India

Vedansh Tomar

Department of Computer Science and Engineering GBPIET Ghurdauri Pauri Garhwal Uttarakhand, India

ABSTRACT

The development of Artificial Intelligence (AI) and deep learning technologies has significantly accelerated the production of deeply realistic deepfake videos especially manipulated with face swap. While they have a number of positive uses in entertainment, media production and virtual communication, they also present significant risks for digital security, misinformation control, identity protection, and public trust if used maliciously. As the creation of face-swap deepfake videos becomes more prevalent, the need for reliable detection mechanisms has never been greater, especially for fraud, political manipulation, cybercrime, and social engineering attacks. In this study, an intelligent approach for the detection of face-swap deepfake videos employing deep learning and machine learning models is proposed. It is proposed to use image preprocessing, facial feature extraction, spatial-temporal analysis, and classification techniques to distinguish manipulated videos with high accuracy from authentic videos. First, a set of video frames are extracted and facial regions are detected from the image using sophisticated computer vision technology. For the learning process, deep learning models like Convolutional Neural Networks (CNN), Long Short-Term Memory (LSTM) and transfer learning architectures are used to learn discriminative visual and temporal patterns related to deep fake manipulation. Additionally, classifiers such as Support Vector Machine (SVM), Random Forest (RF) and XGBoost are incorporated to boost classification accuracy and robustness of the classifiers. The system is tested with benchmarks deepfake datasets on various performance metrics such as accuracy, precision, recall, F1 score, and the Area Under Curve (AUC). The experimental results indicate that the proposed hybrid approach can improve the accuracy of detection, robustness to sophisticated manipulations and minimization of false detection rate in comparison with the traditional methods. The proposed model can be helpful for various applications in the field of multimedia forensics, cyber security, digital authentication and social media content verification.

Abstract Terms—Deepfake, Face-Swap Video, Artificial Intelligence, Machine Learning, Deep Learning, Convolutional Neural Network, LSTM, Multimedia Forensics, Video Authentication, Cyber Security, Transfer Learning, Computer Vision.

THE PROBLEM OF MICROPLASTICS IN ENVIRONMENTAL MEDICINE

Mariami Managadze

Student of the Faculty of Public Health, Tbilisi State Medical University

ABSTRACT

Introduction: Microplastics represent one of the most significant challenges in modern environmental medicine due to their widespread distribution and potential adverse effects on human health. These compounds enter the environment through various routes, including marine and freshwater sources, ambient air, and food products, increasing human exposure.

The study aimed to analyze the main sources, global distribution, and pathophysiological effects of microplastics on human health based on recent scientific literature.

Study Methods and Materials: This study is based on a narrative literature review conducted in accordance with PRISMA guidelines to ensure methodological transparency and accuracy. A comprehensive search was performed in the PubMed and Google Scholar databases, covering the period from 2014 to 2024. The following keywords were used: "microplastics," "human health," "bioaccumulation," "microplastics ingestion," and "toxicology of microplastics."

Inclusion criteria were: Peer-reviewed studies focusing on the impact of microplastics on human health, Systematic reviews, meta-analyses, original research articles. After initial screening of 134 articles, 37 met the final eligibility criteria and were analyzed in depth.

Literature management was conducted using Zotero, while Microsoft Excel was used for data synthesis and thematic organization.

Results: The findings indicate that microplastics have bio accumulative properties and are linked to serious health effects, including endocrine disruption, inflammation, immune dysfunction, cancer risk, and neurodegenerative diseases.

Conclusion:
Strengthening control measures across drinking water, food, and air quality to mitigate microplastic exposure, supported by coordinated efforts in environmental regulation, public health, and education.

Keywords: Microplastics, Health risks, Environmental medicine, Bioaccumulation.

Bibliography

Browne, M.A., et al. (2011). *Accumulations of Microplastic on Shorelines Worldwide: Sources and Sinks.* Environmental Science and Technology, 45, 9175–9179.

Hao-Peng Wang, Xu-Hui Huang, Jia-Nan Chen, Meng Dong, Cheng-Zhen Nie, Lei Qin. (2023). *Micro- and nano-plastics in food systems: Distribution, combined toxicity with environmental contaminants, and removal strategies.* Chemical Engineering Journal, 476, 15 November, 146430.

Ivar do Sul, J.A., & Costa, M.F. (2014). *The present and future of microplastic pollution in the marine environment.* Environmental Pollution, 185, 352–364.

Li, Y., Tao, L., Wang, Q., Wang, F., Li, G., Song, M., & Sung. (2023). *Potential Health Impact of Microplastics: A Review of Environmental Distribution, Human Exposure, and Toxic Effects.* Environmental Health, 1(4), 249–257.

Schwabl, P., Köppel, S., Königshofer, P., Bucsics, T., Trauner, M., Reiberger, T., & Liebmann, B. (2019). [Title missing]. [Journal name missing], 171(7), 453–457.

Thompson, R., & Napper, I. (2019). *Microplastics in the Environment.* In Plastics and the Environment (pp. 60–81).

SYNTHESIS OF 5-PHENYL-N-(PYRIDIN-3-YLMETHYL) FURAN-2-CARBOXAMIDE DERIVATIVES THROUGH PD (0) CATALYZED REACTION.

Muhammad Zubair

Prof. Dr., Department of Chemistry, Govt College University, Faisalabad, Pakistan

ABSTRACT

Carboxamide is an amide linkage compound with numerous industrial and medicinal uses. A two-step procedure was used to prepare the carboxamide compound derivatives. The amide compound, such as 5-bromo-*N*-(Pyridine-3-ylmethyl) furan-2-caboxamide, was first synthesized by reacting 5-bromofuran-2-carboxylic acid and pyridin-3-ylmethanamine in a safe and straightforward reaction that was carried out at room temperature with a yield of 80% using DCC, DMAP or dry DCM. The Suzuki-Miyaura cross coupling reaction was used to prepare all the derivatives of 5-bromo-*N*-(Pyridine-3-ylmethyl) furan-2-caboxamide in the second step of this work, which was conducted with the help of different aryl-boronic acids reacting with the appropriate carboxamide with the use of palladium catalyst, this reaction becomes more significant in the formation of C-C bonds. A moderate yield of 45-78% was the percentage product of newly synthesized compounds. All newly synthesized compounds were characterized using a variety of analytical techniques, including ^{1}H NMR, ^{13}C NMR and FT-IR.

ZOONOTIC DISEASES: A COMPREHENSIVE REVIEW OF TOXOPLASMOSIS AND ITS IMPACT ON PUBLIC HEALTH

Shalvi Pawar

JES's SND College of Pharmacy, Babhulgaon, Dist. Nashik, India.

ABSTRACT

Toxoplasmosis is a widespread zoonotic infection caused by the protozoan parasite Toxoplasma gondii, which primarily infects cats and can be transmitted to humans through various routes. The infection is prevalent worldwide, with varying degrees of severity depending on the host's immune status. While many cases are asymptomatic, individuals with compromised immune systems, such as those with HIV/AIDS, organ transplant recipients, or pregnant women, are at a higher risk for severe complications. These complications can include toxoplasmic encephalitis (a life-threatening inflammation of the brain), ocular toxoplasmosis (retinal inflammation leading to vision loss), and congenital toxoplasmosis, which can result in miscarriage, stillbirth, or severe neurological disorders in newborns. The clinical manifestations of toxoplasmosis range from mild, flu-like symptoms in immunocompetent individuals to more severe, life-threatening conditions in those with weakened immunity. Diagnosis relies on a combination of serological tests, such as the detection of IgM and IgG antibodies, as well as molecular diagnostics (e.g., PCR) for detecting T. gondii DNA, and imaging techniques (e.g., CT or MRI) to identify characteristic lesions in the brain. For severe cases, a histopathological examination of tissue samples may be required. Treatment for toxoplasmosis is primarily based on a combination of pyrimethamine and sulfadiazine, which inhibit the parasite's ability to replicate, although alternative therapies such as clindamycin or spiramycin can be used depending on the patient's condition and response to treatment. Immunocompromised patients, including HIV/AIDS patients, may require long-term maintenance therapy to prevent reactivation of the infection. Prevention strategies are essential in reducing the transmission of T. gondii. Control measures in the management of pet cats and prevention of stray animals are also critical in limiting the environmental sources of infection. In conclusion, toxoplasmosis remains a significant public health issue with the potential for severe health consequences, especially for immunocompromised individuals and pregnant women. Early diagnosis, effective treatment, and preventive measures are essential for controlling the spread of this zoonotic disease and mitigating its impact on vulnerable populations. Ongoing research into the molecular biology, epidemiology, and management of toxoplasmosis is crucial to develop more effective strategies for prevention and treatment.

DROUGHT STRESS AND ITS INFLUENCE ON MORPHOLOGICAL, PHYSIOLOGICAL, AND BIOCHEMICAL TRAITS OF MEDICINAL AND AROMATIC PLANTS. A REVIEW

Hamza EL KISSANY

Biotechnology and Sustainable Development of Natural Resources Unit, Polydisciplinary Faculty of Beni Mellal, Sultan Moulay Slimane University, Beni Mellal, Morocco

Hicham EL-BOUKHARY

Biotechnology and Sustainable Development of Natural Resources Unit, Polydisciplinary Faculty of Beni Mellal, Sultan Moulay Slimane University, Beni Mellal, Morocco

Hicham EL KISSANI

Biotechnology and Sustainable Development of Natural Resources Unit, Polydisciplinary Faculty of Beni Mellal, Sultan Moulay Slimane University, Beni Mellal, Morocco

Adil LAAZIZ

Laboratory of Biotechnology, Environment, Agri-food and Health, Faculty of Sciences Dhar El Mahraz, Sidi Mohamed Ben Abdellah University, Fez, Morocco

Abdelouahed HAJJAJI

Biotechnology and Sustainable Development of Natural Resources Unit, Polydisciplinary Faculty of Beni Mellal, Sultan Moulay Slimane University, Beni Mellal, Morocco.

Laboratory of Biotechnology, Environment, Agri-food and Health, Faculty of Sciences Dhar El Mahraz, Sidi Mohamed Ben Abdellah University, Fez, Morocco.

ABSTRACT

Drought stress is one of the most critical abiotic factors limiting the growth, productivity, and quality of aromatic and medicinal plants (AMPs). These plants are particularly valued for their bioactive compounds; however, water deficit significantly affects their morphological, physiological, and biochemical characteristics. Drought stress commonly reduces plant height, leaf area, biomass accumulation, and root development. At the physiological level, it alters photosynthetic activity, stomatal conductance, transpiration rate, and water use efficiency. Moreover, water deficit disrupts cellular homeostasis by increasing reactive oxygen species (ROS) production, leading to oxidative stress. In response, AMPs activate various defense mechanisms, including the accumulation of osmolytes (proline, soluble sugars), enhancement of antioxidant enzyme activities (superoxide dismutase, catalase, peroxidase), and modulation of secondary metabolite production such as phenolics, flavonoids, and essential oils. Interestingly, moderate drought stress may stimulate the biosynthesis of certain secondary metabolites, thereby influencing the medicinal quality of these plants. This review highlights the complex effects of drought stress on morphological, physiological, and biochemical traits of AMPs and discusses adaptive strategies that enhance their tolerance and maintain their phytochemical potential under water-limited conditions.

Keywords: drought stress, AMPs, morphological, physiological, biochemical traits, defense mechanisms, secondary metabolite

QS INHIBITION BY ALGAL COMPOUNDS AGAINST MARINE BIOFILMS

Iram Liaqat

Dr., Tenured Associate Professor, Department of Zoology, Government College University, Lahore,

ABSTRACT

We examined that whether patulin and penicillic acid, two well-known quorum sensing inhibitors (QSI) for human pathogen *Pseudomonas aeruginosa* PAO1, can prevent biofilm formation. The study aims for amplification of a putative *luxS* gene homologue in the marine microorganism *H. pacifica* ATCC 27122, as well as monitoring AI-2 QS in marine organisms. Degenerated primers were designed based on the *luxS* protein sequence of ten gram-negative, □-, □- and □- proteobacteria, and used for *luxS* gene amplification in *H. pacifica*. AI-2 assays were carried out using the well-established *Vibrio harveyi* BB170 AI-2 bioluminescence assay. Effect of penicillic acid on AI-2 induction of *H. pacifica* showed strong inhibitory effect at non-growth inhibitory concentrations compared to patulin having adverse effect at the highest concentration (25 µM) tested in our study. QSIs effect on biofilm forming capability of marine isolates was isolate specific. Detection of bioluminescence in the autoinducer bioassay and the presence of a putative *luxS* gene orthologue are biochemical and genetic evidence for the production of a signalling molecule(s) and provide a first step in characterizing *H. pacifica* quorum sensing. Our study emphasize that QSI compounds must be selected in the specific system in which they are to function and they cannot easily be transferred from one QS system to another.

Keywords: Biofilm formation, *H. pacifica*, AI-2 assay, *LuxS* gene, Patulin, Penicillic acid

Category: Oral presentation

PHOTOCATALYTIC DEGRADATION OF PEFLOXACIN AND CIPROFLOXACIN USING PPY-NIO-MOO_3 COMPOSITE: PERFORMANCE, KINETICS STUDY AND REUSABILITY

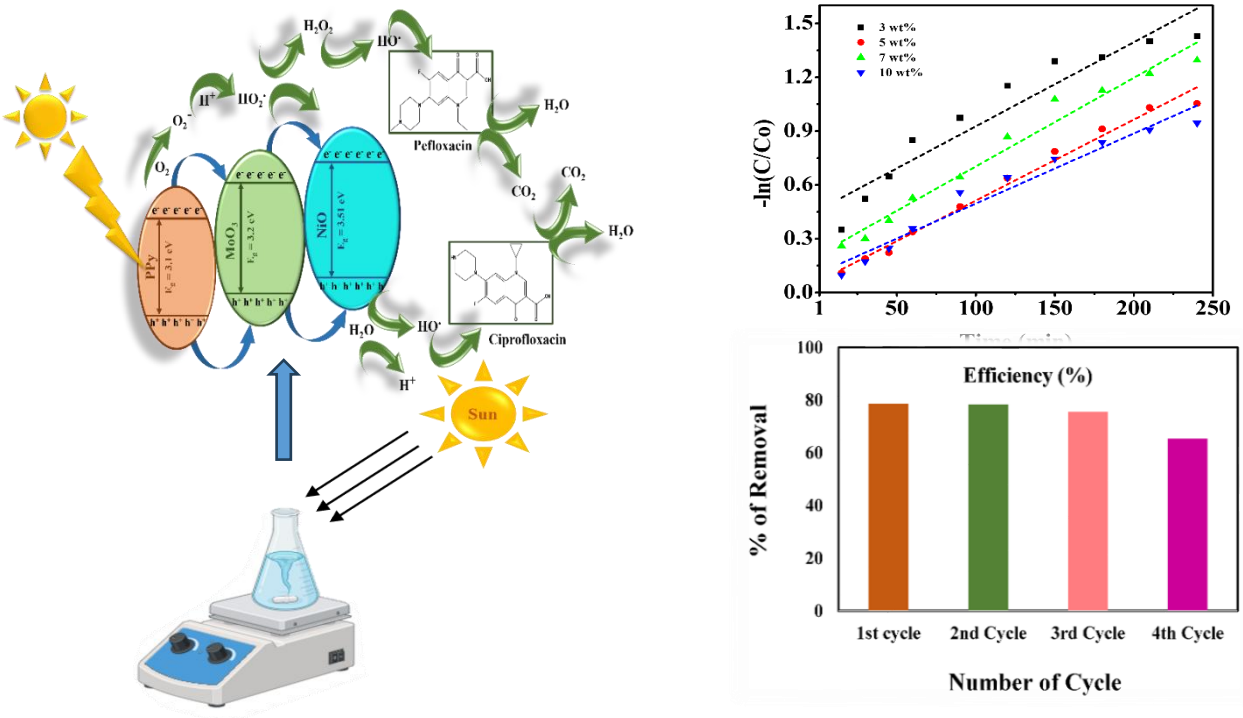
Atia Sanzida

Pabna University of Science and Technology

ABSTRACT

Antibiotics in water are becoming increasingly harmful to the environment. Photocatalytic elimination of antibiotics such as pefloxacin and ciprofloxacin utilizing PPy-NiO-MoO_3 composite and kinetic studies have been examined in this work. PPy-NiO-MoO_3 composite have been produced via in-situ oxidative polymerization using varying quantities of NiO and MoO_3 ranging from 3 wt% to 10 wt%. Techniques including FTIR, FESEM, and EDX have been employed to characterize structural and morphological features of composites. An investigation into the influence of several independent parameters to improve photodegradation efficiency such as pH, photocatalyst dose, antibiotic concentration and temperature has also been studied. Results indicate that the composite containing less NiO and MoO_3 (3 wt%) show greater removal efficiencies of 80.58% for pefloxacin and 83.95% for ciprofloxacin compared to all other formulation combinations. The study of pH revealed that maximum removal (78.25%) of pefloxacin occurs under alkaline conditions (pH 9) whereas maximum removal (76.01%) of ciprofloxacin occurs under acidic conditions (pH 5). A composite dosage of 9 mg yielded the highest removal of pefloxacin (80.58%) and degradation rate. Temperature and antibiotic concentration also had an effect on removal rate. For example, 76.02% removal was achieved at 3 ppm antibiotic concentration and 78.25% removal at 45°C. Conversely, ciprofloxacin yielded the highest removal (83.95%) at antibiotic concentration of 3 ppm. Removals due to variation in composite dosage and temperature were 77.44% and 76.01%, respectively. Composites were shown to be reusable, maintaining removal efficiencies of 75.52% and 65.39% for pefloxacin and 69.85% and 65.15% ciprofloxacin, over three cycles and four cycles, respectively. These data suggest that the PPy-NiO-MoO_3 composite is a highly efficient and sustainable photocatalyst for the treatment of wastewater contaminated with antibiotics.

GRAPHICAL ABSTRACT



FORMULATION, DEVELOPMENT AND COMPARATIVE EVALUATION OF SOLID DISPERSIONS, NANOSUSPENSIONS, AND SELF-NANO EMULSIFYING DRUG DELIVERY SYSTEMS (SNEDDS) FOR ENHANCED ORAL DELIVERY OF AN ANTIRETROVIRAL DRUG

Lakshmi Devi Gottemukkula

Dr., Joginpally B.R. Pharmacy College, Moinabad, R.R. District, Hyderabad, Telangana-500075.

Ravindra Nagasuri

Dr., Joginpally B.R. Pharmacy College, Moinabad, R.R. District, Hyderabad, Telangana-500075.

Sunitha Sampathi

Dr., Department of Pharmacy, Vishwakarma University, Pune, Maharashtra, India-411048

ABSTRACT

The oral bioavailability of many antiretroviral drugs is significantly hindered by their poor aqueous solubility and limited gastrointestinal absorption, leading to suboptimal therapeutic outcomes. To overcome these challenges, this study focuses on the formulation, development, and comparative evaluation of solid dispersions, nanosuspensions, and self-nanoemulsifying drug delivery systems (SNEDDS) to enhance the oral delivery of a selected antiretroviral drug. Solid dispersions were prepared using physical mixing, kneading, rotary solvent evaporation, and lyophilization methods, employing β-cyclodextrins and Soluplus as carriers. Nanosuspensions were developed by sonoprecipitation, while SNEDDS were formulated by water titration using optimised oils, surfactants, and co-surfactants. The formulations were characterised for particle size, polydispersity index, zeta potential, drug content, entrapment efficiency, Fourier transform infrared spectroscopy, crystallinity (XRD, DSC), morphology (SEM), and in vitro drug release profiles. The optimised formulations were prepared for stability studies per the ICH guidelines. *In vivo* studies were performed with New Zealand white rabbits. Among all formulations, SNEDDS showed a significant increase in dissolution rate (98.9%) compared with the plain drug (8.12±1.70) at 60 min. In vivo pharmacokinetic profiles suggest that SNEDDS were dominant with greater C_{max} (4932.7±470.32 ng/ml) as well as AUC_0^t (59458± 200.18 ng-hr/ml) values compared to the plain drug DTG C_{max} (1457.4±321.54ng/ml) and AUC_0^t (19004 ±1100.54ng-hr/ml) due to greater diffusion and dissolution by the nano-sized dispersion formed *in situ*. Finally, administering dolutegravir via oral SNEDDS could be a promising approach to reduce viral replication in the immune system.

Keywords: Antiretroviral drug delivery, nanotechnology, nanosuspensions, Oral bioavailability, Solid dispersions, self-nanoemulsifying drug delivery system (SNEDDS) and solubility enhancement.

ANALYSIS OF DETERMINISTIC AND STOCHASTIC ALCOHOL CONSUMPTION MODELS: STABILITY AND SENSITIVITY

Sara Soulaimani

Chouaib Doukkali University of El Jadida, Natl Sch App Sci, Sci Engineer Lab Energy, El Jadida, Morocco

ABSTRACT

In this paper, we propose a deterministic and stochastic alcohol drinker models, incorporating treatment and relapse mechanisms, to describe the dynamics of alcohol consumption. The population is structured into four interacting compartments: non-drinkers, active alcohol consumers, individuals undergoing treatment, and abstinent individuals. In the deterministic case, an appropriate Lyapunov function is constructed to derive sufficient conditions for the global asymptotic stability of the equilibria. To capture random environmental and behavioral influences, the model is extended to a stochastic formulation through multiplicative perturbations. Numerical simulations are presented to illustrate the theorical results.

Keywords: Alcohol consumption dynamics, deterministic and stochastic modeling, stability analysis, Lyapunov methods, behavioral systems, sensitivity analysis, numerical simulations

THE IMPACT OF SOCIOECONOMIC AND MACROECONOMIC FACTORS ON PHYSICAL ACTIVITY LEVELS IN POLISH WOMEN

Monika LOPUSZANSKA-DAWID

Assoc. Prof., Józef Piłsudski University of Physical Education in Warsaw, Poland, Faculty of Physical Education, Department of Human Biology, ORCID ID: https://orcid.org/0000-0002-3533-5754

ABSTRACT

The social, professional, and political landscape of a given socjety, and specifically the status of women within that socjety, appears to significantly influence both the mental and physical health of this population segment. Over the last few decades, Poland has undergone a series of profound economic, social, and biological transformations, including the systemic transition, accession to the European Union, the COVID-19 pandemic, and the outbreak of war just beyond its eastern border. Living and working conditions have changed drastically, with various groups adapting to these shifts in different ways.

The aim of this study was to evaluate the direction and intensity of changes in the physical activity levels of adult Polish women and to determine whether these changes varied according to macroeconomic factors.

Data from 5,806 women aged 40–50 were analyzed. The variables included physical activity levels, socioeconomic status (level of education), and macroeconomic indicators (Gini coefficient, Gender Inequality Index, total female employment, women in managerial positions, and women in academia). Six birth cohorts were examined in the years 1986, 1991, 1996, 2006, 2019, and 2021, using a consistent methodology across all groups.

Highly statistically significant changes in physical activity levels were observed. The lifestyle of the surveyed women depended significantly on both their socioeconomic status and their specific birth cohort. Macroeconomic indicators were found to exert a highly significant influence on fundamental health behaviors, including physical activity. The data suggest that the better the social standing of women within a society, the more pronounced the trend toward pro-health behaviors.

Research into social disparities and their correlation with macroeconomic indicators regarding health behaviors provides an opportunity to analyze the biological consequences of changes in perceived psychosocial stress within the living environment.

Keywords: physical activity, health behaviors, stress, Covid-19, Poland

STUDY OF THE PREVALENCE OF MALNUTRITION IN RELATION TO SOCIOECONOMIC FACTORS AMONG CHILDREN IN THE CITY OF SALÉ, MOROCCO

SAID AIT MESSAAD

Higher Institute of Nursing Professions and Health Techniques, Safi, Morocco.

Chouaib Doukkali University, Faculty of Sciences El Jadida, Laboratory of Marine Biotechnology and Environment (BIOMARE).

ABSTRACT

The malnutrition affects physical growth, morbidity, cognitive development, reproduction, and work capacity, and consequently has an impact on human performance, health, and survival. It is also one of the main factors underlying many diseases, especially among children, and is particularly prevalent in developing countries, where it affects one in three preschool-aged children.

This is a prospective cross-sectional study. The study focused on children with parasitic diseases who were hospitalized at the Moulay Abdellah Hospital in the city of Salé, Morocco. The children surveyed were between the ages of 0 and 15.

Our study showed a significant association between age and anthropometric status. Indeed, the [4–9] age group is the most affected by chronic malnutrition. Upon analyzing socioeconomic factors, we found that intestinal parasitism is not linked to these factors. Regarding Body Mass Index, it was shown that the factor “number of rooms per household” influences the weight status of the children surveyed.

Keywords: children, mMalnutrition, Socio-economic, Salé, Morocco

MUSCULOSKELETAL HEALTH RISK PROFILING IN ELITE ATHLETES: INTERACTIONS BETWEEN BONE MINERAL DENSITY, LEAN TISSUE AND STRESS-RELATED BONE INJURIES

Anna Kopiczko

Prof. (Assoc.) PhD., Józef Piłsudski University of Physical Education in Warsaw, Faculty of Physical Education, Department of Human Biology, Warsaw, Poland Field of study: Sports Sciences, Anthropology of Sport, ORCID ID: https://orcid.org/0000-0002-1222-113X

Patrycja Widłak

PhD., Józef Piłsudski University of Physical Education in Warsaw, Faculty of Physical Education, Department of Human Biology, Warsaw, Poland. Field of study: Sports Sciences, Physiotherapy and Rehabilitation ORCID ID: https://orcid.org/0000-0003-3433-1310

Joanna Cieplińska

PhD., Józef Piłsudski University of Physical Education in Warsaw, Faculty of Rehabilitation, Department of Clinical Physiotherapy, Warsaw, Poland Field of study: Sports Sciences, Physiotherapy and Rehabilitation ORCID ID: https://orcid.org/0000-0002-6836-6741

ABSTRACT

Aim: The aim of this study was to evaluate determinants of musculoskeletal health in elite athletes, with a focus on the relationship between bone mineral density (BMD), lean body mass, sport discipline (endurance disciplines and combat sports) and the lifetime occurrence of bone stress fractures (BSFs).

Materials and Methods: A total of 129 male professional athletes were included, representing endurance disciplines (long-distance and ultra-distance running) and combat sports (wrestling, judo, Brazilian jiu-jitsu). BMD at the lumbar spine and femoral neck was assessed using dual-energy X-ray absorptiometry (DXA). Body composition parameters were obtained through bioelectrical impedance analysis and anthropometric measurements. Injury history and overuse symptoms were collected using standardized questionnaires and retrospective training records. Exclusion criteria included metabolic and endocrine disorders affecting bone metabolism. The study was conducted in accordance with international ethical standards. The project received a positive opinion on compliance with the principles of ethics from the Bioethics Committee National Institute of Public Health PZH - National Research Institute (Protokol 2/2025). This work was written with financial support of the Ministry of Education and Science as part of the Research Project (UPB No. 14) in Józef Piłsudski University of Physical Education in Warsaw (Poland).

Results: Endurance athletes presented significantly lower BMD values across all analyzed skeletal sites compared to combat sport athletes, alongside a higher prevalence of BSFs. Reduced BMD below age-expected norms was observed exclusively in the endurance group. Athletes in combat sports more frequently reported no history of stress-related fractures. Multivariate analysis revealed that femoral neck BMD was significantly associated with lean mass, sport discipline, and history of BSFs. Lumbar spine parameters were strongly related to muscle mass and training type. Bone quality indicators were also influenced by prior injury occurrence.

Conclusion: Musculoskeletal health in elite athletes is strongly influenced by sport-specific loading patterns and body composition. Endurance athletes may represent a higher-risk group for impaired bone health and stress-related injuries. Routine monitoring of BMD and muscle mass may support early risk identification and inform targeted prevention strategies.

Keywords: bone mineral density; stress fractures, elite athletes; musculoskeletal health, injury prevention

BEYOND FMS: INTEGRATING FUNCTIONAL, MORPHOLOGICAL, AND BIOCHEMICAL MARKERS IN SPORT INJURY RISK ASSESSMENT

Patrycja Widłak

PhD., Józef Piłsudski University of Physical Education in Warsaw, Faculty of Physical Education, Department of Human Biology, Warsaw, Poland, Field of study: Sports Sciences, Physiotherapy and Rehabilitation, ORCID ID: 0000-0003-3433-1310

Anna Kopiczko

Prof. (Assoc.) PhD., Józef Piłsudski University of Physical Education in Warsaw, Faculty of Physical Education, Department of Human Biology, Warsaw, Poland, Field of study: Sports Sciences, Anthropology of Sport, ORCID ID: 0000-0002-1222-113X

Aspasia Dania

PhD., National and Kapodistrian University of Athens, Department of Physical Education and Sport Science, Athens, Greece, Field of study: Physical Education, Pedagogy, ORCID ID: 0000-0003-2829-0479

Piotr Bartnicki

Prof. (Assoc.) PhD., Medical University of Łódź, Faculty of Medicine, Clinic of Nephrology, Arterial Hypertension and Family Medicine, Łódź, Poland, Field of study: Medical Sciences, ORCID ID: 0000-0002-2260-5225

ABSTRACT

Efficient movement patterns and postural stability are key aspects of athletes' readiness and are linked to overuse injury risk. Functional tests identify deficits in mobility, neuromuscular function, and asymmetry, but on their own they are not sufficiently predictive, indicating the need for additional biological and training-related measures.

Injury risk is multifactorial, involving morphological (e.g., body composition) and physiological factors such as energy availability, fatigue, and inflammation. Integrating these variables improves understanding of how training load affects motor function and overload mechanisms.

The study included 48 professional athletes representing team sports. The research protocol involved the assessment of movement pattern quality and dynamic balance using the Functional Movement Screen (FMS) and Y Balance Test (YBT). Additionally, body composition analysis was conducted, along with the assessment of selected biochemical markers related to exercise response, fatigue, and inflammatory processes.

In the analysed group, most athletes achieved FMS scores indicating low to moderate injury risk, while only a small proportion were classified as high risk. ANCOVA analysis revealed a significant effect of body mass on cortisol and CRP concentrations, and of training experience on CK activity. The model for CRP was statistically significant and demonstrated good fit (high R^2), indicating a strong combined influence of the analysed variables on this inflammatory marker. No significant associations were found for IL-6, TNF-α, or TGF-β, and the corresponding models showed low explanatory power.

The findings confirm that although most athletes present a low to moderate injury risk, functional assessment alone is insufficient for accurate prediction. Physiological and morphological factors, such as body mass and training experience, also play a meaningful role through their influence on biochemical markers. The particularly strong associations observed for CRP highlight the importance of inflammatory processes in the context of training load. Overall, the results support the application of a multifactorial approach to injury risk assessment in athletes.

Keywords: functional movement screen; biochemical markers; team sport athletes; injury risk; functional assessment

Source of funding

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no. 13) titled “Assessment of the Relationship Between Selected Lifestyle Factors and the Risk of Sports Injuries in a Young Adult Population.”

LONG-TERM CLINICAL AND METABOLIC OUTCOMES OF LAPAROSCOPIC SLEEVE GASTRECTOMY IN PATIENTS WITH MORBID OBESITY: A RETROSPECTIVE SINGLE-CENTER EXPERIENCE

P.H. Najafguliyeva

Azerbaijan Medical University, Baku, Azerbaijan

Introduction: Morbid obesity is a chronic multifactorial disease associated with severe metabolic, cardiovascular, endocrine, and respiratory complications that significantly reduce quality of life and life expectancy. In recent decades, bariatric surgery has become the most effective long-term treatment method for patients with severe obesity, particularly in cases where conservative management fails to achieve sustained weight reduction. Among modern bariatric procedures, laparoscopic sleeve gastrectomy has gained worldwide acceptance because of its technical simplicity, safety profile, and positive metabolic effects.

Aim the purpose of this study was to evaluate the clinical effectiveness of laparoscopic sleeve gastrectomy in patients with morbid obesity and to analyze postoperative metabolic, hormonal, and functional outcomes during the follow-up period.

Materials and Methods. This retrospective study included 68 patients who underwent bariatric surgery between 2013 and 2024 at the Department of Surgical Diseases of Azerbaijan Medical University. The study population consisted of 12 male and 56 female patients aged between 23 and 64 years.

Preoperative assessment included body mass index (BMI), laboratory investigations, endocrine evaluation, and radiological examinations. BMI values ranged from 35.3 kg/m² to 65.7 kg/m². Patient body weight varied between 94 kg and 193 kg. Associated comorbidities included type II diabetes mellitus and impaired glucose tolerance in 24 patients, dyslipidemia in 39 patients, obstructive sleep apnea in 28 patients, and arterial hypertension in 34 patients. Hyperinsulinemia was detected in 25 patients.

Among female patients, reproductive and hormonal disorders were common and included menstrual irregularities, ovarian dysfunction, hormonal imbalance, and infertility in several cases. All patients underwent laparoscopic sleeve gastrectomy using standard minimally invasive surgical techniques. Postoperative monitoring included assessment of weight loss, metabolic parameters, and resolution of obesity-related disorders.

Results. Postoperative follow-up ranged from 1 to 20 months. Significant weight reduction was observed in the majority of patients, with excess weight loss reaching 50–70% during the first 6 postoperative months. Total body weight reduction ranged from 25% to 48%.Improvement in obesity-related comorbidities was observed in most cases. Sleep apnea resolved completely in 27 patients. Normalization of blood glucose levels occurred in 19 patients with diabetes or impaired glucose tolerance. Cholesterol and triglyceride levels significantly improved in 26 and 32 patients, respectively. Serum insulin levels returned to normal values within the first 6 months in most affected patients.In female patients, substantial improvement in reproductive health was noted, including normalization of menstrual cycles in 34 women. No significant postoperative weight regain was identified during the observation period. Postoperative complications were minimal, and recovery was generally uneventful.

Conclusion. Laparoscopic sleeve gastrectomy is an effective and reliable surgical method for the treatment of morbid obesity and obesity-related metabolic disorders. The procedure provides substantial weight loss, improves metabolic and hormonal balance, and contributes to the resolution of multiple comorbid conditions. Early postoperative outcomes demonstrate that minimally invasive bariatric surgery significantly enhances patient health status and quality of life while maintaining a favorable safety profile.

Keywords: bariatric surgery, morbid obesity, sleeve gastrectomy, metabolic syndrome, laparoscopic surgery

ANTHELMINTIC DRUG RESISTANCE AND THE POTENTIAL OF PLANT-BASED ALTERNATIVES: THE CASE OF *Azadirachta indica (A Review)*

Abah, David Unekwuojo

Department of Biological Sciences, Federal University Lokoja, P.M.B 1154 Lokoja, Kogi state, Nigeria.

Faith Agiounim

Department of Botany, University of Lagos, P.M.B 12003 Akoka, Yaba, Lagos State, Nigeria.

ABSTRACT

Helminthiasis remains one of the most prevalent and debilitating infectious diseases globally, disproportionately affecting populations in tropical and subtropical regions including Nigeria. The prolonged and often indiscriminate use of conventional synthetic anthelmintic drugs, including benzimidazoles, macrocyclic lactones, imidazothiazoles, and salicylanilides, has led to the emergence and spread of anthelmintic drug resistance in helminth populations, threatening the effectiveness of established control programmes. This seminar critically reviews the current global status, molecular mechanisms, and principal drivers of anthelmintic drug resistance in gastrointestinal helminths, and evaluates the scientific evidence supporting plant-based alternatives, with particular focus on *Azadirachta indica* (Neem) as a case study. The review is based on secondary data sourced from peer-reviewed scientific literature, textbooks, and reports from recognised health and agricultural organisations. Findings reveal that resistance to benzimidazoles is now widespread in veterinary helminths across multiple continents, driven by selection pressure from frequent, underdosed, and indiscriminate drug use, poor refugia management, and the absence of effective resistance monitoring systems. Key molecular mechanisms identified include polymorphisms in beta-tubulin isotype 1 genes, increased drug efflux via P-glycoprotein overexpression, and altered receptor binding. Plant-based anthelmintics offer a promising, accessible, and scientifically supported alternative or complement to conventional drugs, with numerous phytochemicals, including tannins, alkaloids, flavonoids, terpenoids, and saponins, demonstrating significant antiparasitic activity *in vitro* and *in vivo*. *Azadirachta indica*, richly endowed with bioactive compounds such as azadirachtin, nimbin, nimbidin, and gedunin, has demonstrated consistent anthelmintic efficacy against major gastrointestinal helminth species in multiple experimental studies, through mechanisms including neuromuscular disruption, interference with helminth reproductive biology, and immunomodulation. This seminar concludes that the anthelmintic potential of *A. indica* is scientifically compelling and warrants further rigorous investigation.

Keywords: Anthelmintic Resistance, *Azadirachta indica*, Gastrointestinal Helminths, Neem, Phytochemicals, Plant-Based Anthelmintics

ISOLATION, CHARACTERIZATION AND THERAPEUTIC APPLICATIONS OF BACTERIOPHAGES AGAINST PATHOGENIC BACTERIA OF THE ESKAPE GROUP

Imane Elbelghiti

Laboratory of Cellular Biology and Molecular Genetics, Faculty of Sciences, Ibn Zohr University, Agadir, Morocco

Noureddine Slimani

Laboratory of Aquatic Systems: Marine and continental ecosystems, Faculty of Sciences, Ibn Zohr University, Agadir, Morocco

Zohra Lemkhente

Laboratory of Medical-Surgical, Biomedicine and Infectiology Research, Faculty of Medicine and Pharmacy, Ibn Zohr University, Agadir, Morocco

Fatima Boubrik

Laboratory of Cellular Biology and Molecular Genetics, Faculty of Sciences, Ibn Zohr University, Agadir, Morocco

Ahmed Belmouden

Laboratory of Cellular Biology and Molecular Genetics, Faculty of Sciences, Ibn Zohr University, Agadir, Morocco

ABSTRACT

Resistance to antimicrobials, including commonly used antibiotics, is a serious global health problem with significant risks to the public.

The emergence of antibiotic resistance compromises our ability to treat common infections, increases the cost of treatment, disrupts the progress we have made in the fight against disease, and thus poses a serious problem for our communities, healthcare systems and economies.

According to the WHO, every year antibiotic-resistant infections cause more than 750,000 deaths, equivalent to more than one death every minute, a figure predicted to rise to 10 million by 2050.

Faced with the scarcity of new antimicrobials on the market and the rapid evolution of bacterial resistance mechanisms, alternative strategies to antibiotic therapy are being developed for the treatment of bacterial infections. These new approaches include the fight against virulence factors, vaccination and modulation of host immunity, as well as protection or regulation of the microbiota and phagotherapy.

Phage therapy is based on the use of natural phages to infect and lyse bacteria at the site of infection. Advances in biotechnology have further expanded the repertoire of potential phage therapies to include new strategies using bioengineered phages and purified phage lytic proteins. Current research into the use of phages and their lytic proteins, particularly against multi-drug resistant bacterial infections, suggests that phage therapy could be used as an alternative or complement to antibiotic treatments.

The aim of this study is to build up a bank of bacteriophages specific to bacteria in the ESKAPE group and then to characterize them functionally and genetically.

Keywords: Antibiotic resistance; Bacteriophages; Phagotherapy; ESKAPE pathogens; Wastewater.

HEALTHCARE EMPLOYEE WELLBEING AS A PREDICTOR OF QUALITY PATIENT CARE: A SYSTEMATIC LITERATURE REVIEW

Najiba Sultani

Research Scholar, Department of Commerce, Mangalore University, India

Dr. Subhashini Srivatsa

Professor, Department of Post Graduate Studies in Commerce, University College Mangalore, India

ABSTRACT

Healthcare employee wellbeing has emerged as an important factor impacting the quality of patient care in healthcare sector. Increasing workplace stress, burnout, workload pressures, and emotional exhaustion among healthcare workers have developed concerns related to their impact on healthcare service delivery. This systematic literature review aims to examine the relationship between healthcare employee wellbeing and quality patient care by analyzing existing scholarly studies published in the fields of healthcare management, occupational health, and organizational behavior. Relevant literature was collected from databases including Google Scholar, Scopus, PubMed, and ScienceDirect using keywords such as healthcare employee wellbeing, job satisfaction, burnout, and patient care quality. The findings show that positive employee wellbeing significantly contributes to improved patient care quality, enhanced healthcare performance, and reduced medical errors. The study further indicates the importance of supportive organizational policies and employee-centered healthcare management practices.

Keywords: Healthcare employee wellbeing, patient care quality, job satisfaction, healthcare workforce, burnout, healthcare management, systematic literature review.

MEDT AND MOLECULAR DYNAMICS INVESTIGATION OF 1,3-DIPOLAR CYCLOADDITION REACTIONS OF FUSED PYRROLE-2,3-DIONES WITH DIPHENYLNITRONE

Soukaina AMEUR

Dr, Molecular Modeling and Spectroscopy Research Team, Chouaib Doukkali University, Faculty of Sciences, Molecular Modeling and Spectroscopy Research Team, El Jadida, Morocco, (ORCID: 0009-0004-4087-8069)

ABSTRACT

This study explores the 1,3-dipolar cycloaddition (1,3-DC) reactions between heterocycle-fused 4-acyl-1H-pyrrole-2,3-diones (FPDs) and diphenylnitrone using Molecular Electron Density Theory (MEDT). Global reactivity indices indicate that the FPD derivatives behave as electrophilic species, whereas diphenylnitrone acts as a nucleophile. The investigated reactions proceed through a one-step asynchronous mechanism, characterized by Bonding Evolution Theory (BET) analysis as a “one-step two-stage” process. In addition, 100 ns molecular dynamics simulations demonstrated the stability of both 2P3B–Ligand1 and 2P3B–Zidovudine complexes. The analyses revealed different stabilization modes, where Ligand1 promotes shape compression of the binding pocket, while Zidovudine enhances active-site stability through an extensive hydrogen-bonding network.

Keywords: 1,3-dipolar cycloaddition; 1H-pyrrole-2,3-diones; nitrones; density functional theory; molecular docking; MD simulation

PHYLOGENETIC CHARACTERIZATION AND *IN VITRO* CONTROL OF *ASPERGILLUS FUMIGATUS*: A CONCERNED FUNGAL CONTAMINANT OF SHRIMP BALACHAO IN BANGLADESH

Tamanna, T

Department of Zoology, Faculty of Biological Sciences, Jahangirnagar University, Savar, Dhaka-1342

Ara, I

Department of Zoology, Faculty of Biological Sciences, Jahangirnagar University, Savar, Dhaka-1342

Siddika, A

Department of Zoology, Faculty of Biological Sciences, Jahangirnagar University, Savar, Dhaka-1342

Amin, R

Department of Zoology, Faculty of Biological Sciences, Jahangirnagar University, Savar, Dhaka-1342

Ahmmed, M.S

Department of Botany, Faculty of Biological Sciences, Jahangirnagar University, Savar, Dhaka1342

Sikder, M.M

Department of Botany, Faculty of Biological Sciences, Jahangirnagar University, Savar, Dhaka1342

Alam, M.N

Department of Botany, Faculty of Biological Sciences, Jahangirnagar University, Savar, Dhaka1342

ABSTRACT

Aspergillus fumigatus has emerged as a potential contaminant of shrimp balachao, a traditional fermented dry fish condiment widely consumed in Bangladesh and is recognized as a common spoilage fungus associated with fermented and semi-fermented food products. This study aimed to morphologically identify *A. fumigatus*, evaluate its growth characteristics, and assess its in vitro control following isolation from shrimp balachao. The fungus was isolated using standard culture techniques and identified based on colony morphology and microscopic features. It exhibited rapid growth, forming black, granular colonies at maturity. Microscopically, the mycelium was hyaline, septate, and well-branched; conidiophores were long and unbranched, terminating in globose vesicles bearing biseriate phialides; and conidia were round to oval, arranged in long chains— confirming its identity as *A. fumigatus*. Among six tested culture media, malt extract agar (MEA) supported the highest mycelial growth, followed by potato dextrose agar (PDA), glucose peptone (GLP), and yeast extract mannitol (YEM). On MEA, the fungus produced black, velvety colonies with profuse sporulation within 7 days of post-inoculation. Optimal growth occurred at 35 °C, followed by 30 °C, and under slightly acidic conditions, with maximum growth observed at pH 5– 6. Under these conditions, colonies were dense, darkly pigmented, rapidly expanding, and highly sporulative. In vitro control assays demonstrated that all tested phytoextracts significantly inhibited fungal growth compared to untreated control. Among them, garlic and ginger extracts showed the most pronounced antifungal activity, achieving complete inhibition at 50% and 75% concentrations. Of the two food preservatives evaluated, sodium benzoate proved more effective than sodium chloride, completely suppressing fungal growth at nearly all tested concentrations. Given that *A. fumigatus* is predominantly airborne, the implementation of improved processing techniques, controlled storage conditions, and the appropriate use of food-grade preservatives is recommended to minimize contamination. To the best of our knowledge, this is the first report of *A. fumigatus* associated with shrimp balachao in Bangladesh.

Keywords: Dry fish fungus, *Aspergillus fumigatus*, growth characteristics, phytoextracts, salt preservatives

STUDY OF THE FRACTURE BEHAVIOR OF DIFFERENT STRUCTURES BY THE EXTENDED FINITE ELEMENT METHOD

Zagane Mohammed El Sallah

University of Tiaret, Department of Mechanical Engineering, city Zaâroura BP 78, Tiaret 14000, Algeria.

University of SidiBel Abbes, Department of Mechanical Engineering, Laboratory Mechanics Physics of Materials (LMPM), BP 89, cite Ben M'hidi, SidiBel Abbes, 22000, Algeria.

Moulgada Abdelmadjid

University of Tiaret, Department of Mechanical Engineering, city Zaâroura BP 78, Tiaret 14000, Algeria.

University of SidiBel Abbes, Department of Mechanical Engineering, Laboratory Mechanics Physics of Materials (LMPM), BP 89, cite Ben M'hidi, SidiBel Abbes, 22000, Algeria.

Baltach Abdelghani

University of Tiaret, Department of Mechanical Engineering, city Zaâroura BP 78, Tiaret 14000, Algeria.

ABSTRACT

The fracture mechanics make it possible to characterize the behavior with cracking of structures using parameters quantifiable in the sense of the engineer, in particular the stress field, the size of the crack and the resistance to cracking of the material. Any structure contains defects, whether they introduced during the production of the part (machining or molding defects for example). The aim of this work is to determine numerically by the finite element method the stress concentration factor Kt of a plate subjected to a tensile loading containing a lateral form defect with different sizes: a semicircle of different radii, a notch with different opening angles and a crack of different lengths. The crack propagation is then determined using the extended finite element technique (X-FEM). The modeling carried out using the ABAQUS calculation code.

Keywords: Finite element method, stress concentration factor Kt, crack, X-FEM

MICROPLASTIC POLLUTION AND HUMAN HEALTH

Alaekwe, I.O.

Department of Chemistry, Federal University Gusau, Zamfara State

ABSTRACT

Microplastics, which are defined as plastic particles smaller than 5 mm that originate from the fragmentation of larger plastics or from purposefully manufactured micro-sized products, are highly persistent, widely distributed, and capable of interacting with environmental and biological systems. This study examines the sources, classification, environmental distribution, and transport pathways of microplastics across aquatic, terrestrial, and atmospheric compartments. The production and widespread use of plastic materials across industrial, domestic, agricultural, and commercial sectors have become a major global environmental problem. The main human exposure routes ingestion, inhalation, and skin contact are further examined, and related health risks such as respiratory conditions, gastrointestinal disturbances, endocrine disruption, immune dysfunction, and possible carcinogenic effects connected to adsorbed toxic chemicals are highlighted. The ecological repercussions of microplastics are also covered, including habitat damage, bioaccumulation in food chains, and effects on aquatic and soil organisms. Along with current control methods like better waste management, regulatory frameworks, public awareness, and the creation of sustainable alternatives, the paper also describes current analytical techniques used for detection and characterization. The study highlights that microplastic contamination is a complex environmental and public health problem that calls for coordinated scientific, technological, and policy-driven solutions. In order to protect ecosystems and human health, combating microplastic contamination necessitates concerted international action centred on prevention, mitigation, and long-term sustainability methods.

Keywords: Microplastics, toxic chemicals, immune dysfunction, global action, bioaccumulation

AI-DRIVEN AND IN SILICO INVESTIGATION OF NOVEL TETRAHYDROPYRAZOLO SCAFFOLDS AS PROMISING SELECTIVE PIM-1 KINASE INHIBITORS AGAINST PROSTATE CANCER

Youssra Ech-Chahdi
Laboratory of Processes, Materials, and Environment (LPME), Faculty of Science and Technology, Sidi Mohamed Ben Abdellah University, Fez, Morocco

Hicham Zaitan
Laboratory of Processes, Materials, and Environment (LPME), Faculty of Science and Technology, Sidi Mohamed Ben Abdellah University, Fez, Morocco

Fouad Khalil
Laboratory of Processes, Materials, and Environment (LPME), Faculty of Science and Technology, Sidi Mohamed Ben Abdellah University, Fez, Morocco

ABSTRACT

Prostate cancer remains a major public health concern due to its high prevalence and the frequent emergence of resistance to existing therapies. Pim-1 kinase, overexpressed in several malignancies, plays a key role in cell proliferation and survival, making it a promising therapeutic target. In this context, our study aimed to identify novel selective Pim-1 inhibitors derived from tetrahydropyrazolo-quinazoline and tetrahydropyrazolo-pyrimidocarbazole scaffolds through an integrated in silico approach. We applied 2D-QSAR modeling, molecular docking, molecular dynamics (MD) simulations, and ADMET profiling to investigate structure–activity relationships, binding affinity, conformational stability, and pharmacokinetic potential. The QSAR model, developed using molecular descriptors computed with RDKit (Python), showed strong predictive performance and helped prioritize the most promising candidates. Docking and MD analyses confirmed favorable binding interactions and stability within the Pim-1 active site, while ADMET evaluations supported their drug-likeness. These findings underscore the power of computational tools in the early phases of drug discovery and highlight the potential of tetrahydropyrazolo-based compounds as selective Pim-1 kinase inhibitors for targeted cancer therapy.

Keywords: Prostate Cancer; PIM-1 Kinase; 2D-QSAR; Molecular Docking; Molecular dynamics; ADMET

OMURGA İMPLANT ENFEKSİYONLARININ TANI VE TEDAVİSİNDE BİLİMSEL KONSENSÜS BİLDİRİMİ: LİTERATÜR DEĞERLENDİRMESİ

Merih ŞİMŞEK

Afyonkarahisar Sağlık Bilimleri Üniversitesi, Tıp Fakültesi, Tıbbi Mikrobiyoloji AD. Afyon, Türkiye

ORCID ID: 0000-0003-2484-5609

Muhammed Zahid ASLAN

Afyonkarahisar Sağlık Bilimleri Üniversitesi, Tıp Fakültesi, Beyin ve Sinir Cerrahisi AD. Afyon, Türkiye

ORCID ID: 0009-0001-3846-6119

ÖZET

Amaç ve Kapsam: Omurga implant enfeksiyonları, omurga ameliyatından sonra ortaya çıkan yani, uzun süreli sakatlığa, ek ameliyatlara ve kronik ağrı sendromuna yol açan enfeksiyonlardır. Omurga implantı ile ilişkili enfeksiyonların kliniği artan boyun-sırt ağrısı, nörolojik bozukluk veya radyolojik inflamasyon bulgusu ile karakterizedir. Bu tip enfeksiyonlar, postoperatif dönemde ya da kronikleşme sürecinde oluşabilmektedir (1,2). Bu çalışmanın amacı güncel literatür ışığında tanı ve tedavi yaklaşımlarını değerlendirmektir.

Materyal ve Yöntem: Çalışma, özellikle son 10 yıl içerisinde yayınlanmış güncel konsensüs bildirimlere ve yüksek etki faktörlü dergilerde yayımlanan klinik çalışmalara ait sonuçlar temel alınarak hazırlanmış bir literatür derlemesidir.

Bulgular: Güncel kanıtlar, enfeksiyonun eradikasyonu ile spinal stabilitenin korunması görüşü arasında önemle ve dikkatle bir denge kurulması gerektiğini bildirmektedir (1,2). Erken dönem enfeksiyonları genellikle cerrahi işlemden sonra 90 gün içinde gelişmektedir. Tanı da manyetik rezonans görüntüleme en duyarlı yöntem olarak kabul edilir. Ancak metal artefaktlar sebebiyle kesin tanı için klinik, laboratuvar ve görüntüleme bulgularını da göz önünde bulundurarak birlikte değerlendirilmesi önem arz etmektedir (1,3,4). Mikrobiyolojik tanı, tedavideki başarının temel şartıdır. Yapılan aerobik ve anaerobik kültürler sonucunda, genellikle ilk izole edilen patojen *Staphylococcus aureus*'dur (5). *Cutibacterium acnes*, spinal implantlarda en sık biyofilm oluşturan patojen olarak bildirilmektedir (6). En sık etken lumbosakral enfeksiyon bölgesinde gram negatif basillerin daha sık izole edildiği bildirilmektedir. Tedavide konsensüs yaklaşım cerrahi debridman ve antibiyotik tedavisidir. Antibiyotik tedavisinin genellikle 12 hafta sürmesi iyileşmeyi sağlamaktadır. Özellikle biyofilm açısından aktif antimikrobiyal ajanlarda kullanılması tedavi başarısını artırmaktadır (7). Özellikle kronik enfeksiyonlarda implantın çıkartılma kararı tedavi için önemlidir (1,5). Bütün bunlarla birlikte, literatürde antibiyotik tedavi süresi konusunda bir konsensüs bulunmamaktadır.

Sonuç: Omurga implantı ilişkili enfeksiyonların tanı ve tedavisinde multidisipliner yaklaşım esastır. Tıbbi mikrobiyoloji, enfeksiyon hastalıkları, radyoloji ve nöroşirurji uzmanlarının birlikte çalışması bu tarz enfeksiyonların tanı ve tedavisindeki başarının kriteridir. Tedavi hastaya göre ayarlanması gereken bir durumdur. Bir başka deyişle, implantın korunması veya çıkartılması ve eş zamanlı olarak antibiyotik kullanımı ve bu antibiyotiğe ait süre gibi kararlar hastaya spesifik verilmesi gereken kararlardır. Sonuç olarak, omurga implant ilişkili enfeksiyonlar yüksek riskli klinik komplikasyonları beraberinde getiren tablolar oluşturur. Bu tarz enfeksiyonlarda erken tanı, antibiyotik tedavisi ve uygun cerrahi operasyonlar başarılı sonuçlar için kritik öneme sahiptir. Ancak son kanıtlarda, özellikle antibiyotik tedavi süreleri bakımından bir konsensüs bulunmamaktadır. Bu nedenle bu alanda daha fazla prospektif çalışmaya ihtiyaç duyulmaktadır.

Anahtar kelimeler: Omurga implant enfeksiyonu, spinal enfeksiyon, antibiyotik tedavisi.

Kaynaklar

1.Tai DBG, Patel R, Lovecchio F, et al. State-of-the-Art Review: Diagnosis and Management of Spinal Implant Infections, Clinical Infectious Diseases. 2024; 79: e65-e71.

2.Kowalski TJ, Berbari EF, Huddleston PM, et al. The management and outcome of spinal implant infections: contemporary retrospective cohort study. Clin Infect Dis. 2007; 44: 91-20.

3.Karczewski D, Schnake KJ, Osterhoff G, et al. Postoperative spinal implant infections (PSII)-a systematic review: what do we know so far and what is critical about it? Global Spine J. 2022; 12: 1231–46.

4.Stradiotti P, Curti A, Castellazzi G, et al. Metal-related artifacts in instrumented spine. Techniques for reducing artifacts in CT and MRI: state of the art. Eur Spine J. 2009; 18: 102-8.

5.Cho OH, Bae IG, Moon SM, et al. Therapeutic outcome of spinal implant infections caused by *Staphylococcus aureus*: a retrospective observational study. Medicine (Baltimore). 2018; 97: e12629.

6. Baroudi M, Daher M, Parks RD, et al. *Cutibacterium acnes* in spine surgery: pathophysiology, diagnosis, and treatment. Spine J. 2024; 24(9): 1545-1552.

7. Renz N, Trampuz A, Zimmerli W. Controversy about the Role of Rifampin in Biofilm Infections: Is It Justified?. Antibiotics (Basel). 2021; 10(2): 165.

STATEMENT OF SCIENTIFIC CONSENSUS ON THE DIAGNOSIS AND TREATMENT OF SPINAL IMPLANT INFECTIONS: LITERATURE REVIEW

ASTRACT

Aim and Scope: Spinal implant infections are infections that occur after spinal surgery, leading to long-term disability, additional surgeries, and chronic pain syndrome. The clinical presentation of spinal implant-related infections is characterized by increased neck and back pain, neurological disorders, or radiological findings of inflammation. These types of infections can occur in the postoperative period or during the chronicity process (1,2). The aim of this study is to evaluate diagnostic and treatment approaches in light of current literature.

Material and Methods: This study is a literature review based on current consensus reports and clinical trial results published in high-impact journals, particularly those published in the last 10 years.

Results: Current evidence indicates that a careful balance must be struck between eradicating the infection and maintaining spinal stability (1,2). Early infections usually develop within 90 days after surgery. Magnetic resonance imaging is considered the most sensitive method for diagnosis. However, due to metal artifacts, it is important to consider clinical, laboratory, and imaging findings together for a definitive diagnosis (1,3,4). Microbiological diagnosis is a fundamental requirement for treatment success. Aerobic and anaerobic cultures usually result in Staphylococcus aureus being the first pathogen isolated (5). Cutibacterium acnes is reported as the most common biofilm-forming pathogen in spinal implants (6). Gram-negative bacilli are more frequently isolated in the lumbosacral infection area. The consensus approach to treatment is surgical debridement and antibiotic therapy. Antibiotic treatment, usually lasting 12 weeks, ensures healing. The use of biofilm-active antimicrobial agents, in particular, increases treatment success (7). The decision to remove the implant is crucial for treatment, especially in chronic infections (1,5). However, there is no consensus in the literature regarding the duration of antibiotic treatment.

Conclusion: A multidisciplinary approach is essential in the diagnosis and treatment of spinal implant-related infections. Collaboration among medical microbiology, infectious diseases, radiology, and neurosurgery specialists is crucial for the success of diagnosing and treating these types of infections. Treatment is tailored to the individual patient. In other words, decisions such as preserving or removing the implant, and the simultaneous use and duration of antibiotic treatment, must be made specifically for each patient. Consequently, spinal implant-related infections present with high-risk clinical complications. Early diagnosis, antibiotic treatment, and appropriate surgical procedures are critical for successful outcomes in such infections. However, recent evidence lacks a consensus, particularly regarding antibiotic treatment durations. Therefore, more prospective studies are needed in this area.

Keywords: Spinal implant infection, spinal infection, antibiotic treatment.

References

1.Tai DBG, Patel R, Lovecchio F, et al. State-of-the-Art Review: Diagnosis and Management of Spinal Implant Infections, Clinical Infectious Diseases. 2024; 79: e65-e71.

2.Kowalski TJ, Berbari EF, Huddleston PM, et al. The management and outcome of spinal implant infections: contemporary retrospective cohort study. Clin Infect Dis. 2007; 44: 91-20.

3.Karczewski D, Schnake KJ, Osterhoff G, et al. Postoperative spinal implant infections (PSII)-a systematic review: what do we know so far and what is critical about it? Global Spine J. 2022; 12: 1231–46.

4.Stradiotti P, Curti A, Castellazzi G, et al. Metal-related artifacts in instrumented spine. Techniques for reducing artifacts in CT and MRI: state of the art. Eur Spine J. 2009; 18: 102-8.

5.Cho OH, Bae IG, Moon SM, et al. Therapeutic outcome of spinal implant infections caused by *Staphylococcus aureus*: a retrospective observational study. Medicine (Baltimore). 2018; 97: e12629.

6. Baroudi M, Daher M, Parks RD, et al. *Cutibacterium acnes* in spine surgery: pathophysiology, diagnosis, and treatment. Spine J. 2024; 24(9): 1545-1552.

7. Renz N, Trampuz A, Zimmerli W. Controversy about the Role of Rifampin in Biofilm Infections: Is It Justified?. Antibiotics (Basel). 2021; 10(2): 165.

BRUSELLOZDA SPİNAL TUTULUM NEDENİYLE UZATILMIŞ VE KOMBİNE EDİLMİŞ ANTİBİYOTİK TEDAVİSİ: GÜNCEL YAKLAŞIM

Merih ŞİMŞEK

Afyonkarahisar Sağlık Bilimleri Üniversitesi, Tıp Fakültesi, Tıbbi Mikrobiyoloji AD. Afyon, Türkiye

ORCID ID: 0000-0003-2484-5609

Muhammed Zahid ASLAN

Afyonkarahisar Sağlık Bilimleri Üniversitesi, Tıp Fakültesi, Beyin ve Sinir Cerrahisi AD. Afyon, Türkiye

ORCID ID: 0009-0001-3846-61

ÖZET

Amaç ve Kapsam: Bruselloz, *Burcella spp.* bakteri türlerinin neden olduğu sistemik bir enfeksiyon hastalığıdır. Fokal komplikasyonların büyük bir kısmında kas iskelet tutulumu görülebilmektedir. Bruselloz yıkıcı etkisinden dolayı, erken tanı ve tedavisi oldukça önemlidir. Spinal bruselloz'un tedavisi için doğru antimikrobiyal rejim ve uygulama süresi konusu hala tartışmalı bir konudur. Günümüzde, nüksler ve hastalığa bağlı oluşan sekeller bildirilen vakalar arasındadır (1). Bu çalışmanın amacı, güncel literatür ışığında spinal bruselloz'un uzatılmış ve kombine edilmiş tedavi yaklaşımlarını değerlendirmektir.

Materyal ve Yöntem: Çalışma, özellikle son 10 yıl içerisinde yayınlanmış güncel bildirimlere ve yüksek etki faktörlü dergilerde yayımlanan klinik çalışmalara ait sonuçlar temel alınarak hazırlanmış bir literatür derlemesidir.

Bulgular: Dünya sağlık örgütü önerilerine göre, spinal tüberkülozun antibiyotik tedavisinde birinci basamak tedavi seçeneği, bir aminoglikozid ile bir tetrasiklin kombinasyonunun 6 hafta süreyle uygulanmasıdır. Tetrasiklinlerden doksisilin aminoglukozidlerden streptomisin tercih edilen kombinasyondur. Yine, dünya sağlık örgütünün önerdiği alternatif antibiyotik rejimi, rifampin ve doksisilinin 6 hafta boyunca uygulanabileceği yönündedir. Ancak spinal bruselloz için tedavi süresinin 8 hafta ve daha fazla olması gerektiği yönünde görüş birliği bulunmaktadır (2). Bu önerilere göre yapılan antibiyotik uygulamalarının sonucunda zaman zaman tedavi başarısızlığı ve nükseden vakalar hala bildirilmektedir (1). Bununla birlikte farklı raporlarda osteoartiküler tutulumda enfeksiyonun tekrar etme oranı %12 olarak bulunmuştur ve en yüksek enfeksiyon tekrarı için tetrasiklin+streptomisin kombinasyonunda bildirilmiştir (3). Son kanıtlara göre, alternatif tedavi rejimleri belirlenmeye çalışılmaktadır. Bunlardan ilki florokinolonlardır. Bunlar, bakterisidal aktiviteleri ve *Brucella spp.* türleri için yüksek duyarlılık oranları ile öne çıkmaktadır. Ayrıca, son kanıtlarda, bu ajanlar kemik ve yumuşak doku enfeksiyonlarına yüksek etkileri nedeniyle spinal bruseloz'da da rifampin ile kombinasyonlarının kullanılabileceği görüşü bildirilmektedir (4,5). Tedavinin başarısız olduğu durumlarda cerrahi operasyona başvurulmaktadır. Ancak operasyonu kabul etmeyen hastalarda Streptomisin+doksisilin+rifampin ve Streptomisin+rifampin+trimetroprim/sülfametoksazol gibi üçlü antibiyotik tedavisinin oldukça başarılı olabileceği bildirilmiştir (5,6,7).

Sonuç: Spinal bruselloza dair yaşanacak sekellerin ve nükslerin önlenmesi için erken tanı ve tedavi hayati önem taşımaktadır. En çok ortaya çıkan klinik sekel tedaviden sonra iyileşmenin gecikmesidir. Spinal bruselozda ilk tercih edilen antibiyotik rejimi 12 hafta süren doksisilin tedavisi ile 3 hafta süren streptomisin kombinasyonudur. Ancak tedavinin başarılı olmadığı durumlarda üçlü antibiyotik tedavisi de öne çıkmaktadır. Antimikrobiyal tedavinin optimal süresi'nin uzatılması cerrahi müdahalelerin sayısını azaltmakla birlikte, sekellerin ve nüksün oranını da azaltmaktadır. Sonuç olarak, spinal tüberkülozda bu oranı daha da aşağıya çekebilmek adına yeni antimikrobiyal ajanlara yönelmek ve bu ajanlarla büyük örneklemli, çok merkezli ve uzun süreli prospektif çalışmalara ihtiyaç duyulmaktadır.

Anahtar Kelimeler: Brucella, spinal bruselloz, antibiyotik tedavisi

Kaynaklar

3. Alp E, Doganay M. Current therapeutic strategy in spinal brucellosis. International Journal of Infectious Diseases. 2008;12: 573-577.

4. Corbel MJ, Alton GG, Ariza J, Banai M, Cosivi O, Diaz R ve diğerleri. İnsanlarda ve hayvanlarda bruselloz. Dünya Sağlık Örgütü. WHO/CDS/EPR/2006.7. Cenevre; 2006.

5. Turgut, M., Turgut, A. & Koşar, U. Spinal brucellosis: Turkish experience based on 452 cases published during the last century. *Acta Neurochir (Wien)*. 2006;**148;**1033–1044.

6. Akova M, Uzun O, Akalin HE, Hayran M, Unal S, Gur D. Quinolones in treatment of human brucellosis: comparative trial of ofloxacin—rifampin versus doxycycline—rifampin. Antimicrob Agents Chemother 1993;37:1831—4.

7. Karabay O, Sencan I, Kayas D, Sahin I. Ofloxacin plus rifampicin versus doxycycline plus rifampicin in the treatment of brucellosis: a randomized clinical trial. BMC Infect Dis 2004;4:18.

8. Pappas G, Seitaridis S, Akritidis N, Tsianos E. Treatment of brucella spondylitis: lesson from an impossible meta-analysis and initial report of efficacy of a fluoroquinolone-containing regimen. Int J Antimicrob Agents 2004;24:502—7.

9. Aljuaid AS, Badirah SB, Abusaeed R, et al. Analysis of antibiotic regimens and outcomes in spinal brucellosis:
insights from a retrospective cohort study in Makkah, Saudi Arabia. J Spine Surg 2024;10(2):264-273

EXTENDED AND COMBINED ANTIBIOTIC TREATMENT DUE TO SPINAL INVOLVEMENT IN BRUCELLOSIS: CURRENT APPROACH

ABSTRACT

Aim and Scope: Brucellosis is a systemic infectious disease caused by the bacterial species Brucella spp. Musculoskeletal involvement can be seen in a large proportion of focal complications. Due to the devastating effects of brucellosis, early diagnosis and treatment are extremely important. The correct antimicrobial regimen and duration of treatment for spinal brucellosis is still a controversial issue. Currently, relapses and sequelae related to the disease are among the reported cases (1). The aim of this study is to evaluate extended and combined treatment approaches for spinal brucellosis in light of current literature.

Material and Methods: This study is a literature review prepared based on current reports, especially those published in the last 10 years, and the results of clinical trials published in high impact factor journals.

Results: According to the World Health Organization recommendations, the first-line treatment option for antibiotic treatment of spinal tuberculosis is the application of a combination of an aminoglycoside and a tetracycline for 6 weeks. Among tetracyclines, doxycycline and among aminoglycosides, streptomycin are the preferred combinations. Again, the alternative antibiotic regimen recommended by the World Health Organization is that rifampin and doxycycline can be applied for 6 weeks. However, there is a consensus that the treatment duration for spinal brucellosis should be 8 weeks or more (2). Treatment failure and relapses are still reported occasionally as a result of antibiotic applications made according to these recommendations (1). However, in different reports, the recurrence rate of infection in osteoarticular involvement has been found to be 12%, and the highest recurrence rate has been reported with the tetracycline+streptomycin combination (3). According to recent evidence, alternative treatment regimens are being sought. The first of these is fluoroquinolones. These stand out with their bactericidal activity and high sensitivity rates for Brucella spp. species. In addition, recent evidence suggests that these agents, due to their high efficacy against bone and soft tissue infections, can also be used in combination with rifampin in spinal brucellosis (4,5). Surgery is resorted to in cases where

treatment fails. However, it has been reported that triple antibiotic therapy such as Streptomycin+doxycycline+rifampin and Streptomycin+rifampin+trimethoprim/sulfamethoxazole can be quite successful in patients who do not accept surgery (6,7).

Conclusion: Early diagnosis and treatment are vital for preventing sequelae and relapses in spinal brucellosis. The most common clinical sequelae is delayed recovery after treatment. The first-choice antibiotic regimen in spinal brucellosis is a combination of 12 weeks of doxycycline treatment and 3 weeks of streptomycin. However, triple antibiotic therapy is also preferred in cases where treatment is unsuccessful. Extending the optimal duration of antimicrobial treatment reduces the number of surgical interventions and also reduces the rate of sequelae and relapses. In conclusion, in order to further reduce this rate in spinal tuberculosis, there is a need to focus on new antimicrobial agents and to conduct large-sample, multicenter, and long-term prospective studies with these agents.

Keywords: Brucella, spinal brucellosis, antibiotic treatment

References

1. Alp E, Doganay M. Current therapeutic strategy in spinal brucellosis. International Journal of Infectious Diseases. 2008;12: 573-577.

2. Corbel MJ, Alton GG, Ariza J, et al. Brucellosis in humans and animals. World Health Organization. WHO/CDS/EPR/2006.7. Geneva; 2006.

3. Turgut M, Turgut A, Koşar U. Spinal brucellosis: Turkish experience based on 452 cases published during the last century. *Acta Neurochir (Wien)*. 2006;**148;**1033–1044.

4. Akova M, Uzun O, Akalin HE, Hayran M, Unal S, Gur D. Quinolones in treatment of human brucellosis: comparative trial of ofloxacin—rifampin versus doxycycline—rifampin. Antimicrob Agents Chemother 1993;37:1831—4.

5. Karabay O, Sencan I, Kayas D, Sahin I. Ofloxacin plus rifampicin versus doxycycline plus rifampicin in the treatment of brucellosis: a randomized clinical trial. BMC Infect Dis 2004;4:18.

6. Pappas G, Seitaridis S, Akritidis N, Tsianos E. Treatment of brucella spondylitis: lesson from an impossible meta-analysis and initial report of efficacy of a fluoroquinolone-containing regimen. Int J Antimicrob Agents 2004;24:502—7.

7. Aljuaid AS, Badirah SB, Abusaeed R, et al. Analysis of antibiotic regimens and outcomes in spinal brucellosis:
insights from a retrospective cohort study in Makkah, Saudi Arabia. J Spine Surg 2024;10(2):264-273

CYSTIC FIBROSIS AND EXERCISE TRAINING

Özge Kuşcu

İzmir Democracy University, Institute of Health Sciences, Department of Physiotherapy and Rehabilitation, İzmir, Turkey, ORCID ID: 0009-0009-0435-1311

Betül Taşpınar

İzmir Democracy University, Faculty of Health Sciences, Department of Physiotherapy and Rehabilitation, İzmir, Turkey, ORCID ID: 0000-0002-3106-2285

Ferruh Taşpınar

İzmir Democracy University, Faculty of Health Sciences, Department of Physiotherapy and Rehabilitation, İzmir, Turkey, ORCID ID: 0000-0002-5084-2949

ABSTRACT

Cystic fibrosis (CF) is an autosomal recessively inherited genetic condition, with a one in four probability of occurrence in children of two carrier parents. This multisystemic disease is more prevalent in populations of European descent, with an estimated incidence ranging between 1 in 3,000 and 1 in 6,000. The evolving demographic structure of CF, along with an increasing number of aging adults presenting with multiple chronic conditions and elevated cardiovascular risk factors, creates challenges for healthcare professionals. Reduced exercise capacity remains common in individuals with CF and is associated with decreased life expectancy. Therefore, early promotion of an active lifestyle and individualized guidance addressing barriers and facilitators to long-term participation are essential.

Physical activity is recognized as one of the top five treatment modalities by individuals with CF. Regular physical activity has been shown to slow decline in lung function by enhancing airway clearance and facilitating sputum expectoration through mechanisms such as hyperventilation, mechanical vibration, coughing, and changes in sputum rheology. In addition, exercise contributes to reduction of exertional dyspnea and improves exercise tolerance. The implementation of individualized exercise programs and promotion of long-term adherence are key factors in maximizing functional outcomes. Furthermore, the use of remote technologies, including mobile applications, wearable devices, and telemedicine, is expected to enhance treatment adherence.

In this study, literature published within the last 10 years on clinical characteristics, genetic basis, and treatment approaches of CF was reviewed using databases such as PubMed, Cochrane, and Google Scholar. The studies consisted of randomized controlled trials and systematic reviews focusing on exercise training, physical activity, and exercise capacity.

CF is characterized by a broad clinical spectrum and leads to significant systemic involvement, particularly affecting the pulmonary system and quality of life. Based on evidence, physiotherapy and rehabilitation play a critical role in multidisciplinary management of the disease.

Keywords: Cystic fibrosis, exercise training, rehabilitation.

COMPARATIVE TRANSCRIPTOMIC ANALYSIS OF DEVELOPMENTAL STAGE OF LUCILIA SERICATA WITH NEXT GENERATION RNA SEQUENCING

Zeyneb ÖZTÜRK

Merve YÜRÜK

ABSTRACT

Purpose of the Study: The benefit of Lucilia sericata arthropod parasite to humans, gained through debridman therapy is already known but there are very restricted number of resources in the world literature about the molecules of the parasite that are active in wound treatment and the character of these molecules. Additionally, it appears that no RNA libraries were created by next-generation sequencing. It is aimed to perform RNASeq analysis of Lucilia sericata and an interpretation of the molecular character of the parasite's secretory enzymes at the RNA level and to reveal their bioinformatics relationship.

material and method: In the study, Lucilia sericata samples were generated under laboratory conditions, samples taken from different life stages were sterilized and developed in the liver environment. Total RNA was isolated from the samples obtained and analyzed using the next generation sequencing method.

Results: High quality was achieved with RNA-seq data obtained from Lucilia sericata samples from all life periods, and the highest number of reads was obtained with 52,869,910 (99.7%) filtered reads in the egg sample and 48,041,726 (99.7%) filtered reads in the pupa sample. While 7,476,208 (98.9%) readings were obtained in the adult sample, Q30> 90% quality was achieved in all samples and it was displayed that the data set was appropriate and profound enough for further analysis. FastQC analyzes revealed high duplication rates, especially in the larval and pupal stages (pupa 97.7%; Larva2 93.2%), which was associated with high gene expression or technical duplications. In differential gene expression analyses, significant differences were observed between life stages. These findings put forward that there are distinct transcriptomic changes specific to developmental stages.

Conclusions: The use of next-generation sequencing technologies in parasitology research; It aids in a more comprehensive understanding of parasite biology, host–parasite interactions, and potential therapeutic targets. RNA-Seq and associated NGS approaches will be one of the fundamental tools in the development of diagnosis, treatment and control methods of parasitic diseases in the future.

Keywords: Lucilia sericata, Transcriptomics, Bioinformatics, RNA-Seq.

1. Master’s Degree, Erciyes University, Faculty of Medicine, Department of Parasitology, zeyneb.yuksel99@gmail.com, +90 5412072603, ORCID ID: https://orcid.org/0009-0001-8206-2859,

2. Assistant Professor, Erciyes University, Faculty of Medicine, Department of Parasitology, merveyuruk@erciyes.edu.tr, +90 5555179955, ORCID ID: https://orcid.org/0000-0003-3295-5322

DEVELOPMENT AND IN VITRO ASSESSMENT OF GINGER (ZINGIBER OFFICINALE) ESSENTIAL OIL-LOADED NANOEMULSION AND NANOEMULGEL FORMULATIONS FOR TOPICAL APPLICATION

Beyza ÇELEN

Department of Pharmaceutical Technology, Hamidiye Institute of Health Sciences, University of Health Sciences, Istanbul, Türkiye, 0009-0007-2137-3323

İmren ESENTÜRK-GÜZEL

Department of Pharmaceutical Technology, Hamidiye Faculty of Pharmacy, University of Health Sciences, Istanbul, Türkiye, 0000-0002-4069-2035

Evren ALGIN YAPAR

Department of Pharmaceutical Technology, Faculty of Pharmacy, Sivas Cumhuriyet University, Sivas, Türkiye, 0000-0002-6504-4608

Ebrar İNAL-KILIÇARSLAN

Department of Pharmacognosy, Faculty of Pharmacy, Bezmialem Vakif University, Istanbul, Türkiye, 0000-0002-6022-1644

Murat KARTAL

Phytotheraphy Research Center, Bezmialem Vakif University, Istanbul, Türkiye, 0000-0003-3538-2769.

Cemre ÖZKANCA

Hamidiye Vocational School of Health Services, University of Health Sciences, 34668, Istanbul, Türkiye, 0000-0002-0342-2060

Sibel DÖŞLER

Department of Pharmaceutical Microbiology, Faculty of Pharmacy, Istanbul University, 34116, Istanbul, Türkiye, 0000-0001-5223-4755

ABSTRACT

Aim: Ginger (*Zingiber officinale*) essential oil is a natural compound with strong antimicrobial and anti-inflammatory effects, and developing suitable carrier systems to enhance its effectiveness in topical applications is important. This study aimed to develop nanoemulsion and nanoemulgel formulations containing ginger essential oil and evaluate their *in vitro* performance, including physicochemical characterization and efficacy against acne vulgaris.

Materials and Methods: The chemical composition of ginger essential oil was analyzed by GC-FID/MS to identify major bioactive components. Nanoemulsions were prepared by ultrasonication, and suitable formulations were selected based on droplet size and polydispersity index (PDI); stability was also assessed. Droplet size, PDI, pH, zeta potential, and conductivity were measured. Morphology was evaluated using STEM. Nanoemulgels were prepared using Carbopol (0.5%) and hyaluronic acid (1.5%), and their rheological, textural, and *ex vivo* bioadhesion properties on pig skin were investigated. Antimicrobial activity was evaluated using agar diffusion, microdilution, and time–kill methods, while cytotoxicity and wound healing were assessed through *in vitro* cell culture and scratch assays.

Results: GC-MS analysis showed that the essential oil mainly consisted of sesquiterpene hydrocarbons, with α-zingiberene (35.56%) as the major component, followed by β-sesquiphellandrene, α-farnesene, ar-curcumene, and β-bisabolene. Optimal nanoemulsions contained 4% essential oil, with droplet sizes of 142–172 nm and PDI values of 0.17–0.21. Nanoemulsion and nanoemulgel formulations increased bioadhesion to porcine skin and showed significant antimicrobial activity against acne-related strains. Additionally, the formulations showed no cytotoxic effects in vitro and enhanced wound healing.

Conclusion: Ginger essential oil-loaded nanoemulsion and nanoemulgel formulations showed suitable physicochemical properties, strong antimicrobial activity against acne-associated microorganisms, good biocompatibility, and improved wound healing. These findings suggest these systems are promising topical treatments for acne vulgaris; however, further *in vivo* and clinical studies are required.

Keywords: Nanoemulsion, Nanoemulgel, *Zingiber officinale*, Ginger Essential Oil, Topical Acne Treatment

TİROİT İNCE İĞNE ASPİRASYON BİYOPSİSİNDE HEMŞİRELİK TEMELLİ NON-FARMAKOLOJİK GİRİŞİMLER

Sinan KORKMAZ

Dicle University, Internal Medicine Nursing, ORCID: 0009-0006-6608-734X

Hamdiye ARDA SÜRÜCÜ

Dicle University, Internal Medicine Nursing, ORCID: 0000-0001-7052-1002

ÖZET

Amaç: Bu çalışmanın amacı, endokrin sistemin işleyişi ve tiroit bezinin fonksiyonları doğrultusunda, tiroit nodüllerinin tanılanmasında kullanılan yöntemleri ve ince iğne aspirasyon biyopsisi sürecinde uygulanan bir hemşirelik yaklaşımlarını ortaya koymaktır.

Materyal ve yöntem: Bu çalışma, literatür taramasına dayalı olarak hazırlanmıştır. Tiroit bezinin değerlendirilmesinde fizik muayene, laboratuvar bulguları, tiroit sintigrafisi, ultrasonografi (USG), bilgisayarlı tomografi (BT) ve manyetik rezonans (MR) gibi görüntüleme yöntemleri incelenmiştir. Ayrıca ince iğne aspirasyon biyopsisi (İİAB) işlemi; yüksek çözünürlüklü (7,5–14 MHz) lineer prob eşliğinde ultrason kılavuzluğunda ve 22–27 gauge iğneler kullanılarak gerçekleştirilen bir yöntem olarak ele alınmıştır. İşlem sırasında hastanın anksiyetesini azaltmaya yönelik hemşirelik girişimleri (müzik terapi, sanal gerçeklik, görsel uyarıcılar ve stres topu kullanımı) değerlendirilmiştir.

Bulgular: Tiroit nodüllerinin yetişkin popülasyonda yaygın olarak görüldüğü ve prevalansının %19–68 arasında değiştiği belirlenmiştir. Kadınlarda, özellikle yaşla birlikte artış göstererek erkeklere oranla daha sık görüldüğü saptanmıştır. Fizik muayenede nodül saptama oranı %1–5 arasında iken, ultrasonografi ile bu oran %20–70'e kadar yükselmektedir. Ultrasonografi ve renkli Doppler ultrasonografinin; radyasyon içermemesi, non-invaziv olması, düşük maliyetli ve kolay ulaşılabilir olması nedeniyle tanıda önemli avantajlar sağladığı görülmüştür. İnce iğne aspirasyon biyopsisinin ise güvenilir ve yaygın kullanılan bir tanı yöntemi olduğu belirlenmiştir. Ayrıca işlem sırasında uygulanan dikkat dağıtıcı hemşirelik yöntemlerinin hastanın konforunu artırdığı gözlemlenmiştir.

Sonuç: Tiroit nodüllerinin tanılanmasında fizik muayene ve görüntüleme yöntemleri birlikte değerlendirilmelidir. Ultrasonografi ve ince iğne aspirasyon biyopsisi, tanı sürecinde önemli ve etkili yöntemlerdir. Endokrin hemşirelerinin hem tanı sürecinde hem de hasta bakımında aktif rol oynadığı; özellikle girişimsel işlemler sırasında uygulanan non-farmakolojik yöntemlerle hasta konforunu artırmada önemli katkı sağladığı sonucuna varılmıştır.

NURSING-BASED NON-PHARMACOLOGICAL INTERVENTIONS IN THYROID FINE NEEDLE ASPIRATION BIOPSY

ABSTRACT

Objective: The aim of this study is to present the methods used in the diagnosis of thyroid nodules and the nursing approaches applied during fine needle aspiration biopsy, in line with the functioning of the endocrine system and the functions of the thyroid gland.

Material and Methods: This study was prepared based on a literature review. Physical examination, laboratory findings, thyroid scintigraphy, ultrasonography (USG), computed tomography (CT), and magnetic resonance imaging (MRI) were examined in the evaluation of the thyroid gland. In addition, fine needle aspiration biopsy (FNAB) was considered as a method performed under ultrasound guidance with a high-resolution (7.5–14 MHz) linear probe and using 22–27 gauge needles. Nursing interventions

aimed at reducing patient anxiety during the procedure (music therapy, virtual reality, visual stimuli, and stress ball use) were evaluated.

Findings: It was determined that thyroid nodules are commonly seen in the adult population, with a prevalence ranging from 19% to 68%. They are more frequent in women than in men, with the incidence increasing with age. While the nodule detection rate on physical examination is between 1% and 5%, this rate increases to 20% to 70% with ultrasonography. Ultrasonography and color Doppler ultrasonography were found to offer significant advantages in diagnosis due to their lack of radiation, non-invasiveness, low cost, and easy accessibility. Fine needle aspiration biopsy was determined to be a reliable and widely used diagnostic method. Furthermore, it was observed that distraction nursing techniques applied during the procedure increased patient comfort.

Conclusion: Physical examination and imaging methods should be evaluated together in the diagnosis of thyroid nodules. Ultrasonography and fine needle aspiration biopsy are important and effective methods in the diagnostic process. Endocrine nurses play an active role in both the diagnostic process and patient care; It has been concluded that non-pharmacological methods, especially those applied during interventional procedures, make a significant contribution to improving patient comfort.

ATTENTION DEFICIT HYPERACTIVITY DISORDER IN FAMILY MEDICINE: A CURRENT REVIEW FROM DIAGNOSIS TO TREATMENT

A Review Article

Deniz ALMAK

Balıkesir Bandırma Family Medicine Unit No.056, Department of Family Medicine

ORCID: 0000-0001-6744-5299

Objective:
This review aims to synthesize current evidence on the diagnosis, screening, pharmacological and non-pharmacological management, and comorbidity assessment of attention-deficit/hyperactivity disorder (ADHD) in family medicine practice, and to outline strategies for early identification in primary care settings.

Methods:
A structured literature search was conducted in PubMed/MEDLINE and Web of Science for studies published between January 2015 and December 2024. Current clinical guidelines, including the American Academy of Pediatrics (AAP 2019), NICE (2018), and DSM-5-TR criteria, were also reviewed. Eligibility was based on predefined inclusion criteria related to ADHD diagnosis and management in primary care. Observational studies were assessed using the Newcastle–Ottawa Scale, while other study designs were evaluated using appropriate critical appraisal tools. Of 312 screened records, 27 studies met the inclusion criteria and were included in the final synthesis.

Results:
Stimulant medications, including methylphenidate and amphetamine salts, remain the first-line pharmacological option for ADHD, with response rates of 70–80% in children and adolescents. Atomoxetine is an effective alternative for patients who do not respond to stimulants or who present with comorbid anxiety or tic disorders. The use of DSM-5-TR diagnostic criteria in combination with validated rating scales such as SNAP-IV and Conners is associated with improved diagnostic accuracy. Evidence suggests that 60–80% of individuals with ADHD have at least one psychiatric comorbidity. Non-pharmacological interventions, particularly parent training programs and cognitive behavioral therapy (CBT), provide additional benefit when combined with pharmacological treatment.

Conclusion:
Family physicians play a central role in ADHD management by integrating structured screening tools into routine practice, optimizing pharmacological treatment, and facilitating multidisciplinary care. Strengthening shared-care models and expanding ADHD-focused training in family medicine curricula remain essential for improving early diagnosis and long-term outcomes

Keywords: ADHD; primary care, family medicine; diagnosis, screening

BEYAZ KİNOA TOHUMLARINA (*CHENOPODIUM QUINOA* WILLD.) UYGULANAN ÇİMLENDİRME VE/VEYA FERMANTASYON İŞLEMLERİNİN TOPLAM FENOLİK İÇERİK ÜZERİNE ETKİSİ

Semanur GÖZ

Erciyes Üniversitesi, Sağlık Bilimleri Enstitüsü, Beslenme ve Diyetetik Anabilim Dalı, Kayseri, Türkiye

Kevser KARAMAN

Erciyes Üniversitesi, Ziraat Fakültesi, Tarımsal Biyoteknoloji Bölümü, Kayseri, Türkiye
Erciyes Üniversitesi, Genom ve Kök Hücre Araştırma Merkezi (GENKÖK), Kayseri, Türkiye

Armağan YÜRÜK

Erciyes Üniversitesi, Sağlık Bilimleri Fakültesi, Beslenme ve Diyetetik Bölümü, Kayseri, Türkiye

Kanykei KANATBEKOVA

Erciyes Üniversitesi, Fen Bilimleri Enstitüsü, Bahçe Bitkileri Anabilim Dalı, Kayseri, Türkiye

AMAÇ: Kinoa tohumlarına uygulanan biyoproseslerin etkileri literatürde çoğunlukla çimlendirme veya fermantasyon işlemlerinden biri ile sınırlı olarak incelenmiş olup, bu işlemlerin kombine etkilerine yönelik çalışmalar sınırlıdır. Bu çalışmada, çimlendirme ve/veya fermantasyon işlemlerinin beyaz kinoa tohumlarının toplam fenolik içeriği (TPC) üzerindeki etkisinin belirlenmesi amaçlanmıştır.

MATERYAL VE YÖNTEM: Beyaz kinoa tohumları (*Chenopodium quinoa* Willd.) oda sıcaklığında 48 saat süreyle çimlendirilmiş ve liyofilize edilmiştir. Fermantasyon, ham ve çimlendirilmiş kinoa örneklerinde; spontan fermantasyon, *Lactobacillus fermentum*, *Lactobacillus plantarum*, *Lactobacillus sakei* ve bu üç suşun kombinasyonu ile, ilgili starter kültürlerin inokülasyonunu takiben 37 °C'de, 120 rpm'de çalkalamalı inkübasyon koşullarında 30 saat süreyle gerçekleştirilmiş; fermantasyon sonrası örnekler liyofilize edilmiştir. Tüm örneklerden %80 (v/v) etanol kullanılarak ekstraksiyon gerçekleştirilmiş TPC analizi üç paralel olarak yürütülmüştür. TPC tayini Folin–Ciocalteu yöntemi ile gerçekleştirilmiş, 765 nm'de ölçülen absorbans değerleri gallik asit standart eğrisi kullanılarak mg GAE/g cinsinden hesaplanmıştır. Elde edilen veriler tek yönlü varyans analizi (ANOVA) ve Tukey çoklu karşılaştırma testi ile değerlendirilmiştir. Bu çalışma Erciyes Üniversitesi Bilimsel Araştırma Projeleri Koordinasyon Birimi tarafından desteklenmiştir (Proje No: TYL-2025-15616).

BULGULAR: TPC değerlerinin uygulanan işlemlere bağlı olarak istatistiksel olarak anlamlı düzeyde farklılık gösterdiği belirlenmiştir ($p<0.001$). Kontrol grubunda TPC değeri 1.35 ±0.07 mg GAE/g olarak saptanırken, çimlendirme işlemi ile bu değerin 1.52 ±0.05 mg GAE/g'ye yükseldiği, ancak bu artışın istatistiksel olarak anlamlı olmadığı belirlenmiştir ($p>0.05$). Ham tohumlara uygulanan fermantasyon işlemlerinde TPC değerlerinin 2.13 ±0.16–3.29 ±0.11 mg GAE/g aralığında değiştiği ve en yüksek değerin *L. fermentum* ile gerçekleştirilen fermantasyonda (3.29 ±0.11 mg GAE/g) elde edildiği saptanmıştır. Tüm fermantasyon uygulamalarının, kontrol ve çimlendirme gruplarına kıyasla TPC değerlerinde istatistiksel olarak anlamlı artış sağladığı belirlenmiştir ($p<0.05$). Çimlendirme ve fermantasyonun birlikte uygulandığı örneklerde TPC değerlerinin 2.27 ±0.06 ile 4.26 ±0.29 mg GAE/g aralığında olduğu belirlenmiş olup, bu grupların tamamında elde edilen değerlerin kontrol ve yalnızca çimlendirme uygulanan gruplara kıyasla istatistiksel olarak anlamlı düzeyde daha yüksek olduğu saptanmıştır ($p<0.05$).

SONUÇ: Elde edilen bulgular, çimlendirmenin TPC üzerinde sınırlı bir etkiye sahip olduğunu, fermantasyonun ise TPC'yi anlamlı düzeyde yükselttiğini göstermektedir. Çimlendirme ve fermantasyonun birlikte uygulanması ise tekil uygulamalara kıyasla daha yüksek TPC değerleri sağlayarak, bu biyoproseslerin kinoanın fonksiyonel özelliklerinin geliştirilmesinde etkili bir yaklaşım olduğunu ortaya koymaktadır.

Anahtar Kelimeler: Kinoa, çimlendirme, fermantasyon, toplam fenolik içerik

EFFECT OF GERMINATION AND/OR FERMENTATION PROCESSES APPLIED TO WHITE QUINOA SEEDS (*CHENOPODIUM QUINOA* WILLD.) ON TOTAL PHENOLIC CONTENT

OBJECTIVE: The effects of bioprocesses applied to quinoa seeds have mostly been investigated in the literature individually, focusing either on germination or fermentation, whereas studies evaluating their combined effects remain limited. This study aimed to determine the effects of germination and/or fermentation on the total phenolic content (TPC) of white quinoa seeds.

MATERIALS AND METHODS: White quinoa seeds (*Chenopodium quinoa* Willd.) were germinated at room temperature for 48 h and subsequently lyophilized. Fermentation was performed on both raw and germinated samples using spontaneous fermentation, *Lactobacillus fermentum*, *Lactobacillus plantarum*, *Lactobacillus sakei*, and a combination of these strains. Following inoculation, fermentation was carried out at 37 °C and 120 rpm under shaking conditions for 30 h, after which the samples were lyophilized. Extraction was performed using 80% (v/v) ethanol, and TPC analysis was conducted in triplicate. TPC was determined using the Folin–Ciocalteu method, and absorbance measured at 765 nm was expressed as mg GAE/g using a gallic acid standard curve. Data were analyzed using one-way ANOVA followed by Tukey's multiple comparison test. This study was supported by the Erciyes University Scientific Research Projects Coordination Unit (Project No: TYL-2025-15616).

RESULTS: TPC values differed significantly depending on the applied treatments ($p<0.001$). The control group exhibited a TPC value of 1.35 ±0.07 mg GAE/g, which increased to 1.52 ±0.05 mg GAE/g following germination; however, this increase was not statistically significant ($p>0.05$). In fermentation treatments, TPC values ranged from 2.13 ±0.16 to 3.29 ±0.11 mg GAE/g, with the highest value observed in samples fermented with *L. fermentum*. All fermentation treatments resulted in a statistically significant increase in TPC compared to the control and germination groups ($p<0.05$). In combined treatments, TPC values ranged from 2.27 ±0.06 to 4.26 ±0.29 mg GAE/g, and all groups exhibited significantly higher values than the control and germination-only groups ($p<0.05$).

CONCLUSION: Germination had a limited effect on TPC, whereas fermentation significantly increased TPC. The combined application resulted in higher TPC values than individual treatments, indicating that these bioprocesses are effective strategies for enhancing the functional properties of quinoa.

Keywords: Quinoa, germination, fermentation, total phenolic content

SCREEN TIME, SLEEP DISORDERS, AND CHRONOTYPE IN CHILDREN AND ADOLESCENTS WITH AUTISM SPECTRUM DISORDER: A RECENT REVIEW

Tilbe Erten Almak

Bandırma Onyedi Eylül University Faculty of Medicine, Department of Child and Adolescent Psychiatry, ORCID: 0000-0001-7738-0468

Objective: Sleep disturbances affect 40–80% of children and adolescents with autism spectrum disorder (ASD), with circadian rhythm disruption, melatonin dysregulation, and chronotype shifts as key components. With increasing digital device use, the impact of screen time on sleep and chronotype has gained attention; however, existing findings remain fragmented. This review aims to synthesize studies published between 2015 and 2025 to clarify the relationship between screen time, sleep disturbances, and chronotype in youth with ASD and to highlight their clinical implications.

Materials and Methods: A literature search was conducted in PubMed and Web of Science using the keywords "autism spectrum disorder," "screen time," "sleep," "chronotype," "circadian rhythm," and "melatonin." Original studies, systematic reviews, and meta-analyses published in English between 2015 and 2025 were included.Studies were evaluated for methodological quality and clinical relevance, and findings were synthesized using a narrative approach

Results: Individuals with ASD frequently exhibit circadian rhythm abnormalities, delayed melatonin secretion, and an evening chronotype. Studies conducted during the COVID-19 pandemic reported increased sleep problems and a shift toward eveningness. Observational studies and meta-analyses indicate a significant association between screen time and ASD, with blue light exposure contributing to melatonin suppression and delayed circadian phase. Higher screen exposure is associated with prolonged sleep onset latency, increased nocturnal awakenings, and reduced morningness. Melatonin supplementation has been shown to improve sleep onset latency and total sleep duration.

Conclusion: Current evidence suggests that increased screen time negatively affects sleep patterns and chronotype in children and adolescents with ASD. Routine assessment of screen habits and sleep hygiene, along with parental guidance on limiting evening screen exposure and maintaining consistent sleep schedules, is recommended. Further controlled studies, particularly in Turkey, are needed.

Keywords: autism spectrum disorder, screen time, sleep, chronotype

EVALUATION OF THE INHIBITORY EFFECTS OF IMIDAZOLE-THIAZOLE DERIVATIVES ON COX-1/2 AND 5-LOX ENZYMES

Sevde Nur BİLTEKİN KALELİ

Istanbul Medipol University, School of Pharmacy, Department of Pharmaceutical Microbiology, Istanbul, Türkiye, ORCID: 0000-0003-1896-2729

ABSTRACT

Objective: Inflammation is a complex biological response to tissue injury, where mediators synthesized via the arachidonic acid pathway play a pivotal role. Traditional nonsteroidal anti-inflammatory drugs (NSAIDs) are often limited by gastrointestinal and cardiovascular side effects due to their mechanism of action. This study aims to evaluate the potential of a series of 2-[(1,5-disubstituted phenyl-1H-imidazol-2-yl)thio]-N-(thiazol-2-yl)acetamide derivatives as safer, dual-pathway (COX and 5-LOX) inhibitors. This dual-targeting approach represents a promising strategy to overcome the 'leukotriene switch' often associated with selective COX inhibitors, potentially offering a superior safety profile for chronic inflammatory conditions.

Materials and Methods: The inhibitory activities of nine compounds (Compounds 1-9) against COX-1, COX-2, and 5-lipoxygenase (5-LOX) enzymes were assessed *in vitro* using fluorometric and colorimetric enzyme immunoassay kits. 5-LOX inhibition was tested at a concentration of 10 µM, while IC_{50} values were calculated for COX isoenzymes to determine potency and selectivity indices. Additionally, the biosafety profiles of these derivatives were determined through *in vitro* cytotoxicity assays using the HEK293 (human embryonic kidney) cell line via the MTT method.

Results: The findings indicated that Compound 1 exhibited potent and selective COX-2 inhibition with an IC_{50} value of 2.53 µM demonstrating a favorable selectivity ratio over COX-1. Several other derivatives also demonstrated significant inhibitory capacity against the 5-LOX enzyme. Furthermore, cytotoxicity analyses showed that the molecules maintained over 70% cell viability in HEK293 cells at the indicated concentration revealing a promising therapeutic potential.

Conclusion: In conclusion, the high selectivity of Compound 1 and the dual inhibitory activity of certain derivatives on the 5-LOX enzyme suggest that these heterocyclic structures serve as promising lead compounds. These molecules provide a robust scaffold for the development of next-generation anti-inflammatory drugs with reduced side effects and enhanced efficacy in blocking multiple inflammatory cascades.

Key words: COX-2, 5-LOX, imidazothiazole, HEK293.

REFERENCES

Yarla, N. S., Pathuri, G., Gali, H., Terzyan, S., Panneerselvam, J., Chandrakesan, P., ... & Rao, C. V. (2020). Discovery and development of a novel mPGES-1/5-LOX dual inhibitor LFA-9 for prevention and treatment of chronic inflammatory diseases. *Journal of inflammation research*, 1261-1278.

Allaj, V., Guo, C., & Nie, D. (2013). Non-steroid anti-inflammatory drugs, prostaglandins, and cancer. *Cell & bioscience*, *3*(1), 8.

Katori, M., & Majima, M. (2000). Cyclooxygenase-2: its rich diversity of roles and possible application of its selective inhibitors. *Inflammation Research*, *49*(8), 367-392.

Vane, J. R., & Botting, R. M. (1998). Anti-inflammatory drugs and their mechanism of action. *Inflammation Research*, *47*(Suppl 2), 78-87.

DOĞUM SONRASI FASİYAL VALSALVA PURPURASI: OLGU SUNUMU

Taha GÜVEN

Van Eğitim ve Araştırma Hastanesi, Deri ve Zührevi Hastalıkları Kliniği, Van, Türkiye, ORCID ID: 0000-0002-8407-6541

ÖZET

Amaç: Benign parturient purpura, doğumun ikinci evresinde kuvvetli ıkınma sırasında oluşan Valsalva manevraları ile ilişkili peteşiyal-purpurik döküntü olarak tanımlanmıştır (1). Bu bildiride, doğum sırasında ıkınma sonrasında yüzde purpurik lezyonlar gelişen bir olgunun sunulması amaçlandı.

Materyal ve Yöntem: 36 yaşında kadın hasta, normal vajinal doğum sonrası kadın hastalıkları ve doğum servisinde yatmakta iken yüzde gelişen kızarık döküntüler nedeniyle tarafımıza danışıldı. Hastanın doğum eyleminde ıkınma öyküsü mevcuttu ve herhangi bir obstetrik komplikasyon bildirilmedi.

Bulgular: Dermatolojik muayenede, bilateral yanaklarda daha belirgin olmak üzere tüm yüzde basmakla solmayan peteşiyal-purpurik maküller izlendi. Ek sistemik bulgu, mukozal kanama veya ekimoz saptanmadı. Laboratuvar testleri normaldi. Klinik bulgular ve doğum sırasında ıkınma öyküsü birlikte değerlendirildiğinde olgu valsalva purpurası ile uyumlu kabul edildi. Hastaya lezyonların benign ve kendini sınırlayıcı nitelikte olduğu anlatılarak takip önerildi.

Sonuç: Valsalva purpurası, kapalı glottise karşı zorlu ekspirasyon veya benzer basınç artırıcı durumlar sonrasında gelişen purpura olarak bildirilmiştir (2). Valsalva manevrası sırasında artan intratorasik veya intraabdominal basıncın deri kapillerlerinde rüptüre yol açarak purpuraya neden olabileceği belirtilmiştir (3). Kusma, öksürme, hapşırma, balon şişirme ve ağırlık kaldırma gibi çeşitli aktivitelerin Valsalva purpurası ile ilişkili olduğu bildirilmiştir (2, 3). Yüzde gelişen peteşiyal-purpurik lezyonlarda hematolojik, vaskülitik, travmatik ve enfeksiyöz nedenler ayırıcı tanıda değerlendirilmelidir (3).

Anahtar Kelimeler: Valsalva purpurası, ıkınma, doğum, fasiyal purpura



Şekil 1. Yüzde purpuralar

Kaynaklar

1. Wilkin JK. Benign parturient purpura. *JAMA.* 1978;239(10):930. doi:10.1001/jama.1978.03280370026015.

2. Galadari AA, Al Otaibi M. Valsalva purpura on the face of a 7-year-old child. *J Med Life.* 2023;16(12):1869-1871. doi:10.25122/jml-2023-0447.

3. Rifaioğlu EN, Ekiz Ö, Şen BB, Doğramacı AÇ. Facial purpura in a child after inflating a balloon. *J Turk Acad Dermatol.* 2014;8(1):1481c3. doi:10.6003/jtad.1481c3.

POSTPARTUM FACIAL VALSALVA PURPURA: A CASE REPORT

ABSTRACT

Objective: Benign parturient purpura has been defined as a petechial-purpuric eruption associated with Valsalva maneuvers occurring during forceful straining in the second stage of labor (1). In this report, we aimed to present a patient who developed purpuric lesions on the face after straining during labor.

Materials and Methods: A 36-year-old woman was referred to our department for erythematous eruptions facial eruptions while she was hospitalized in the obstetrics and gynecology ward after normal vaginal delivery. The patient had a history of straining during labor, and no obstetric complication was reported.

Results: Dermatological examination revealed non-blanching petechial-purpuric macules on the entire face, more prominent on both cheeks. No additional systemic findings, mucosal bleeding, or ecchymosis were detected. Laboratory tests were normal. Based on the clinical findings and the history of straining during labor, the case was considered consistent with Valsalva purpura. The patient was informed that the lesions were benign and self-limiting, and follow-up was recommended.

Conclusion: Valsalva purpura has been reported as purpura developing after forceful expiration against a closed glottis or similar pressure-increasing conditions (2). It has been suggested that increased intrathoracic or intra-abdominal pressure during the Valsalva maneuver may cause purpura by leading to rupture of dermal capillaries (3). Various activities such as vomiting, coughing, sneezing, inflating a balloon, and weightlifting have been reported to be associated with Valsalva purpura (2, 3). In petechial-purpuric lesions developing on the face, hematologic, vasculitic, traumatic, and infectious causes should be considered in the differential diagnosis (3).

Keywords: Valsalva purpura, straining, labor, facial purpura.



Figure 1. Facial purpura

References

1. Wilkin JK. Benign parturient purpura. *JAMA.* 1978;239(10):930. doi:10.1001/jama.1978.03280370026015.

2. Galadari AA, Al Otaibi M. Valsalva purpura on the face of a 7-year-old child. *J Med Life.* 2023;16(12):1869-1871. doi:10.25122/jml-2023-0447.

3. Rifaioğlu EN, Ekiz Ö, Şen BB, Doğramacı AÇ. Facial purpura in a child after inflating a balloon. *J Turk Acad Dermatol.* 2014;8(1):1481c3. doi:10.6003/jtad.1481c3.

PREAURİKÜLER YERLEŞİMLİ AKSESUAR AURİKULA: OLGU SUNUMU

Taha GÜVEN

Van Eğitim ve Araştırma Hastanesi, Deri ve Zührevi Hastalıkları Kliniği, Van, Türkiye, ORCID ID: 0000-0002-8407-6541

ÖZET

Amaç: Aksesuar aurikula, dış kulağın gelişimsel konjenital malformasyonlarından biridir ve en sık preauriküler bölgede yerleşir. Genellikle doğumda mevcut olmasına rağmen geç tanı alabilir. Deri renginde, saplı veya sapsız olabilen papül veya nodül şeklinde izlenir (1). Bu bildiride, sol kulak tragus ve preauriküler alanda yerleşen nodüller şeklinde aksesuar aurikula saptanan bir olgunun sunulması amaçlanmıştır.

Materyal ve Yöntem: 18 yaşında erkek hasta, sol kulak çevresinde kitle şikâyeti ile kliniğimize başvurdu. Görünüm dışında herhangi bir şikâyeti olmadığı, doğuştan beri var olduğu öğrenildi. Bilinen ek hastalığı, aile öyküsü yoktu. Lezyonların lokalizasyonu, klinik morfolojisi ve eşlik eden sistemik hastalık ya da konjenital anomali varlığı açısından muayene bulguları kaydedildi.

Bulgular: Dermatolojik muayenede sol kulak tragus üzerinde ve sol preauriküler bölgede deri renginde, iki adet saplı nodül izlendi. Başka lokalizasyonda lezyon görülmedi. Hastada eşlik eden sistemik bulgu veya ek konjenital anomali saptanmadı. Klinik bulgular izole aksesuar aurikula ile uyumlu olarak değerlendirildi (Şekil 1). Kozmetik açıdan tedavi talebi olan hasta lezyonun eksizyonu açısından ilgili cerrahi branşa yönlendirildi.

Sonuç: Aksesuar aurikül/aksesuar tragus, dış kulağın konjenital malformasyonlarından olup birinci faringeal ark gelişim anomalisiyle ilişkilidir (2, 3). En sık preauriküler bölgede, tragus anteriorunda görülür; bununla birlikte bukkal ve intraaurikuler yerleşimli de olabilir (2). Klinik olarak yumuşak veya sert, saplı veya sapsız; deri renginde nodül ya da yassı lezyonlar şeklinde izlenebilir (2, 3). Genellikle izole ve soliter görülmekle birlikte, multipl lezyonlar da olabilir; ayrıca ek konjenital anomaliler ve Goldenhar sendromu gibi bazı sendromlar ile ilişkili olabileceğinden tanı konulduğunda eşlik edebilecek patolojiler dışlanmalıdır (3). Ayırıcı tanıda akrokordon, auriküler fistül, fibrom, polip, lipom ve epidermoid kist gibi lezyonlar yer alır; histopatolojik incelemede kıkırdak dokusu içerebilmesi ayırıcı tanıda destekleyici olabilir (2, 3). Tedavide cerrahi eksizyon uygulanabilir ve kozmetik amaçla tercih edilebilir (1, 3).

Anahtar Kelimeler: Aksesuar aurikula, aksesuar tragus, konjenital malformasyon



Şekil 1. Aksesuar aurikula

Kaynaklar

1. Bahrani B, Khachemoune A. Review of accessory tragus with highlights of its associated syndromes. Int J Dermatol. 2014;53(12):1442-1446. doi:10.1111/ijd.12369.

2. Hwang J, Cho J, Burm JS. Accessory auricle: classification according to location, protrusion pattern and body shape. Arch Plast Surg. 2018;45(5):411-417. doi:10.5999/aps.2017.01292.

3. Jansen T, Romiti R, Altmeyer P. Accessory tragus: report of two cases and review of the literature. Pediatr Dermatol. 2000;17(5):391-394. doi:10.1046/j.1525-1470.2000.017005391.x.

PREAURICULAR ACCESSORY AURICLE: A CASE REPORT

ABSTRACT

Objective: Accessory auricle is a developmental congenital malformation of the external ear and is most commonly located in the preauricular region. Although it is usually present at birth, diagnosis may be delayed. It may present as a skin-colored, pedunculated or non-pedunculated papule or nodule (1). In this report, we aimed to present a case of accessory auricle presenting as nodular lesions located on the left tragus and in the preauricular region.

Materials and Methods: An 18-year-old male patient presented to our clinic with a complaint of a lump around the left ear. He had no symptoms other than cosmetic concern, and the lesions had been present since birth. He had no known comorbidities or family history. Examination findings were recorded with regard to lesion localization, clinical morphology, and the presence of any accompanying systemic disease or congenital anomaly.

Results: Dermatological examination revealed two skin-colored, pedunculated nodules located on the left tragus and left preauricular region. No lesions were observed at other sites. No accompanying systemic findings or additional congenital anomalies were detected. The clinical findings were considered consistent with isolated accessory auricle (Figure 1). Since the patient requested treatment for cosmetic reasons, he was referred to the relevant surgical department for excision of the lesions.

Conclusion: Accessory auricle/accessory tragus is a congenital malformation of the external ear associated with a developmental anomaly of the first pharyngeal arch (2, 3). It is most commonly observed in the preauricular region, anterior to the tragus; however, buccal and intra-auricular localizations may also occur (2). Clinically, it may present as a soft or firm, pedunculated or sessile, skin-colored nodular or flat lesion (2, 3). Although it is usually isolated and solitary, multiple lesions may be present; furthermore, because it may be associated with additional congenital anomalies and syndromes such as Goldenhar syndrome, associated pathologies should be excluded after diagnosis (3). The differential diagnosis includes acrochordon, auricular fistula, fibroma, polyp, lipoma, and epidermoid cyst; the presence of cartilage tissue on histopathological examination may support the diagnosis (2, 3). Surgical excision may be performed as treatment and may be preferred for cosmetic reasons (1, 3).

Keywords: Accessory auricle, accessory tragus, congenital malformation



Figure 2. Accessory auricle

References

4. Bahrani B, Khachemoune A. Review of accessory tragus with highlights of its associated syndromes. *Int J Dermatol*. 2014;53(12):1442-1446. doi:10.1111/ijd.12369.

5. Hwang J, Cho J, Burm JS. Accessory auricle: classification according to location, protrusion pattern and body shape. *Arch Plast Surg*. 2018;45(5):411-417. doi:10.5999/aps.2017.01292.

6. Jansen T, Romiti R, Altmeyer P. Accessory tragus: report of two cases and review of the literature. *Pediatr Dermatol*. 2000;17(5):391-394. doi:10.1046/j.1525-1470.2000.017005391.x.

OPTIMAL REHABILITATION STRATEGIES AFTER TOTAL KNEE ARTHROPLASTY: A SYSTEMATIC REVIEW OF ACCELERATED PROTOCOLS AND TELEREHABILITATION IN LIGHT OF CURRENT EVIDENCE

Nurten NAS KIRDAR

Department of Physical Medicine and Rehabilitation, Bandırma Onyedi Eylül University, Faculty of Medicine, Balıkesir, ORCID: 0000000265077880

Abdülhalim AKAR

Department of Orthopedics and Traumatology, Bandırma Onyedi Eylül University, Faculty of Medicine, Balıkesir, ORCID: 0000000231534799

Aim: Total knee arthroplasty (TKA) is a widely performed procedure for end-stage knee osteoarthritis, and postoperative rehabilitation is a key determinant of functional recovery. This systematic review aimed to evaluate current evidence regarding accelerated rehabilitation protocols and telerehabilitation approaches after TKA, and to identify optimal rehabilitation strategies for clinical practice.

Material and Methods: A systematic literature search was conducted in PubMed, Scopus, and Web of Science databases for studies published between 2020 and 2025. The search strategy included the terms “total knee arthroplasty,” “rehabilitation,” “accelerated protocol,” and “telerehabilitation.” Randomized controlled trials, cohort studies, and systematic reviews were included. Study selection and data extraction were performed in accordance with PRISMA guidelines. Due to heterogeneity among studies, a narrative synthesis was conducted.

Results: A total of 32 studies were included. Accelerated rehabilitation protocols were consistently associated with reduced length of hospital stay, earlier mobilization, and improved early functional outcomes without increasing complication rates. Telerehabilitation interventions demonstrated comparable clinical outcomes to conventional face-to-face rehabilitation in terms of pain reduction and functional scores. Additionally, higher patient satisfaction and improved adherence rates were reported in telerehabilitation groups. Hybrid rehabilitation models combining in-person and remote approaches showed promising results in maintaining continuity of care and improving accessibility.

Conclusion: Current evidence suggests that both accelerated rehabilitation protocols and telerehabilitation are effective and safe strategies after TKA. Rather than being competing approaches, they may serve as complementary components of a patient-centered rehabilitation model. Individualized rehabilitation strategies and hybrid care models appear to represent the most optimal approach for improving postoperative outcomes after TKA.

Keywords: Arthroplasty, Knee, Postoperative care, Rehabilitation, Telerehabilitation

LEPTIN AND ADIPONECTIN SIGNAL PATHS AT THE OBESITY-RELATED BREAST CANCER

Mahira Firudin kizi Amirova

Biochemistry Department, Azerbaijan Medical University, https://orcid.org/0000-0001-5598-6995

ABSTRACT

Breast cancer pathogenesis is profoundly influenced by metabolic dysregulation and obesity-associated endocrine alterations. Adipose tissue functions as an active endocrine organ, secreting adipokines that modulate inflammation, insulin sensitivity, angiogenesis, and cellular proliferation/apoptosis. Among these, leptin and adiponectin are the most extensively studied due to their antagonistic roles in breast tumor initiation and progression. Leptin, encoded by the *LEP* gene and acting through its receptor (*LEPR*), is overexpressed in obesity and breast cancer tissues. It promotes tumor growth and metastasis by activating key oncogenic signaling pathways, including JAK2/STAT3, PI3K/Akt, MAPK/ERK, and Wnt/β-catenin. Leptin also upregulates pro-angiogenic and inflammatory mediators such as VEGF, IL-6, TNF-α, cyclin D1 (*CCND1*), and anti-apoptotic genes like *BCL2*, while enhancing estrogen biosynthesis and estrogen receptor (ERα) signaling via aromatase (*CYP19A1*) induction. In contrast, adiponectin, encoded by *ADIPOQ* and signaling through its receptors *ADIPOR1* and *ADIPOR2*, exhibits tumor-suppressive properties. Adiponectin activates AMPK and p38 MAPK pathways, leading to inhibition of mTOR, NF-κB, and STAT3 signaling. These effects result in reduced cell proliferation, increased apoptosis, suppression of angiogenesis, and attenuation of epithelial-mesenchymal transition. Adiponectin also downregulates oncogenes and inflammatory mediators while enhancing tumor suppressor pathways involving *TP53* and *LKB1*. The dysregulated leptin-adiponectin axis, often reflected by an elevated leptin-to-adiponectin ratio, creates a pro-tumorigenic microenvironment that links obesity to aggressive breast cancer phenotypes and poorer prognosis. Elucidating the molecular networks and gene targets regulated by adipokines provides critical insight into obesity-driven breast carcinogenesis and identifies adipokine signaling pathways as promising targets for prevention and personalized therapy.

Keywords: breast cancer; leptin; adiponectin; adipokine signaling; obesity-associated carcinogenesis

SEARCH FOR EARLY DETECTION AND PRECISION MONITORING OF BREAST CANCER

Mahira Amirova

Biochemistry Department, Azerbaijan Medical University, https://orcid.org/0000-0001-5598-6995

Kamila Talibova:

Biochemistry Department, Azerbaijan Medical University, https://orcid.org/0009-0003-5484-3724

ABSTRACT

Breast cancer classical serum tumor markers such as CA 15-3 and carcinoembryonic antigen (CEA) have long been used in clinical practice, mainly for monitoring advanced disease rather than early screening due to limited sensitivity and specificity. Modern biochemical diagnostics extend beyond single-analyte markers toward multi-parameter panels that integrate proteins, metabolites, lipids, and nucleic acids. Proteomics-based assays quantify dysregulated proteins involved in proliferation, apoptosis, angiogenesis, and immune evasion, while metabolomics captures cancer-associated shifts in energy metabolism, amino acid utilization, and oxidative stress. These *omics* signatures are increasingly analyzed with machine-learning models to improve discrimination between malignant and benign breast lesions and to support subtype prediction. A major modern direction is liquid biopsy, which evaluates tumor-derived material in blood. Circulating tumor DNA (ctDNA) enables detection of somatic mutations, copy-number changes, and methylation patterns, with potential applications in early detection, minimal residual disease assessment, and relapse prediction. Circulating tumor cells (CTCs) provide additional biological insight, including epithelial-mesenchymal transition states and potential therapeutic targets. Exosomal cargo - microRNAs, proteins, and fragments of nucleic acids - offers another promising layer of biochemical information that may reflect tumor activity and microenvironmental signaling. Biochemical diagnostics also support precision therapy by identifying actionable molecular features. Tissue-based biomarker testing for estrogen receptor (ER), progesterone receptor (PR), HER2, and proliferation indices (e.g., Ki-67) guides systemic therapy selection and prognosis; emerging assays add pathway activation states and immune markers to refine treatment decisions. Despite rapid progress, translation into routine care requires robust analytical validation, standardized pre-analytical handling, clear clinical utility, and equitable access. Future biochemical diagnosis of breast cancer is likely to be *multi-omic*, algorithm-assisted, and longitudinal moving from one-time detection toward continuous, personalized disease monitoring.

Keywords: breast cancer; biochemical diagnosis; biomarkers; proteomics; metabolomics.

INCREASING BURDEN OF MULTIDRUG-RESISTANT *KLEBSIELLA PNEUMONIAE* IN COMMUNITY AND HOSPITAL-ACQUIRED UTIS

Md. Jan Sadur Rahman Moon

Department of Microbiology, Rajshahi Institute of Biosciences, Affiliated with University of Rajshahi, Rajshahi-6205, Bangladesh

Soikot Kawria

Department of Microbiology, Rajshahi Institute of Biosciences, Affiliated with University of Rajshahi, Rajshahi-6205, Bangladesh

Prof. Dr. Mst. Ismat Ara Begum

Department of Veterinary and Animal Sciences, University of Rajshahi, Rajshahi-6205, Bangladesh

ABSTRACT

Urinary tract infections (UTIs) are common worldwide, and *Klebsiella pneumoniae* has emerged as an important uropathogen because of increasing multidrug resistance. Forty-five *Klebsiella spp.* İsolates recovered from symptomatic UTI patients at several diagnostic centers were tested for antibiotic susceptibility using the Kirby–Bauer disk diffusion method following CLSI guidelines. Zones of inhibition were interpreted as susceptible, intermediate, or resistant. Resistance rates were: azithromycin (90%), cefixime (60%), gentamicin (10%), ciprofloxacin (20%), cefuroxime (60%), erythromycin (100%), and tetracycline (60%). Corresponding susceptibility rates were: azithromycin (0%), cefixime (20%), gentamicin (80%), ciprofloxacin (70%), cefuroxime (10%), erythromycin (0%), and tetracycline (20%). Intermediate results were observed as follows: azithromycin (10%), cefixime (20%), gentamicin (10%), ciprofloxacin (10%), cefuroxime (30%), erythromycin (0%), and tetracycline (20%). These results demonstrate a substantial burden of multidrug-resistant *Klebsiella pneumoniae* among UTI isolates, notably high resistance to azithromycin and erythromycin. Routine antimicrobial susceptibility testing and strengthened antibiotic stewardship are essential to guide effective therapy and limit further spread of resistance.

Keywords: UTIs patients; multidrug resistance, *Klebsiella pneumonia.*

ORTHOPEDIC CONSEQUENCES OF MILITARY LOAD CARRIAGE: MECHANISMS OF STRESS FRACTURE AND OVERUSE INJURY DURING PROLONGED ROUTE MARCHING

Gargano, Giuseppe

UCAM Universidad Católica de Murcia

INTRODUCTION

Load carriage during prolonged military route marching is a major cause of musculoskeletal injury and functional impairment, particularly in young and otherwise healthy populations. Historically described as “march foot,” load-related injuries primarily affect bone, joints, and periarticular soft tissues, with stress fractures representing one of the most clinically relevant outcomes. From an orthopedic perspective, bone remodeling with accumulation of bone microdamage can be altered by repetitive overload.

The magnitude of the load determines the risk of injury, but other influencing factors include walking speed, terrain, footwear, and certain individual anatomical and physiological factors.

Our review aims to summarize and highlight the biomechanical, physiological, and clinical characteristics relevant to the mechanisms of musculoskeletal injury associated with military load-bearing.

METHOD

A qualitative narrative review was conducted including experimental studies, prospective cohorts, epidemiological analyses, and systematic reviews focusing on military load carriage and prolonged route marching. The literature addressed lower limb biomechanics, bone stress injuries, neuromuscular fatigue, and injury incidence in military and military-analog populations. Outcomes of interest included stress fractures, joint and soft-tissue injuries, biomechanical loading parameters, metabolic cost, and neuromuscular function assessed through laboratory, field-based, and wearable sensor methodologies.

RESULTS

Orthopedic evidence consistently demonstrates that load carriage alters gait mechanics and increases ground reaction forces, joint moments, and metatarsal loading, thereby predisposing individuals to bone stress injuries, particularly of the foot, tibia, and knee. Stress fractures are most strongly associated with abrupt increases in training volume, prolonged marching duration, and heavy load relative to body mass. Neuromuscular fatigue, especially of the knee extensors and plantar flexors, contributes to altered load attenuation and increased skeletal strain. Current studies show an incidence of back and foot injuries during prolonged marches. Regarding heavy loads, injuries are found to be more common among female soldiers than among male soldiers. This phenomenon appears to be gender-related due to differences in mechanical structure.

CONCLUSION

Military load carriage represents a complex orthopedic stressor that affects bone, joints, and neuromuscular function through cumulative mechanical overload. Soldiers' individual factors appear to dominate the risk of injury. External factors, such as terrain and environmental conditions, appear to be more significant than the weight of the load carried. To reduce the risk of injury, more targeted training design could be conducted, taking into account the individual characteristics of the soldier and the equipment in use.

KEYWORDS: load carriage; stress fractures; march foot; military orthopedics; overuse injuries

DETERMINANTS OF BONE MINERAL DENSITY IN THE FOREARM OF YOUNG GYMNASTS AND SWIMMERS

Wiktoria Pietrzak

PhD Student, Doctoral School of the Józef Piłsudski University of Physical Education in Warsaw, Poland

ORCID ID: https://orcid.org/0009-0001-7325-8091

ABSTRACT

Aim: The aim of the study was to identify the main determinants of forearm BMD and BMC in young gymnasts and swimmers compared with non-training peers.

Materials and Methods: The study included a total of 45 girls aged 10.70±0.90 years, divided into three groups: gymnasts (G), swimmers (S), and non-training girls (N). Forearm BMD and BMC in the distal (dis) and proximal (prox) segments were assessed using densitometry (DXA). Dairy product consumption and eating habits were analyzed based on a dietary interview. Basic anthropometric measurements were taken, and the degree of somatic maturity and rate of sexual maturation were determined. The study was conducted in accordance with international ethical standards. The project received a positive opinion on compliance with the principles of ethics from the Bioethics Committee National Institute of Public Health- National Research Institute (Protokol 2/2025). This research was supported by the Ministry of Education and Science (Research Project UPB 14) at the Józef Piłsudski University of Physical Education in Warsaw, Poland.

Results: All analyzed bone parameters were significantly higher in group G compared to groups S and N ($\eta 2>0.14$; large effect; $P<0.001$). The incidence of below-normal BMD was significantly higher in groups S and N compared to group G. Analysis of covariance (ANCOVA) showed that BMD dis was significantly influenced by somatic maturity and physical activity (adj. $R^2=0.65$; $P<0.001$). A similar relationship was observed for BMC prox (adj. $R^2=0.51$; $P<0.001$). Physical activity had a significant effect on BMD prox (adj. $R^2=0.60$; $P<0.001$), and a similar relationship was found for BMC dis (adj. $R^2=0.38$; $P<0.01$). The Z-score value was significantly determined by dairy product consumption (n/day) and physical activity (adj. $R^2=0.54$; $P<0.001$).

Conclusion: Physical activity, in particular intensive weight-bearing gymnastic training, is the strongest factor in determining forearm bone mineralization parameters in the girls studied.

Keywords: bone mineralization, gymnastics, swimming, nutrition, dairy products, osteogenic index, pubertal age

ANTENATAL CARE FACTORS INFLUENCING BABIES' WEIGHT AT BIRTH

SAADATU IBRAHIM

Federal University of Technology Minna, Niger State

IBRAHIM ABDULRAHMAN

National Hydro Electric Power Producing Areas Development Commission

ABSTRACT

Low birth weight remains a major public health concern, particularly in developing countries, due to its strong association with infant morbidity and mortality. Antenatal care (ANC) plays a crucial role in promoting healthy pregnancy outcomes, including optimal birth weight. This study examined the influence of antenatal care factors on babies' weight at birth at the General Hospital Minna, Niger State, Nigeria. A cross-sectional study design was adopted, involving pregnant women who attended antenatal clinics and delivered at the facility. Data were collected using structured questionnaires and hospital records. Statistical analysis was conducted using the Statistical Package for Social Sciences (SPSS) version 26. Descriptive statistics, chi-square tests, and binary logistic regression were employed to determine the relationship between antenatal care factors and birth weight. The findings revealed that early initiation of ANC, adequate number of visits, good maternal nutritional status, compliance with iron and folic acid supplementation, tetanus toxoid immunization, and effective management of anemia and infections were significantly associated with normal birth weight. In contrast, inadequate ANC attendance, poor dietary practices, and untreated maternal illnesses were linked to low birth weight. The study concludes that strengthening antenatal care services and promoting maternal health education can significantly improve birth outcomes. Improving access to quality ANC services is essential for reducing the prevalence of low birth weight and enhancing neonatal survival.

Keywords: Antenatal Care, Birth Weight, Low Birth Weight, Maternal Nutrition, Pregnancy Outcomes, Neonatal Health, General Hospital Minna

THE EFFECT OF REGULAR FITNESS ACTIVITY ON PAIN, FUNCTIONAL DISABILITY, CORE ENDURANCE, FUNCTIONAL CAPACITY, AND QUALITY OF LIFE IN INDIVIDUALS WITH NON-SPECIFIC LOW BACK PAIN

Sama Borounmand

Biruni University, Institute of Graduate Education, Department of Physiotherapy and Rehabilitation, Istanbul, Türkiye | Study Area: Physiotherapy and Rehabilitation ORCID: 0009-0001-5390-1174

Ayda Padash

Biruni University, Institute of Graduate Education, Department of Physiotherapy and Rehabilitation, Istanbul, Türkiye | Study Area: Physiotherapy and Rehabilitation ORCID: 0009-0001-7180-5282

Majed J. Amro

Biruni University, Institute of Graduate Education, Department of Physiotherapy and Rehabilitation, Istanbul, Türkiye | Study Area: Physiotherapy and Rehabilitation | ORCID: 0009-0005-1048-3709

Şensu Dinçer

Istanbul University, Istanbul Faculty of Medicine, Department of Sports Medicine, Istanbul, Türkiye | Study Area: Sports Medicine | ORCID: 0000-0003-1425-2543

Berivan Beril Kılıç

Biruni University, Institute of Graduate Education, Department of Physiotherapy and Rehabilitation, Istanbul, Türkiye | Study Area: Physiotherapy and Rehabilitation | ORCID: 0000-0002-5588-4371

ABSTRACT

Objective: This study aimed to examine whether regular fitness participation is associated with lower pain, better function, greater core endurance, improved functional capacity, and better quality of life in individuals with non-specific low back pain.

Materials and Methods: This cross-sectional comparative study included 40 volunteers who reported non-specific low back pain within the previous 4 weeks. Participants were divided into a Fitness Group (FG; n=20; age: 22.65 ± 3.24 years; BMI: 24.97 ± 3.48 kg/m²), who had exercised regularly for at least 3 days per week and 50 minutes per day over the last 6 months, and a Sedentary Group (SG; n=20; age: 22.85 ± 3.60 years; BMI: 23.58 ± 3.79 kg/m²). Pain intensity was assessed with the Visual Analog Scale, disability with the Oswestry Disability Index, core endurance with the McGill Core Endurance Test, functional capacity with the Five-Repetition Sit-to-Stand Test, and quality of life with the SF-36. Statistical analyses were performed using SPSS 22.0.

Results: The groups were similar in age and BMI ($p>0.05$). Pain intensity was significantly higher in the SG ($Z=-2.142$, $p=0.038$), whereas trunk extensor endurance was significantly higher in the FG ($Z=-2.326$, $p=0.020$). No significant between-group differences were detected in the remaining variables ($p>0.05$). In both groups, pain and disability showed moderate positive correlations (SG: $r=0.619$, $p=0.004$; FG: $r=0.582$, $p=0.007$). In the SG, sit-to-stand duration was positively correlated with trunk flexor and lateral endurance, while in the FG, greater trunk extensor endurance was moderately associated with shorter sit-to-stand duration ($r=-0.554$, $p=0.011$).

Conclusion: Regular fitness activity in individuals with non-specific low back pain appears to be associated with lower pain levels and better trunk extensor endurance. The relationship between higher extensor endurance and improved sit-to-stand performance in the fitness group suggests that posterior chain capacity may contribute to functional performance. Targeted endurance-based exercise approaches may therefore be clinically valuable in this population.

Keywords: non-specific low back pain, fitness, core endurance, functional capacity

UPCYCLING AGRICULTURAL BY-PRODUCTS: ESSENTIAL OIL AND HYDROSOL FROM PRUNING BIOMASS IN TOPICAL FORMULATION

Fouzia Benoudjit

Laboratory of coatings, Materials & Environment, M'hamed Bougara University, Boumerdès, Algeria

Djihad Cherifi

Faculty of Sciences, Department of Chemistry, M'hamed Bougara university, Boumerdès, Algeria

Fatma Zohra Benyoucef

Faculty of Sciences, Department of Chemistry, M'hamed Bougara university, Boumerdès, Algeria

Imene Hamoudi

Faculty of Sciences, Department of Chemistry, M'hamed Bougara university, Boumerdès, Algeria

ABSTRACT

The valorisation of agricultural residues into high-value bioactive ingredients is a cornerstone of the circular economy. The present study investigates the upcycling of local *Pistacia lentiscus* pruning biomass to develop stable topical emulsions incorporating either the essential oil or the hydrosol. Both extracts have been reported to possess significant anti-inflammatory properties. Three oil-in-water emulsions were prepared: a control, an hydrosol-based cream, and an essential oil-based cream. Stability was monitored over 28 days at room temperature and at 4 ºC. All formulations maintained macroscopic integrity, and pH values (5–6) were compatible with human skin. Rheological analysis revealed shear-thinning behaviour, ensuring easy spreadability and a pleasant skin feel. Antibacterial assays against clinical isolates demonstrated enhanced efficacy of the bioactive formulations. At room temperature, essential oil-based cream showed the highest inhibition against *Escherichia coli* (12 mm), whereas hydrosol-based cream was most effective against *Staphylococcus aureus* (12 mm), doubling the inhibition relative to the control (6 mm). Storage conditions influenced activity while under refrigeration, hydrosol-based cream exhibited increased efficacy against *Pseudomonas aeruginosa* (11 mm). These results indicate that *Pistacia lentiscus* pruning biomass are is a sustainable and effective source for stable, bioactive cosmeceutical applications. Incorporating both essential oil and hydrosol into topical emulsions provides complementary anti-inflammatory and antimicrobial effects, while maintaining stable physical properties and good skin compatibility. This study demonstrates that distillation by-products can successfully enhance the protective and functional profile of topical formulations, illustrating a practical implementation of circular economy principles in cosmetic science.

Keywords: *Pistacia lentiscus*, upcycling, essential oil, hydrosol, topical emulsion, characterisation.

BIOGENIC SILVER NANOGEL FROM BRUGMANSIA SUAVEOLENS: ANTIMICROBIAL AND THERAPEUTIC POTENTIAL

Prathmesh Y. Khandare

Department of Pharmacognosy, Bharati Vidyapeeth College of Pharmacy, Kolhapur -416013 Maharashtra, India, ORCID ID: https://orcid.org/0009-0004-7233-9860

Firoj A. Tamboli

Department of Pharmacognosy, Bharati Vidyapeeth College of Pharmacy, Kolhapur -416013 Maharashtra, India

Mandira S. More.

Department of Pharmacognosy, Bharati Vidyapeeth College of Pharmacy, Kolhapur -416013 Maharashtra, India

ABSTRACT

The growing demand for eco-friendly technologies has promoted the adoption of plant-based approaches for nanoparticle synthesis. Brugmansia suaveolens is rich in bioactive compounds that facilitate the green synthesis of silver nanoparticles (AgNPs). The present study aimed to synthesize and characterize AgNPs using leaf and flower extracts of B. suaveolens and to evaluate their antimicrobial and therapeutic potential in gel formulations. AgNPs were synthesized using plant extracts and characterized by UV-visible spectroscopy, Fourier-transform infrared spectroscopy, X-ray diffraction, scanning electron microscopy, and DPPH assay. The extracts were also subjected to phytochemical screening and evaluated for antibacterial, antifungal, and anti-inflammatory activities. The results revealed that the synthesized AgNPs possessed crystalline structures with average particle sizes of 75.2 nm (leaf extract) and 102.7 nm (flower extract). The nanoparticles exhibited significant antioxidant activity and demonstrated effective antimicrobial action against Staphylococcus aureus, Escherichia coli, and Aspergillus niger. Among the formulations, batch F6 showed enhanced skin penetration (84.96%), indicating improved delivery characteristics. B. suaveolens-mediated AgNPs exhibit promising antimicrobial and therapeutic potential. The developed nanogel formulation may serve as an effective treatment option for wounds and burns; however, further in vivo studies are required to confirm its safety and efficacy.

Keywords: Green synthesis, Silver nanoparticles, Brugmansia suaveolens, Nanogel, Wound healing

PILOT-SCALE PRODUCTION OF BIOCHAR FROM LIGNOCELLULOSIC BIOMASS: VALIDATION, MODIFICATIONS AND APPLICATIONS

Younes Beddach

Laboratory of Applied Chemistry and Biomass, Department of Chemistry, Faculty of Sciences Semlalia, Cadi Ayyad University, BP 2340, Marrakech, Morrocco

Imad Rabichi

Laboratory of Applied Chemistry and Biomass, Department of Chemistry, Faculty of Sciences Semlalia, Cadi Ayyad University, BP 2340, Marrakech, Morrocco

Fatima Ezzahra Yaacoubi

Laboratory of Applied Chemistry and Biomass, Department of Chemistry, Faculty of Sciences Semlalia, Cadi Ayyad University, BP 2340, Marrakech, Morrocco

Abdelaziz Ounas

Laboratory of Applied Chemistry and Biomass, Department of Chemistry, Faculty of Sciences Semlalia, Cadi Ayyad University, BP 2340, Marrakech, Morrocco

Abdelrani Yaacoubi

Laboratory of Applied Chemistry and Biomass, Department of Chemistry, Faculty of Sciences Semlalia, Cadi Ayyad University, BP 2340, Marrakech, Morrocco

Abdelaziz Bacaoui.

Laboratory of Applied Chemistry and Biomass, Department of Chemistry, Faculty of Sciences Semlalia, Cadi Ayyad University, BP 2340, Marrakech, Morrocco

ABSTRACT

This study compares biochar production at the laboratory and pilot scales, focusing on its relevance for agroecological agriculture and the sustainability of production systems. At the laboratory scale, precise control over pyrolysis conditions enables detailed analysis of how temperature and biomass type affect biochar properties. These experiments generate essential insights for optimizing biochar as a soil amendment to improve fertility, soil structure, and water retention, while stimulating beneficial microbiological activity. At the pilot scale, biochar yields are substantially higher (33 to 68%) compared to conventional techniques (10 to 22%). Biochar produced notably from olive stones shows a low H/C ratio, high stable organic carbon content, and, when activated, increased specific surface area and porosity—facilitating nutrient retention and carbon sequestration. Enhanced electrical conductivity and ash content help regulate soil–plant–microorganism interactions, which are crucial to agroecological resilience. Integrating results from both scales opens possibilities for designing tailored biochars, sustaining durable improvements in agroecosystems, promoting natural fertility, stabilizing yields, and valorizing local resources in agroecological farming systems.

Keywords: Biochar, Pilot-Scale, Soil health, Carbon sequestration, Nutrient retention

USE OF AI/MACHINE LEARNING IN VACCINE DESIGN

K. Vaishnavi

V.Keerthana

S. Shakthishree

ABSTRACT

The integration of artificial intelligence (AI) and machine learning (ML) is transforming vaccine research by accelerating antigen discovery, optimizing immunogen design, and improving prediction of immune responses. Traditional vaccine development relies heavily on trial-and-error approaches and lengthy preclinical testing, whereas AI-driven platforms enable rapid screening of vast genomic and proteomic datasets to identify promising epitopes and antigenic targets. Deep learning models, structural bioinformatics, and generative algorithms have been applied to predict antigenicity, model protein–pathogen interactions, and design novel immunogens with enhanced stability and immunogenicity. Furthermore, ML frameworks are being used to optimize adjuvant selection, predict population-level vaccine efficacy, and tailor formulations to diverse genetic and immunological backgrounds. Recent applications include COVID-19 variant-adapted vaccines, development of next-generation influenza vaccines, and exploration of broadly protective candidates against HIV and malaria. Despite significant progress, challenges remain in data quality, interpretability of models, and validation in clinical trials. The convergence of computational prediction with experimental immunology holds promise for a new paradigm of "precision vaccinology," enabling faster, more cost-effective, and potentially more universal vaccine development.

Keywords: artificial intelligence (AI) and machine learning (ML), antigen discovery, covid-19 variant adaptive vaccines, precision vaccinology,

CAUSAL ASSOCIATION OF CIRCULATING VITAMIN D LEVELS WITH CARDIOVASCULAR DISEASES AND DIABETES: INSIGHTS FROM MENDELIAN RANDOMIZATION ANALYSIS

Arup Singha Roy

Department of Pharmacy, Jashore University of Science and Technology, Jashore – 7408, Bangladesh

Md. Rafiqul Islam

Department of Pharmacy, Jashore University of Science and Technology, Jashore – 7408, Bangladesh

ABSTRACT

Background:

Vitamin D deficiency has been associated with cardiovascular and metabolic diseases in observational studies; however, whether these associations are causal remains uncertain. This study aimed to investigate the causal effects of circulating vitamin D levels on cardiovascular diseases and diabetes using Mendelian randomization (MR) and generalized summary-data–based Mendelian randomization (GSMR).

Methods:

Genome-wide association study summary statistics from European ancestry populations were used to assess the association of genetically predicted vitamin D levels with type 1 diabetes, type 2 diabetes, myocardial infarction, heart failure, coronary artery disease, and hypertension. Two-sample MR was performed using inverse-variance weighted analysis as the primary method, supported by weighted median, MR-Egger, and MR-PRESSO sensitivity analyses. GSMR was further applied to validate causal estimates after excluding pleiotropic variants.

Results:

In the IVW analysis, genetically predicted higher vitamin D levels were significantly associated with reduced risk of myocardial infarction (OR 0.78, 95% CI 0.65–0.93; P=0.007), heart failure (OR 0.89, 95% CI 0.80–0.99; P=0.04), and type 1 diabetes (OR 0.99, 95% CI 0.97–1.00; P=0.038). MR-PRESSO supported protective associations for myocardial infarction and type 2 diabetes. GSMR analysis confirmed significant inverse associations with type 2 diabetes, myocardial infarction, and hypertension.

Conclusion:

This genetic epidemiological study suggests a potential protective causal role of circulating vitamin D levels in selected cardiometabolic diseases, particularly myocardial infarction. GSMR findings further support possible causal effects on type 2 diabetes and hypertension, highlighting the relevance of vitamin D biology in cardiometabolic disease prevention.

Keywords: Vitamin D; Mendelian randomization; GSMR; myocardial infarction; type 2 diabetes; hypertension; cardiovascular disease; genetic epidemiology.

MINERALOGICAL, THERMAL AND RHEOLOGICAL CHARACTERIZATION OF A CLAY-BASED FORMULATION FOR EXTRUSION APPLICATIONS

El Mustapha El-Aissi

Materials and Process and Environmental Engineering Lboratory, Higher School of Technology, Hassan II university of Casablanca, Morocco

Abdel hafid Essadki

Materials and Process and Environmental Engineering Lboratory, Higher School of Technology, Hassan II university of Casablanca, Morocco

ABSTRACT

This study investigates the mineralogical, thermal, and rheological behavior of a clay-based formulation intended for shaping applications, particularly extrusion and potentially 3D printing. X-ray diffraction (XRD) was used to identify the main crystalline phases, Fourier-transform infrared spectroscopy (FTIR) was employed to detect the characteristic functional groups, and thermogravimetric/differential thermal analysis (TGA-DTA) was carried out to evaluate the thermal stability and transformation behavior of the material. In parallel, rheological measurements were performed to assess the flow behavior, apparent viscosity, and yield stress of the prepared paste.

The results showed that the clay formulation is mainly composed of typical aluminosilicate phases, with the possible presence of accessory minerals depending on the raw material composition. FTIR analysis confirmed the characteristic bands associated with hydroxyl groups and Si–O/Al–O vibrations, supporting the mineralogical interpretation obtained by XRD. TGA-DTA results revealed the expected mass losses and thermal events related to physically adsorbed water removal, dehydroxylation of clay minerals, and structural reorganization at higher temperature. From a rheological point of view, the paste exhibited a non-Newtonian behavior, characterized mainly by shear-thinning and a measurable yield stress, which are favorable features for extrusion-based processing. Overall, the combined results indicate that the studied formulation has a coherent mineralogical and thermal profile and presents promising rheological properties for extrusion and shape retention after deposition.

Keywords: Clay; XRD; FTIR; TGA-DTA; Rheology; Extrusion; Clay paste; Shear-thinning; Yield stress; Thermal analysis

ACTIVITY GUIDED FRACTIONATION OF METHANOLIC EXTRACT OF CITRULLUS COLOCYNTHIS FOR SPASMOGENS

Dr. Muhammad Saleh Faisal

Associate Professor, Department of Pharmacology, Khyber Medical College, Peshawar, Pakistan

ABSTRACT

Background & Objectives

Citrullus Colocynthis is an ancient herbal plant, commonly called as the Colocynth, Bitter cucumber or Bitter apple. There are many traditional uses of this plant including diarrhea, which proposed the presence of spasmogenic principles in its constituents. Using rabbit's Jejunal model, spasmogenic activity of the crude methanolic extract of C. colocynthis has been reported. This work was an attempt to isolate those spasmogens by activity guided fractionation of methanolic extract of C. colocynthis using rat's ileum model.

Methodology

An experimental study was conducted in the department of Pharmacology, Institute of Basic Medical Sciences, Khyber Medical University, Hayatabad, Peshawar. After preparing the animal models of rat's ileum and rabbit's jejunum, different fractions i.e. n-hexane, chloroform, Ethyl acetate, n-butanol and aqueous fractions of methanolic extract were tried in concentrations of 0.01, 0.03, 0.1, 0.3, 1.0, 3.0, 5.0, 10 and 15 mg/ml to identify the portion with maximum spasmogens.

Results

Aqueous and n-Butanol fractions showed spasmogenic effects on the spontaneous contractions of rat's ileal preparations at the concentrations of 0.1, 0.3, 1.0, 3.0 and 5.0 mg/ml while at 10 and 15 mg/ml, they showed spasmolytic effects. Ethyl acetate and chloroform fractions did not show significant spasmogenic effects, rather showed spasmolytic effects in rabbit's jejunal preparations with respective EC50 values of 0.1283 ± 0.007 mg/ml and 2.703 ± 0.235 mg/ ml. Respective EC50 values for spasmolytic effects of Ethyl acetate and chloroform fractions upon KCl induced contractions were 5.37 ± 0.515 mg/ml and 12.36 ± 1.484 mg/ml. Respective EC50 (log [Ca++] M) of ethyl acetate fraction at 1mg/ml vs control were -2.563 ± 0.04 and -2.846 ± 0.035. Similarly, respective EC50 (Log[Ca++]M) in the absence and presence of 0.1 µM verapamil were -2.45 ± 0.06 and -1.7 ± 0.07. EC50 (log [Ca++] M) for control vs chloroform fraction at 3 mg/ml and 5 mg/ml were -2.95 ± 0.035 vs -3.02 ± 0.03 and -3.06 ± 0.0264, respectively. Similarly, respective EC50 (Log[Ca++]M) in the absence and presence of 0.1 µM verapamil were -2.45 ± 0.06 and -1.7 ± 0.07.

Conclusion

It is concluded that maximum spasmogens were extracted in the residual aqueous fraction followed by n-butanol fraction. They follows voltage gated calcium channels to produce spasmogenic response. It was also found that spasmolytic constituents are concentrated in the ethyl acetate fraction followed by chloroform fraction. Ethyl acetate fraction follows voltage gated calcium channels to exhibit its relaxant effect while mechanism for chloroform fraction still need to be confirmed.

Key words: Citrullus Colocynthis, Fractionation, Spasmogens

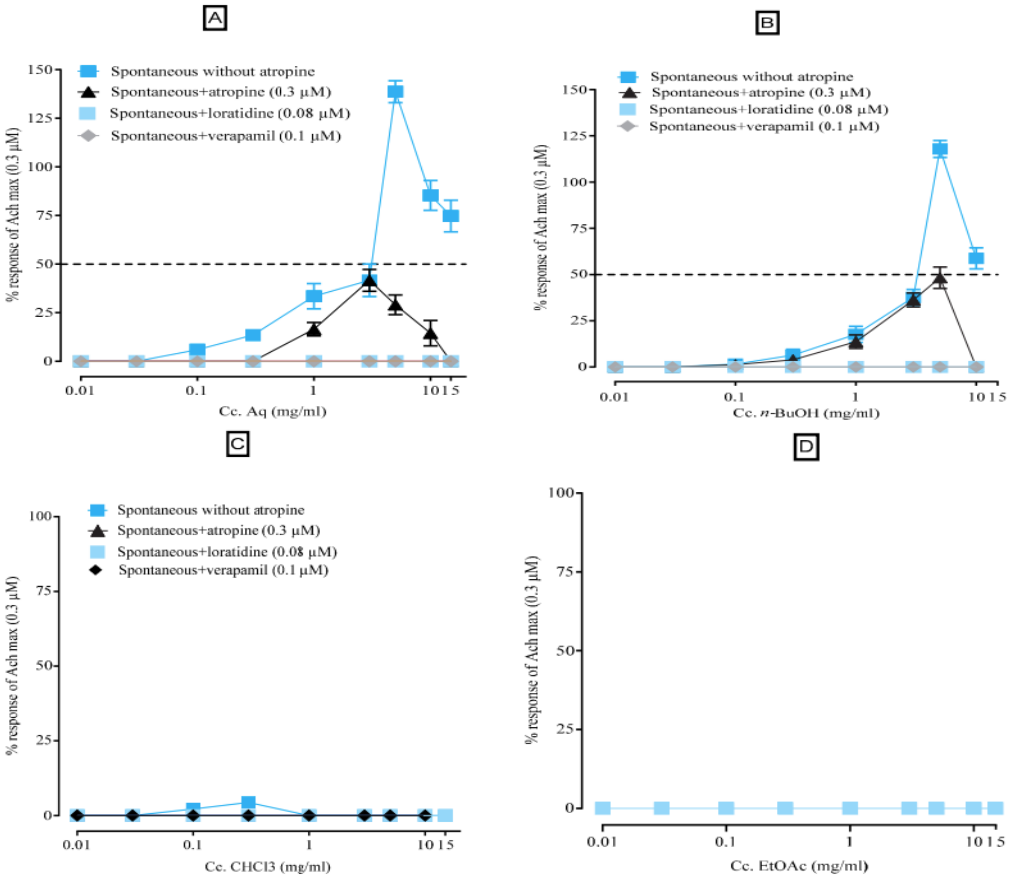


Figure-1. Effects of various concentrations of different fractions of Citrullus colocynths on rat's ileum. Spasmogenic effects are expressed as % response of Ach max (0.3 µM), n=3.

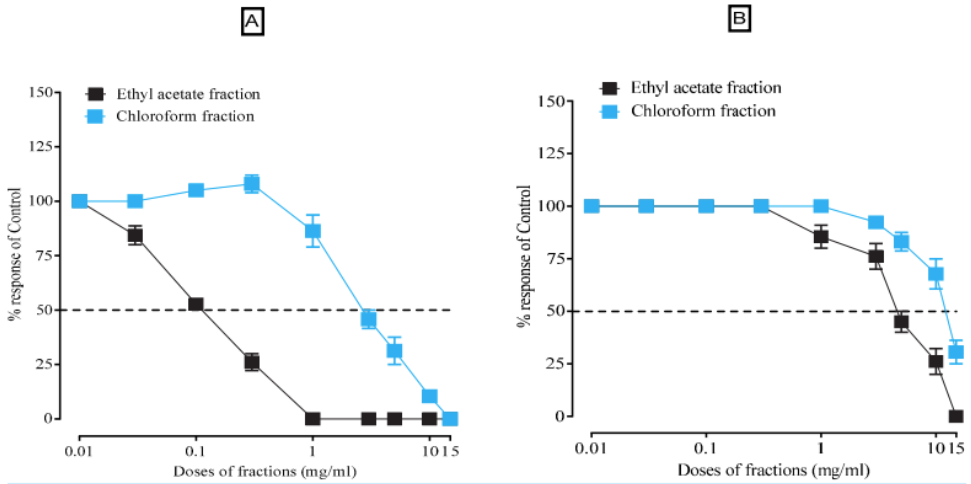


Figure-2(A). Effects of Cc. EtOAc and Cc. CHCl3 on spontaneous jejunal contractions.
(B) Effects of Cc. EtOAc and Cc. CHCl3 on KCl (80mM) induced contractions in rabbit's jejunal preparations, n=3.

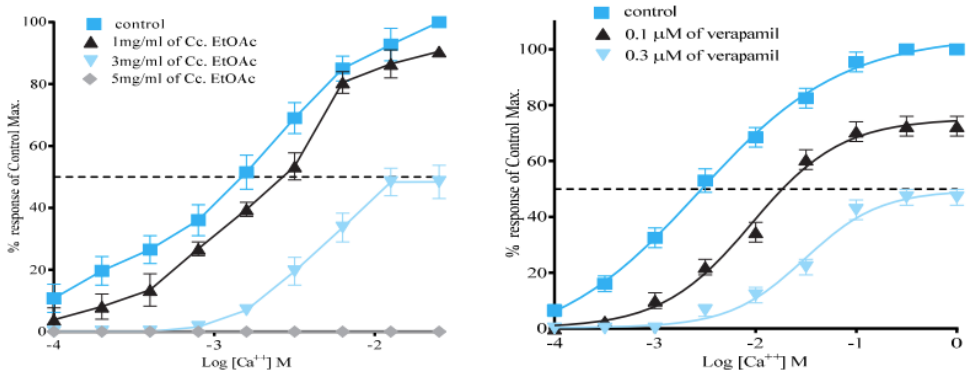


Figure-3(A). Calcium chloride curves in the absence and presence of Cc. EtOAc.
(B) Calcium chloride curves in the absence and presence of verapamil, n=3.

COMPUTATIONAL SCREENING OF FLEMINGIA MACROPHYLLA BIOACTIVE COMPOUNDS FOR TARGETING THE PI3K/AKT1 PATHWAY IN COLORECTAL CANCER

Md. Sabit Hossan

Department of Pharmacy, Jahangirnagar University, Savar, Dhaka-1342, Bangladesh

ABSTRACT

Colorectal cancer (CRC) is one of the leading causes of cancer-related mortality worldwide, and the identification of effective targeted therapeutic agents remains a major challenge. The PI3K/AKT signaling pathway plays a key role in regulating cell proliferation, survival, and tumor progression, making it an important molecular target for anticancer drug development. Natural phytochemicals are increasingly recognized as potential sources of novel therapeutic agents due to their structural diversity and biological activity. In this study, an in silico molecular docking approach was performed to evaluate the inhibitory potential of bioactive compounds derived from *Flemingia macrophylla* against colorectal cancer-associated protein targets 4JPS and 6NPZ, which are involved in the PI3K/AKT signaling pathway. Celecoxib and Capivasertib were used as standard reference inhibitors for comparative analysis. The docking results demonstrated that several phytochemicals exhibited strong binding affinities toward the target proteins. Among them, IMPHY008557 showed the highest binding affinity against 4JPS with a docking score of −9.9 kcal/mol, forming stable hydrogen bond interactions with ASP883, GLN879, and LYS884, along with π–π stacking interaction with TRP880. Additionally, IMPHY008566 exhibited significant binding affinity against 6NPZ with a docking score of −9.4 kcal/mol through hydrogen bonding and hydrophobic interactions. These findings suggest that bioactive compounds from *Flemingia macrophylla* possess promising inhibitory potential against PI3K/AKT pathway-related targets in colorectal cancer. However, further ADMET profiling, molecular dynamics simulations, and experimental validation are required to confirm their safety, stability, and therapeutic potential.

Keywords: Flemingia macrophylla; colorectal cancer, PI3K/AKT1 pathway; molecular docking.

FROM PRENATAL ETHANOL NEUROTOXICITY TO ALTERED SOCIAL BEHAVIOUR: IMPAIRMENT OF SOCIAL MEMORY AND INTERACTION

Kamal Smimih

Biological Engineering Laboratory, Faculty of Sciences and Technology (FST), Sultane Moulay Slimane University, Beni Mellal 23000, Morocco;

Omar El Hiba

Laboratory of Anthropogenic, Biotechnology and Health, Nutritional Physiopathologies, Neuroscience and Toxicology Team, Faculty of Sciences, Chouaib Doukkali university, El Jadida, 24000, Morocco;

ABSTRACT

Developmental neurotoxicity associated with prenatal exposure to ethanol is considered an international public health concern due to its profound and long-lasting effects on the central nervous system, as well as its potential to cause various physical and psychological malformations in the developing fetus, ultimately leading to behavioral disorders in affected individuals. The present study aimed to assess susceptibility to the effects of Fetal Alcohol Spectrum Disorder (FASD) on social behavior.

Female mice with positive vaginal plugs were divided into 3 groups: group 1: (Et+Pyr), received 1g/kg ethanol i.p. in two doses (D10 and D13 of pregnancy). Group 2: (Pyr), received an i.p. injection of 100mg/kg pyrazole on the same days as the Et+Pyr group, while Group 3: (C), received an equivalent volume of saline solution (NaCl 0.9%), in an equal volume on the same days.

Subsequently, the offspring were assessed using the social interaction test and the social score test to evaluate their social interest and social communication abilities. Our study revealed that mice exposed to alcohol exhibited impaired social behaviours.

These results highlight the potent neurotoxic effect of a low dose (1 g/kg) of ethanol administered during the prenatal period, on social neurobehavioral functions.

Keywords: *prenatal alcohol exposure, social interaction test, social score test, mice.*

DEVELOPMENTAL NEUROTOXICITY OF PRENATAL ETHANOL EXPOSURE: IMPLICATIONS FOR WORKING MEMORY DYSFUNCTION IN MICE

Kamal Smimih

Biological Engineering Laboratory, Faculty of Sciences and Technology (FST), Sultane Moulay Slimane University, Beni Mellal 23000, Morocco

Omar El Hiba

Laboratory of Anthropogenic, Biotechnology and Health, Nutritional Physiopathologies, Neuroscience and Toxicology Team, Faculty of Sciences, Chouaib Doukkali university, El Jadida, 24000, Morocco

ABSTRACT

Alcohol is a teratogen capable of easily crossing the placental barrier, thereby directly exposing the fetus to its toxic effects during critical stages of development. This exposure can disrupt the normal maturation of organs, particularly the brain, and lead to various neurodevelopmental, neurological, and cognitive impairments. In this context, the aim of the present study was to evaluate the impact of prenatal alcohol exposure on working memory using a mouse model.

Female mice with positive vaginal plugs were divided into 3 groups: group 1: Ethanol+Pyrazole (Et+Pyr), received 1g/kg ethanol i.p. in two doses (D10 and D13 of pregnancy). Group 2: Pyrazole (Pyr), received an i.p. injection of 100mg/kg pyrazole on the same days as the Et+Pyr group, while Group 3: Control (C), received an equivalent volume of saline solution (NaCl 0.9%), in an equal volume on the same days.

Subsequently, the adult offspring were assessed using the T-maze test, the Morris Water Maze, and the Novel Object Recognition Test to evaluate their learning and memory functions.

Our study revealed that mice exposed to alcohol exhibited significant impairments in behavioural performance related to learning and memory functions.

Keywords: prenatal alcohol exposure, T-maze test, the Morris Water Maze, and the Novel Object Recognition Test, mice.

OVERVIEW AND EPIDEMIOLOGY OF NON-TUBERCULOUS MYCOBACTERIA ISOLATED FROM WILD ANIMALS IN AFRICA

BELLIL Dassine

Université de Bejaia, Faculté des Sciences de la Nature et de la Vie, Laboratoire d'Ecologie Microbienne, 06000 Bejaia, Algérie.

GHAROUT-SAIT Alima

Université de Bejaia, Faculté des Sciences de la Nature et de la Vie, Laboratoire d'Ecologie Microbienne, 06000 Bejaia, Algérie.

DJOUDI Ferhat

Université de Bejaia, Faculté des Sciences de la Nature et de la Vie, Laboratoire d'Ecologie Microbienne, 06000 Bejaia, Algérie.

BELLIL Zahra

Université de Bejaia, Faculté des Sciences de la Nature et de la Vie, Laboratoire d'Ecologie Microbienne, 06000 Bejaia, Algérie.

MENDIL Ouidad

Université de Bejaia, Faculté des Sciences de la Nature et de la Vie, Laboratoire d'Ecologie Microbienne, 06000 Bejaia, Algérie.

MANSEUR Lyticia

Université de Bejaia, Faculté des Sciences de la Nature et de la Vie, Laboratoire d'Ecologie Microbienne, 06000 Bejaia, Algérie.

DIB-SAIT Sabrina

Université de Bejaia, Faculté des Sciences de la Nature et de la Vie, Laboratoire de Biochimie Biophysique Biomathématique et Scientométrie, 06000 Bejaia, Algérie.

Abstract

INTRODUCTION: Non-tuberculous mycobacteria (NTM) represent a group of significant pathogens with a global distribution in wildlife. Their presence at the interface between livestock and wild animals is of particular concern, as wildlife species can act as reservoirs, facilitating transmission to domestic cattle and potentially humans. These dynamic underscores the importance of monitoring NTM as a key One Health issue.

OBJECTIVE: This study aimed to conduct a comprehensive assessment of the reported prevalence and temporal trends of NTM in wildlife across African countries over a 15-year period from 2010 to 2025.

METHODOLOGY: We performed a systematic review of the scientific literature on NTM epidemiology in African wildlife. Data were retrieved from electronic databases, including PubMed, ScienceDirect, and African Journals Online (AJOL), and subsequently compiled and analyzed.

RESULTS: The systematic review identified a validated dataset comprising 57 distinct occurrence reports of NTM across a range of wild animal species in Africa. From a total of 3,384 animal observations, 706 confirmed NTM cases were identified, yielding an aggregate prevalence of 20.8% across the studied wildlife populations during the 2010-2025 period.

CONCLUSION: Our analysis confirms the environmental endemicity of NTM and establishes that wildlife populations in Africa constitute a significant reservoir. Furthermore, multivariable statistical

analyses demonstrated a significant association between NTM detection and clinical disease in animals, reinforcing the veterinary and ecological importance of these pathogens.

Keywords: Mycobacterium non-tuberculosis, wild animals, review, Africa.

CHALLENGES AND FUTURE PERSPECTIVES IN THE BIOLOGICAL EVALUATION OF MOROCCAN MEDICINAL PLANTS WITH IMMUNOMODULATORY POTENTIAL

Boutaina YAHYAI

Laboratory of Botany, Biotechnology and Plant Protection, Faculty of Sciences, Kenitra, BP 133, Kenitra, Morocco

Ahmed CHRIQUI

Laboratory of Natural Resources and Sustainable Development, Faculty of Sciences, Kenitra, BP 133, Kenitra, Morocco

Meyrem DOUBI

Laboratory of Natural Resources and Sustainable Development, Faculty of Sciences, Kenitra, BP 133, Kenitra, Morocco

Rajae AGNAOU

Laboratory of Botany, Biotechnology and Plant Protection, Faculty of Sciences, Kenitra, BP 133, Kenitra, Morocco

Chaimae TORRES

Laboratory of Natural Resources and Sustainable Development, Faculty of Sciences, Kenitra, BP 133, Kenitra, Morocco

Driss HMOUNI

Laboratory of Natural Resources and Sustainable Development, Faculty of Sciences, Kenitra, BP 133, Kenitra, Morocco

Brahim BOURKHIS

Laboratory of Botany, Biotechnology and Plant Protection, Faculty of Sciences, Kenitra, BP 133, Kenitra, Morocco

ABSTRACT

Chronic inflammatory diseases and immune dysfunctions remain important health concerns worldwide. Although conventional treatments are effective in many cases, their side effects, high costs, and certain therapeutic limitations have increased interest in natural alternatives. In this context, medicinal plants have gained growing scientific interest because of their reported anti-inflammatory, antioxidant, and immunomodulatory properties.

Morocco is characterized by a rich biodiversity and a long tradition of medicinal plant use, offering valuable natural resources for the identification of bioactive compounds with potential immunomodulatory effects. However, the biological evaluation of these plants still faces several scientific and methodological challenges, including variability in phytochemical composition, lack of extract standardisation, and limited mechanistic and clinical studies.

This communication aims to provide an overview of current knowledge on medicinal plants with potential immunomodulatory activities, with particular focus on Moroccan plant resources. Some biological mechanisms involved in inflammation modulation, such as oxidative stress reduction and cytokine regulation, will be briefly discussed. In addition, attention will be given to the main challenges related to biological validation, safety assessment, and future research perspectives.

Overall, Moroccan medicinal plants represent promising natural resources for future studies in immunomodulation. Further interdisciplinary investigations combining ethnobotany, phytochemistry, and experimental biology are still needed to better understand their biological effects and support their scientific valorisation.

Keywords: Medicinal plants; Immunomodulation; Inflammation; Moroccan biodiversity; Bioactive compounds.

OCCURRENCE AND RISK ASSESSMENT OF ORGANOCHLORINE PESTICIDES AND PCB MARKERS IN LIVER AND MUSCLE TISSUES OF THE ENDEMIC BELUSHKA (*SALMO OHRIDANUS*) FROM LAKE OHRID

Aurel Nuro

Department of Chemistry, Faculty of Natural Sciences, University of Tirana, Albania

Ilirjana Osmani

Department of Chemistry, Faculty of Mathematical and Natural Sciences, University of Pristina "Hasan Prishtina", Kosovo

Arben Haziri

Department of Chemistry, Faculty of Mathematical and Natural Sciences, University of Pristina "Hasan Prishtina", Kosovo

Bledar Myrtaj

Department of Chemistry, Faculty of Natural Sciences, University of Tirana, Albania

Kleva Shpati

Department of Pharmacy, Faculty of Medicinal Sciences, Albanian University, Tirana, Albania

Aurora Napuce

Department of Pharmacy, Faculty of Medicinal Sciences, Albanian University, Tirana, Albania

Aurora Nuro

Department of Pharmacy, Faculty of Medicinal Sciences, Albanian University, Tirana, Albania

Ardit Shehi

Department of Pharmacy, Faculty of Medicinal Sciences, Albanian University, Tirana, Albania

Indrit Brahollari

Department of Pharmacy, Faculty of Medicinal Sciences, Albanian University, Tirana, Albania

Doriana Beqiraj

Department of Morfo-functional Field, Faculty of Veterinary, Agricultural University of Tirana, Albania

ABSTRACT

This study investigated the occurrence of organochlorine pesticides (OCPs) and seven markers of polychlorinated biphenyls (PCBs) in liver and edible tissue samples of *Salmo ohridanus* species collected in April 2026. Fish specimens of different size and sex were analysed in order to evaluate contaminant distribution between liver and muscle tissue and to assess the possible risk for consumers. Samples were extracted by ultrasonic-assisted extraction using a hexane: dichloromethane mixture (3:1), followed by acid hydrolysis, Florisil column clean-up and determination by GC/ECD using a Varian GC 450 apparatus. The results showed detectable levels of several persistent organic contaminants in both matrices. Total OCP concentrations ranged from 1.69 to 6.97 µg/kg ww in liver and from 1.00 to 5.46 µg/kg ww in edible tissue, with mean values of 3.42 and 2.32 µg/kg ww, respectively. Total marker PCB concentrations ranged from 0.85 to 2.35 µg/kg ww in liver and from 0.68 to 1.86 µg/kg ww in tissue, with mean values of 1.59 and 1.21 µg/kg ww, respectively. The liver generally contained higher contaminant levels than edible tissue, confirming its role as a preferential accumulation and detoxification organ. The dominant OCPs were endosulfan sulfate, endosulfan II, endosulfan I, heptachlor epoxide and dieldrin, while PCB 101 was the main PCB congener. DDT and its metabolites were not detected in any sample. A preliminary human health risk assessment indicated hazard quotient values below 1, suggesting no evident non-carcinogenic risk for adult consumers under the assumed fish

consumption scenarios. However, continued monitoring is recommended due to the endemic status and ecological importance of *S. ohridanus*.

Keywords: Ohrid Lake, *Salmo ohridanus*, Water analyse, OCP, PCB markers, GC/ECD

NOVEL CO(II) AND NI(II) PYRIMIDINE SCHIFF BASE COMPLEXES AS POTENTIAL ANTICANCER AGENTS

Vjollca Berisha

University of Prishtina, Faculty of Mathematical and Natural Sciences, Department of Chemistry, Prishtina, Republic of Kosova, (ORCID: https://orcid.org/0009-0000-9493-4864)

Sevdije Govori

University of Prishtina, Faculty of Mathematical and Natural Sciences, Department of Chemistry, Prishtina, Republic of Kosova

ABSTRACT

The development of novel metal-based anticancer agents remains an important approach in the search for more effective chemotherapeutic compounds. In this study, new Co(II) and Ni(II) complexes derived from a pyrimidine Schiff base ligand were synthesized and comprehensively characterized by FT-IR, NMR, elemental analysis, and mass spectrometry, confirming the successful formation of stable coordination compounds.

The antiproliferative activity of the synthesized compounds was evaluated against human breast adenocarcinoma (MCF-7), lung carcinoma (H460), and colon carcinoma (HCT116) cell lines using the MTT assay. The obtained results demonstrated that coordination of the Schiff base ligand with transition metal ions significantly enhanced the biological activity compared to the free ligand. Among the investigated compounds, the cobalt complexes exhibited the most pronounced cytotoxic effects, particularly against HCT116 cells, showing significant antiproliferative activity and improved biological performance.

The enhanced activity observed after metal coordination may be associated with increased lipophilicity, improved cellular uptake, and stronger interactions with intracellular biomolecular targets. Overall, the findings suggest that pyrimidine-based Schiff base Co(II) and Ni(II) complexes represent promising candidates for further development as potential anticancer agents.

Keywords: Pyrimidine Schiff base; Co(II) complexes; Ni(II) complexes; Anticancer activity; MTT assay.

MATERNAL KNOWLEDGE AND PERCEPTIONS OF NUTRITION IN THE FINAL WEEKS OF PREGNANCY: A CROSS-SECTIONAL STUDY IN VLORA, ALBANIA

Ph. D(c). Saemira Durmishi

Department of Healthcare, Faculty of Health, "Ismail Qemali" University, Vlorë, Albania

Prof.Assoc. Rezarta Lalo,

Department of Healthcare, Faculty of Health, "Ismail Qemali" University, Vlorë, Albania

Dr. MitildaGugu,

Faculty of Medical Technical Sciences, "Aleksandër Xhuvani" University, Elbasan

ABSTRACT

Introduction: Maternal nutrition during the third trimester is essential for maintaining maternal health and supporting optimal pregnancy progression. Adequate intake of key macro- and micronutrients in late pregnancy contributes to physiological preparedness for childbirth and fetal well-being. Despite the recognized importance of antenatal nutritional counseling, limited data are available regarding pregnant women's knowledge and perceptions about diet in the final weeks of pregnancy. This study aimed to assess maternal knowledge and perceived information sources related to nutrition during late pregnancy.

Methods: A cross-sectional study was conducted in Vlora, Albania, between January and September 2025. A total of 110 women in the third trimester (28–40+ weeks of gestation) completed an adapted version of the Pregnancy Nutrition Knowledge Questionnaire (PNKQ). The instrument evaluated knowledge of key nutrients, perceived beneficial foods, and primary sources of information. Statistical analysis was performed using IBM SPSS Statistics, version 27.0 **Results:** Only 32% of participants demonstrated awareness of the importance of nutrition in late pregnancy, while 43% reported no knowledge and 25% were uncertain. Cereals/grains (41%) and fruits (34%) were most frequently perceived as beneficial foods. Iron (38%) was the most recognized micronutrient, followed by magnesium (24%), calcium (21%), and vitamin C (17%). Gynecologists (38%) and nurses (21%) were the main information sources, although 25% relied on the internet. Despite 46% perceiving themselves as sufficiently informed, overall knowledge levels were limited.

Conclusions: The findings highlight significant knowledge gaps among pregnant women in this local Albanian setting. Strengthening structured, evidence-based nutritional education within routine antenatal care is essential to improve maternal health literacy and support informed dietary practices during late pregnancy.

Keywords: Maternal nutrition; knowledge; pregnancy; antenatal care; district of Vlore; health education.

COST CONTROL AND FIRM PERFORMANCE OF SELECTED MANUFACTURING COMPANIES IN NIGERIA

Ademola, Emmanuel Akinyele

Department of Accountancy, The Federal University of Technology Ilaro Ogun State

Akinola Morufu Biodun

Department of Accountancy, The Federal University of Technology Ilaro Ogun State

Adekunle Julianah Kikelomo

Department of Accountancy, The Federal University of Technology Ilaro Ogun State

Ajimati Blessing Oluwatosin

Department of Accountancy, The Federal University of Technology Ilaro Ogun State

ABSTRACT

The study examined the effect of cost control on firm performance of selected manufacturing company in Nigeria. This was achieved through the following specific objectives: To examine the effect of finance cost on return on asset of selected manufacturing Company in Nigeria; To determine the effect of salaries and wages on return on asset of selected manufacturing Company in Nigeria; To evaluate the effect of cost of sales on return on asset of selected manufacturing Company in Nigeria. The study used sample size of five (5) manufacturing companies in Nigeria from 2015 to 2024. Secondary data was the main source of data collection and this was obtained from financial annual report of the selected manufacturing companies. Data were evaluated using descriptive statistics, correlation, fixed effect and random effect estimates, and the Hausman test was used to evaluate consistency and efficiency. The regression results reveal that finance cost has a negative and statistically significant effect on ROA. This suggests that higher financing costs erode profitability by increasing the burden of debt servicing on manufacturing firms. In contrast, salaries and wages exhibit a positive and statistically significant relationship with ROA. The study further reveals that cost of sales negatively and significantly affects ROA. This finding suggests that high production and operational costs diminish profitability by squeezing margins. it was therefore recommended that; Manufacturing firms should minimize reliance on excessive debt financing and adopt alternative funding strategies such as equity financing, retained earnings, or strategic partnerships.

Keywords: cost control, cost of sales, finance cost, performance, return on asset, salaries and wages,

ENVIRONMENTAL HEALTH IMPLICATIONS OF BRINE MANAGEMENT IN INDUSTRIAL WATER SOFTENING SYSTEMS

Mohamed EL MORSY

PhD student (Responsible Author), Ibnou Zohr University, Faculty of Sciences, Department of chemistry, Laboratory of Materials and Environment (LME), ORCID ID: https://orcid.org/0009-0005-3979-1940

Laila AFIA

Prof. Dr., Ibnou Zohr University, Faculty of Sciences, Department of chemistry, Laboratory of Materials and Environment (LME), ORCID ID: https://orcid.org/0009-0003-6324-8396

ABSTRACT

Industrial water softening systems are widely applied to reduce water hardness caused by calcium and magnesium ions, thereby preventing scaling in industrial and domestic water networks. Although ion exchange processes are efficient, they generate regeneration brine characterized by high salinity and residual chemical content, which may contribute to environmental contamination if improperly managed. Such discharges can indirectly affect water quality in receiving ecosystems and, consequently, pose potential risks to public health through long-term exposure pathways.

This study evaluates industrial water softening processes from a water quality and health-environment perspective, with emphasis on process stages including pretreatment, ion exchange softening, resin regeneration, and wastewater management. Particular attention is given to regeneration brine, identified as a critical effluent stream due to its high ionic load and disposal challenges.

Optimization strategies are explored to mitigate environmental and indirect health impacts, including partial brine recycling, reduction of salt dosing during regeneration, and improved process control to minimize chemical excess. In addition, advanced treatment options such as membrane concentration and selective recovery are considered to reduce saline discharge and limit contamination of natural water bodies.

The findings highlight that improved management of regeneration brine significantly reduces pollutant loads and supports safer water resource management. From a health perspective, reducing saline and chemical discharges contributes to protecting water quality and limiting indirect exposure risks associated with contaminated water systems.

This study emphasizes that integrating optimized water treatment practices with environmental health considerations is essential for ensuring sustainable water management and protecting public health in industrialized regions.

Keywords: water softening, brine management, water quality, environmental health, ion exchange, wastewater treatment, public health.

ANALYTICAL STUDY OF WAVE-CURRENT INTERACTION WITH DOUBLE RECTANGULAR TRENCHES

H. MABCHOUR

Engineering and Materials Laboratory (LIMAT), Ben M'Sick Faculty of Science, Hassan II University, Casablanca.

H. AKARNI

Engineering and Materials Laboratory (LIMAT), Ben M'Sick Faculty of Science, Hassan II University, Casablanca

L. EL AARABI

Engineering and Materials Laboratory (LIMAT), Ben M'Sick Faculty of Science, Hassan II University, Casablanca

S. MORDANE

Engineering and Materials Laboratory (LIMAT), Ben M'Sick Faculty of Science, Hassan II University, Casablanca

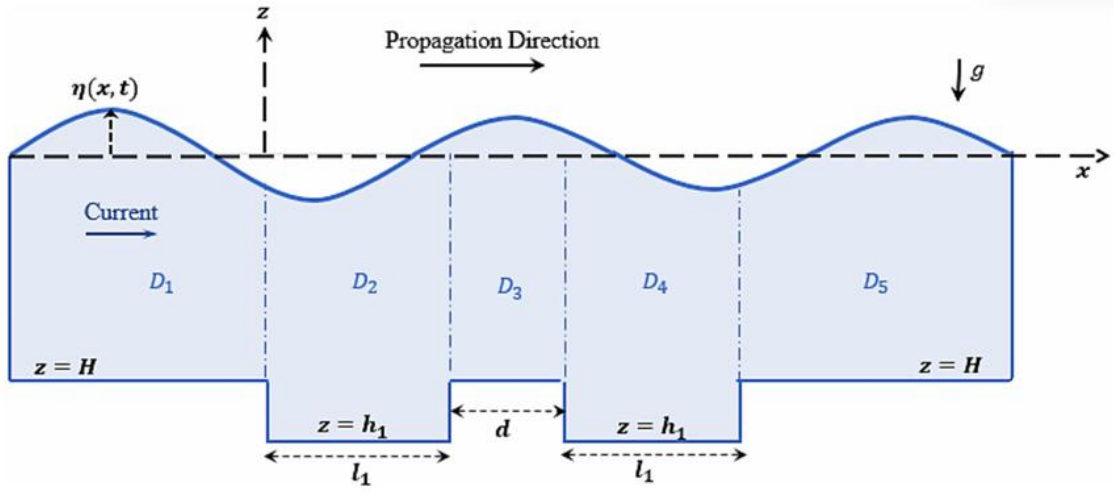
ABSTRACT

Ocean surface waves are influenced by various physical phenomena, leading to the formation of gravity waves that propagate uniformly from offshore to coastal areas. The interaction between these waves and submerged structures poses significant challenges in ocean engineering and naval architecture. Over the past few decades, extensive research has been conducted using analytical, numerical, and experimental approaches to elucidate the mechanisms of wave attenuation and dissipation.

This study presents an analytical investigation of wave interaction with double submerged trenches under the influence of a uniform current, either co-directional or counter-directional to the incident wave propagation. The primary objective is to examine the impact of the current and geometric parameters on the reflection coefficient. The wave dynamics are analyzed within the framework of potential theory, and the submerged structures comprise two rectangular trenches positioned at the bottom of a wave flume, spaced apart. The analytical model employed is based on the plane wave approximation, and the approach is validated through comparison with experimental results.

Keywords: Wave, submerged structures, current, plane wave, reflection coefficient.

Graphical abstract



Reference

[1] H. Akarni, H. Mabchour, L. El Aarabi, S. Mordane, Wave Reflection by Rectangular Breakwaters for Coastal Protection, Fluid Dynamics and Materials Processing 20(3) (2023) 579-593.

[2] MABCHOUR, Hamza, AKARNI, Hasna, AKOUIBAA, Abdelilah, et al. Analytical study of wave-trenches interaction under the effect of current. Journal of Ocean Engineering and Marine Energy, 2025, p. 1-13.

[3] M. Errifaiy, S. Nasse, C, Chahine, Analytical determination of the reflection coefficient by the evanescent modes model during the wave–current– horizontal plate interaction. C. R. Mécanique 344 (2016) 479–48.

[4] S. Mordane, C. Chahine, S. Nasse, M. Chagdali, Propagation de la houle en présence d'obstacles : Etude théorique, numérique et expérimentale, Les cahiers de la recherche, 3 (2001) 161-176.

DISTRIBUTION AND DYNAMICS OF BULINUS TRUNCATUS POPULATIONS IN THE DRÂA-TAFILALT REGION: IMPLICATIONS FOR SCHISTOSOMIASIS TRANSMISSION

Samiha Bouaouich

Laboratory of Integrative Biology, Department of Biology, Faculty of Sciences Ain Chock, Hassan II University, Casablanca, Morocco.

Abdelali Balahbib

Laboratory of Integrative Biology, Department of Biology, Faculty of Sciences Ain Chock, Hassan II University, Casablanca, Morocco.

Higher Institute of Nursing and Health Techniques Professions (ISPITS), Errachidia, Morocco

Souad Bouhout

Directorate of Epidemiology and Disease Control, 335 Avenue Mohammed V, Rabat, Morocco

El Bachir Adlaoui

Department of Parasitology-Mycology-Entomology, National Institute of Hygiene, Rabat, Morocco.

Fatima Amarir

Laboratory of Integrative Biology, Department of Biology, Faculty of Sciences Ain Chock, Hassan II University, Casablanca, Morocco.

ABSTRACT

Urinary schistosomiasis, caused by Schistosoma haematobium, is a parasitic disease whose transmission depends on complex interactions between the intermediate snail host and the parasite. Among these hosts, Bulinus truncatus plays a key role in the transmission cycle.

This study aimed to analyze the distribution and population dynamics of Bulinus truncatus in the Drâa-Tafilalt region and to explore their implications for host–pathogen interactions and the risk of schistosomiasis transmission.

Malacological surveys were conducted at nine aquatic sites. Snail densities were classified into three categories: high, low, and very low. The results revealed a heterogeneous distribution, with 33.3% of the sites showing high density, 33.3% low density, and 33.3% very low density. High densities were mainly observed in favorable environments such as stagnant waters and irrigation systems.

These findings suggest that certain areas constitute ecological niches favorable to interactions between Bulinus truncatus and Schistosoma haematobium, potentially promoting parasite transmission in the event of reintroduction.

Keywords: Urinary schistosomiasis, Schistosoma haematobium, Bulinus truncatus, intermediate host, host–pathogen interactions, malacological surveys, transmission risk

HERBAL MEDICINES

Janani.S. S,

Students, faculty of Pharmacy, Bharath Institute of Higher Education and Research, Selaiyur, Chennai, Tamil Nadu, India.

[1]Preethi.B,

Students, faculty of Pharmacy, Bharath Institute of Higher Education and Research, Selaiyur, Chennai, Tamil Nadu, India.

[1]Ragul.R,

Students, faculty of Pharmacy, Bharath Institute of Higher Education and Research, Selaiyur, Chennai, Tamil Nadu, India.

David.G,

Students, faculty of Pharmacy, Bharath Institute of Higher Education and Research, Selaiyur, Chennai, Tamil Nadu, India.

Jayaramakani.N,

Assistant Professor, Faculty of Pharmacy, Bharath Institute of Higher Education and Research, Selaiyur, Chennai, Tamil Nadu, India.

Dr.R. Srinivasan

Dean and Professor, Faculty of Pharmacy, Bharath Institute of Higher Education and Research, Selaiyur, Chennai, Tamil Nadu, India.

ABSTRACT

Traditional medicine refers to the knowledge, skills, and practices developed from cultural beliefs and experiences, used to maintain health and treat illnesses. In recent years, herbal medicine has regained importance as people seek more holistic and personalized healthcare approaches. This review highlights the integration of traditional knowledge with modern scientific research, focusing on the safety, effectiveness, and biological activity of herbal medicines. It emphasizes the need to scientifically evaluate herbal remedies to confirm their therapeutic value and ensure safe usage. Herbal medicines contain multiple active compounds that interact with the human body in complex ways. Understanding these mechanisms helps bridge the gap between traditional use and modern evidence-based medicine. The study also recognizes systems like Traditional Chinese Medicine (TCM), which has been practiced for over 3000 years, as examples of holistic healthcare approaches still relevant today. Overall, combining traditional wisdom with modern science can improve global healthcare and support the use of herbal medicine as a complementary treatment. Indian traditional medicine is a holistic, ancient healthcare system primarily based on Ayurveda, Yoga, Siddha, and Unani, focusing on body-mind balance through natural remedies, diet, and lifestyle adjustments. It emphasizes preventive care and removing toxins, with Ayurveda being a, if not the, oldest codified system.

Keywords: Traditional medicine, Herbal medicine, Safety and efficacy, Evidence-based medicine, Traditional Chinese Medicine (TCM), Ayurveda.

EPIDEMIOLOGICAL SURVEY OF VIRAL INFECTIONS AMONG BLOOD DONORS AND THEIR ASSOCIATION WITH BLOOD GROUPS IN AL-NAJAF PROVINCE, IRAQ

Hawraa Abdulameer Ali

Prof.Dr., Dean and Professor, Faculty of Pharmacy, Bharath Institute of Higher Education and Research, Selaiyur, Chennai, Tamil Nadu, India, Pathological Analyses Depart. Faculty of Science.University of Kufa.Iraq

Najlaa Abdulameer Ali

Prof.Dr., College of Dentistry. University of Kufa.Iraq

ABSTRACT

This study aimed to evaluate the prevalence of transfusion-transmissible infections (TTIs) among blood donors and to investigate their association with ABO and Rh blood groups in Al-Najaf province, Iraq. A cross-sectional study was conducted on 1000 blood donors over a five-month period from July to December 2025. The samples were collected from the Central Blood Bank in Najaf Province.

Blood samples were collected and analyzed using serological methods, including ELISA techniques, to detect Hepatitis B virus (HBV), Hepatitis C virus (HCV), and syphilis infections. The results showed that 688 donors (68.8%) were positive for at least one infection marker and were therefore excluded from blood donation.

Among the detected infections, HBV exposure (HBc) was the most prevalent (84.05%), followed by syphilis (9.57%), HBsAg (4.44%), and HCV (1.94%). The highest infection rates were observed among males and in middle-aged groups. Blood group O+ showed the highest frequency of infections; however, no significant association was found between blood groups and infection prevalence.

In comparison with international studies, the prevalence rates in this study were higher, particularly for HBV and syphilis, indicating the need for improved screening strategies and public health interventions.

In conclusion, transfusion-transmissible infections remain a major challenge to blood safety in the study area. Strengthening screening protocols, enhancing donor selection criteria, and increasing public awareness are essential to reduce infection rates and ensure safe blood transfusion services.

ZINC STANNATE@GRAPHENE OXIDE NANOCOMPOSITE FOR ELECTROCHEMICAL SENSING OF AQUATIC MICROPLASTICS

A F M Faridul Islam

Advanced Materials and Devices Laboratory, Department of Bio-Convergence Science, Jeonbuk National University, Jeongeup Campus, 56212, Republic of Korea

Eun-Bi Kim

Advanced Materials and Devices Laboratory, Department of Bio-Convergence Science, Jeonbuk National University, Jeongeup Campus, 56212, Republic of Korea

M. Shaheer Akhtar

Department of Engineering, School of Computing, Engineering and Mathematical Sciences, La Trobe University, Melbourne, VIC 3086, Australia

Graduate School of Physical-AI, Jeonbuk National University, Jeonju, 54896, Republic of Korea

Department of JBNU-KIST Industry-Academia Convergence Research, Jeonbuk National University, Jeonju 54896, Republic of Korea

[c]New & Renewable Energy Material Development Center (NewREC), Jeonbuk National University, Jeonbuk, Republic of Korea

Sadia Ameen

Advanced Materials and Devices Laboratory, Department of Bio-Convergence Science, Jeonbuk National University, Jeongeup Campus, 56212, Republic of Korea

Department of Engineering, School of Computing, Engineering and Mathematical Sciences, La Trobe University, Melbourne, VIC 3086, Australia

Department of Bioactive Material Sciences, Jeonbuk National University, Jeonju,

Republic of Korea

Abstract

Microplastics (MPs) have emerged as critical environmental contaminants, posing serious threats to aquatic ecosystems and human health. Conventional detection techniques are often constrained by their complexity, high operational costs, and limited capability for real-time analysis. In this study, zinc stannate (Zn_2SnO_4, ZnTO) and graphene oxide (GO) nanocomposites (ZnTO@GO NCs) containing different GO weight percentages (1 mg/ml–10 mg/ml) were successfully synthesized via a hydrothermal approach and utilized as electrode materials for the electrochemical detection of microplastics, specifically polystyrene (PS, 100 nm). Among the prepared samples, the sensor fabricated using ZnTO@GO NCs with 5 mg/ml GO exhibited excellent sensing performance, achieving a sensitivity of ~186.458 µA $\mu m^{-1}cm^{-2}$, a limit of detection (LOD) of ~9.6755 µM, and an R^2 value of ~0.982935. The fabricated sensor for MP detection was further confirmed through cyclic voltammetry (CV) and linear sweep voltammetry (LSV), demonstrating its strong potential for advanced environmental monitoring applications.

Keywords: Zinc stannate (Zn_2SnO_4), Graphene oxide (GO), Microplastics, Nanocomposite, Sensitivity

HEALTH LITERACY AMONG ADOLESCENTS IN ETHIOPIA: EVIDENCE FOR POLICY AND INTERVENTIONS

Adamu Amanu Asari

Department of Health, Behavior, and Society, Faculty of Public Health, Jimma University, Oromia, Ethiopia
Department of Sociology, College of Social Sciences, Jimma University, Oromia, Ethiopia

Ameyu Godesso

Department of Sociology, College of Social Sciences, Jimma University, Oromia, Ethiopia

Zewdie Birhanu

Department of Health, Behavior, and Society, Faculty of Public Health, Jimma University, Oromia, Ethiopia

ABSTRACT

Background and justifications: Health literacy (HL) among adolescents is a critical determinant of health behavior and long-term wellbeing. In developing countries such as Ethiopia, inadequate HL among adolescents exacerbates challenges such as teenage pregnancy, sexually transmitted infections, substance abuse, and poor mental health outcomes. Understanding HL situation in this population and making tailored interventions is essential for achieving health related Sustainable Development Goals and promoting societal wellbeing. Therefore, this study focuses on HL among adolescents in Ethiopia.

Methods: A cross-sectional study was conducted in 2024 among secondary school adolescents in Ethiopia. Participants were selected using stratified random sampling. Data were collected using a locally developed and validated 33-item HL scale encompassing five dimensions, namely, health information competency, communication, health awareness and knowledge, decision-making and behavior, and citizenship and responsibility. Responses were self-administered on paper, entered into Epidata 3.1 for cleaning, and analyzed in SPSS 27.0 using both descriptive and inferential statistics.

Results: Seven hundred twenty-two adolescents participated in the study. Overall, 74.8% of the respondents had inadequate HL, with consistently high inadequacy across all the five dimensions. In addition, about four-fifths of the respondents exhibited unhealthy behaviors, clustering together in a number of cases. Inadequate HL was significantly associated with unhealthy behaviors and with sociodemographic factors such as attending public schools, low parental education, and low family income.

Implications: The findings highlight the urgent need for tailored interventions to improve HL among adolescents in Ethiopia. Improving HL in adolescents can empower them to make informed decisions, reduce risky behaviors, and enhance their overall wellbeing. Policy should prioritize adolescent HL, integrating it into school curricula as well as community-based programs. And addressing the disparities is also crucial to ensure equitable health outcomes.

Conclusion: HL among adolescents in Ethiopia is concerning, with significant implications for health behaviors, mental wellbeing, and societal development. Strengthening HL among adolescents should be a national priority to foster healthier lifestyles, reduce health risks, and contribute to achieving broader public health and development goals. Further longitudinal or intervention studies are warranted to deepen understanding and establish causal pathways.

Keywords: Adolescents, health literacy, health behavior, Ethiopia, developing country

OPTIMIZING CEFAZOLIN PROPHYLAXIS IN OBESE ADULTS UNDERGOING SURGERY

S. Deepak

Faculty of Pharmacy, Bharath Institute of Higher Education and Research, Chennai, India-600073

A. Palanisamy

Faculty of Pharmacy, Bharath Institute of Higher Education and Research, Chennai, India-600073

S. Kalaivanan

Faculty of Pharmacy, Bharath Institute of Higher Education and Research, Chennai, India-600073

Lavanya Babu

Faculty of Pharmacy, Bharath Institute of Higher Education and Research, Chennai, India-600073

C.Ravi

Faculty of Pharmacy, Bharath Institute of Higher Education and Research, Chennai, India-600073

G. David

Faculty of Pharmacy, Bharath Institute of Higher Education and Research, Chennai, India-600073

ABSTRACT

Cefazolin is widely used as prophylactic antibiotic therapy to prevent surgical site infections (SSI) in clean and contaminated surgical procedures. Traditionally, a 1 g intravenous (IV) dose administered before surgery has been considered effective in both non-obese and obese patients. Recently, higher doses such as 3 g IV have become popular in obese patients based on the assumption that "more is better." However, there is limited comparative evidence supporting this practice. This review evaluates high-dose cefazolin prophylaxis from a pharmacokinetic (PK) perspective. Cefazolin is a hydrophilic antibiotic that poorly penetrates adipose tissue regardless of dose. Since adipose tissue is not usually the target site in SSI prophylaxis, increasing the dose does not improve therapeutic benefit. Higher doses increase serum and non-adipose tissue concentrations proportionally, but adipose tissue levels remain unchanged. Cefazolin demonstrates time-dependent killing kinetics, meaning antibacterial effectiveness depends on maintaining drug concentrations above the minimum inhibitory concentration (MIC) rather than achieving excessively high concentrations. A 1 g IV dose produces peak serum concentrations of approximately 185 mcg/mL and provides up to six hours of intraoperative protection, making re-dosing unnecessary for surgeries lasting less than six hours.The article also highlights concerns regarding antibiotic stewardship, increased healthcare costs, and potential adverse effects such as Clostridium difficile infection associated with unnecessary high-dose antibiotic use. Pharmacokinetic studies in obese patients show no added clinical benefit from 3 g dosing or intraoperative re-dosing. Therefore, routine high-dose cefazolin prophylaxis in obese patients may not be scientifically justified.

Keywords: Cefazolin, Surgical Site Infection (SSI), Antibiotic Prophylaxis, Obesity, Pharmacokinetics (PK), High-Dose Cefazolin, Intravenous Administration, Antibiotic Stewardship Program (ASP), Time-Dependent Killing

PROTECTIVE EFFECT OF THE FLAVONOID EXTRACT OF *RANUNCULUS REPENS* AGAINST HYPERGLYCEMIA AND PANCREATIC DAMAGE IN AN EXPERIMENTAL MODEL OF GLUCOTOXICITY

Safinez BOUTRID

Department of Biology of Organisms, Faculty of Natural and Life Sciences, University of Batna 2, Algeria

BACKGROUND

Chronic hyperglycemia plays a central role in the development of metabolic disorders and is closely linked to oxidative stress and pancreatic β-cell dysfunction. Natural bioactive compounds have attracted growing interest due to their antioxidant and antihyperglycemic properties. *Ranunculus repens* is a medicinal plant rich in flavonoid compounds with potential protective effects. This study aimed to evaluate the protective role of the flavonoid extract of *Ranunculus repens* against hyperglycemia-induced pancreatic alterations in an experimental model of glucotoxicity.

MATERIALS/METHODS

Experimental glucotoxicity was induced in rats using alloxan. Animals were divided into control, diabetic, and treated groups receiving the flavonoid extract of *Ranunculus repens*. Biochemical parameters including blood glucose, lipid profile, and glycogen content were evaluated, along with histopathological analysis of pancreatic tissue to assess glucotoxic alterations.

RESULTS

Treatment with the flavonoid extract significantly reduced blood glucose levels and improved lipid metabolism compared with untreated diabetic animals. A marked restoration of glycogen reserves was also observed, indicating an improvement in glucose homeostasis. Histological analysis revealed attenuation of pancreatic tissue degeneration, with partial preservation of pancreatic architecture and cellular integrity. These findings suggest that the extract exerts a protective effect against oxidative stress-mediated cellular damage and may contribute to the preservation of pancreatic function.

CONCLUSION

The flavonoid extract of *Ranunculus repens* demonstrated promising antihyperglycemic, antioxidant, and cytoprotective effects in experimental glucotoxicity, highlighting its potential as a natural therapeutic candidate for metabolic disorders related to diabetes.

KEYWORDS: *Ranunculus repens*, flavonoids, glucotoxicity, hyperglycemia, oxidative stress, pancreatic protection.

RELATIONSHIP BETWEEN CHRONIC LATERAL EPICONDYLITIS AND ERECTILE DYSFUNCTION: A PROSPECTIVE CROSS-SECTIONAL COMPARATIVE STUDY

Mehmet Ali Dursun, MD

Tavsanli State Hospital, Dept. of Orthopedics and Traumatology, Kutahya, Turkey | *Field:* Orthopedics & Traumatology |*ORCID:* 0000-0003-2679-9351

ABSTRACT

Objective: Chronic musculoskeletal pain is associated with sexual dysfunction; however, the relationship between chronic lateral epicondylitis (CLE) and erectile dysfunction (ED) has not been previously investigated. This study aimed to determine whether ED is more prevalent in men with CLE compared with occupation-matched controls and to examine the relationship between pain severity and erectile function.

Material and Method: In this prospective cross-sectional comparative study, 71 men with clinically diagnosed CLE (group LE) and 84 occupation-matched male controls without CLE (group C) were enrolled. Erectile function was assessed using the validated Turkish version of the IIEF-5 questionnaire (ED defined as IIEF-5 $\leq$ 21). Pain severity was quantified with the Visual Analog Scale (VAS, 0–10). Statistical analyses included the Mann–Whitney U test, chi-square test, Spearman's rank correlation, and multivariable binary logistic regression adjusting for age, smoking, and BMI.

Results: Groups were comparable for age and smoking but differed significantly in BMI (25.4 ± 4.0 vs. 24.0 ± 4.3 kg/m²; p = 0.028). Median IIEF-5 score was significantly lower in the CLE group (20 [IQR 17–22]) than in controls (23 [IQR 18–24]; p = 0.001). ED prevalence was 67.6% in CLE patients versus 38.1% in controls (OR = 3.39, 95% CI: 1.75–6.59; p < 0.001). Within the CLE group, VAS scores were significantly higher in patients with ED than in those without (median 7 vs. 4; p < 0.001), and a significant inverse correlation was found between VAS and IIEF-5 scores ($\rho = -0.500$, p < 0.001). Multivariable logistic regression confirmed CLE as an independent predictor of ED (adjusted OR = 4.65, 95% CI: 1.90–11.39; p < 0.001).

Conclusion: ED is significantly more prevalent in men with CLE than in occupation-matched controls, and pain severity is inversely associated with erectile function. To our knowledge, this is the first study to investigate this association. Clinicians managing patients with CLE should consider screening for ED, particularly in those reporting high pain levels.

Keywords: chronic lateral epicondylitis; erectile dysfunction, musculoskeletal pain; Visual Analog Scale

ASSOCIATION BETWEEN MATERNAL TSH LEVELS AND NEONATAL BIRTH WEIGHT: A RETROSPECTIVE COHORT STUDY

Deniz Taşkıran

Assistant Professor, Department of Obstetrics and Gynecology, Giresun University Faculty of Medicine, Giresun, Turkey, ORCID: 0000-0001-7270-4566

Objective: This study aimed to evaluate the association between maternal thyroid-stimulating hormone (TSH) levels during pregnancy and obstetric and neonatal outcomes, with particular emphasis on the potential effect of elevated TSH levels on neonatal birth weight.

Materials and Methods: This retrospective cohort study included a total of 398 pregnant women who were followed and delivered at Giresun University Faculty of Medicine between January 2022 and January 2025. Patients were categorized into three groups according to maternal TSH levels: TSH 0.2–2.99 mIU/L as the reference group, TSH 3.0–3.99 mIU/L as the borderline elevated group, and TSH ≥4.0 mIU/L as the high TSH group. Maternal demographic characteristics, obstetric complications, and neonatal outcomes were compared between the groups. Continuous variables were presented as median [interquartile range], whereas categorical variables were expressed as number and percentage. Continuous variables were compared using the Kruskal–Wallis test. Categorical variables were analyzed using the Pearson chi-square test or, when appropriate, the Fisher–Freeman–Halton exact test. Univariable and multivariable linear regression analyses were performed to evaluate the association between maternal TSH categories and neonatal birth weight.

Results: Of the 398 pregnant women included in the study, 276 were in the TSH 0.2–2.99 mIU/L group, 88 were in the TSH 3.0–3.99 mIU/L group, and 34 were in the TSH ≥4.0 mIU/L group. There were no significant differences between the groups in terms of maternal age, gravida, parity, history of miscarriage, hemoglobin level, gestational diabetes mellitus, or preeclampsia. Gestational age at delivery was similar across the groups: 38 [37–39], 38 [37–39], and 38 [37–39] weeks, respectively (p=0.850). In contrast, neonatal birth weight differed significantly across TSH categories. Median birth weight was 3305 [3004–3603] g in the reference TSH group, 3285 [3041–3465] g in the borderline elevated TSH group, and 3135 [2788–3344] g in the high TSH group. Median birth weight was particularly lower among women with TSH ≥4.0 mIU/L, and the difference between the groups was statistically significant (p=0.025). Post-hoc Dunn–Bonferroni analysis showed that neonatal birth weight was significantly lower in the TSH ≥4.0 mIU/L group than in the TSH 0.2–2.99 mIU/L group (adjusted p=0.026), whereas the other pairwise comparisons were not statistically significant. No significant differences were observed between the groups regarding preterm birth, cesarean delivery, fetal sex, or 1-minute and 5-minute Apgar scores. Similar findings were observed in regression analyses. A TSH level of ≥4.0 mIU/L was significantly associated with lower neonatal birth weight compared with the reference TSH group in univariable analysis (β=-206.39 g, p=0.010). This association remained statistically significant in the multivariable model adjusted for gestational age at delivery and relevant maternal-fetal variables (adjusted β=-170.27 g, p=0.013).

Conclusion: Elevated maternal TSH levels were associated with lower neonatal birth weight despite similar gestational age at delivery. This finding suggests a potential effect of maternal TSH elevation on fetal growth. However, due to the retrospective design of the study, causality cannot be established, and these results should be supported by larger prospective studies.

Keywords: Maternal TSH; neonatal birth weight; pregnancy outcomes

SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL APPLICATIONS OF MIXED LIGAND METAL COMPLEXES WITH A LIGAND DERIVED FROM 2-AMINO-4-CHLOROPHENOL AND 5-BROMO SALICYLALDEHYDE AND 1,10 PHENANTHROLINE AS A CO-LIGAND

Fatima Qasim

Department of Chemistry, Government College University Faisalabad, Pakistan

Bushra Parveen

Department of Chemistry, Government College University Faisalabad, Pakistan

Kulsoom Ghulam Ali

Department of Chemistry, Government College University Faisalabad, Pakistan

ABSTRACT

Schiff base ligand (HL) was synthesized by reacting 5-bromosalicylaldehyde with 2-amino-4-chlorophenol in methanol. Metal complexes of Ni(II), Cu(II) and Zn(II) complexes (1-3) were synthesized by reaction of Schiff base ligand (HL) with metal salts NiCl2.6H₂O, CuCl2.2H₂O and ZnC4H6O4 in methanolic solution during reflux. Mixed ligand metal complexes (4-6) were formed by refluxing the methanolic solution of Schiff base (HL) with metal salts and by adding 1,10 phenanthroline as a co-ligand. The ligand to metal ratio in all the synthesized complexes is 1:1. Elemental analyses information suggests stoichiometry of the metal compounds. Molar conductance suggested non-electrolytic behavior of Schiff base ligand (HL) and metal complexes. UV-visible data explained mode of transitions of electrons because of ($\pi \rightarrow \pi^*$), ($n \rightarrow \pi^*$) and LMCT transitions. FT-IR data showed bonding of Schiff base ligand (HL) with metal ions by oxygen of deprotonated hydroxyl group and nitrogen of azomethine group. It was predicted that all the metal complexes have octahedral geometry. Antibacterial activity was checked against *E.coli* and *S. aureus*. Antifunagl activity was checked against *A.niger* and *A.flavus*. Metal complexes were more active than the free Schiff base ligand (HL) due to chelation effect.

ASSOCIATION OF ORAL AND PARENTERAL ANTIDIABETIC THERAPY WITH ACUTE MYOCARDIAL INFARCTION IN PATIENTS WITH DIABETES MELLITUS

Maria Fareed Siddiqui

Assistant Professor Pharmaceutical Biotechnology, Faculty of Pharmacy, University of Lahore-Pakistan.

ORCID: https://orcid.org/0000-0001-8515-5260

Umar Raees

MPhil Scholar, Department of Pharmacy, University of Lahore

Aiman Mehmood

Faculty of Pharmacy, Minhaj University, Lahore.

ABSTRACT

Diabetes mellitus is a major risk factor for cardiovascular complications, particularly acute myocardial infarction. Previous studies have shown that diabetic individuals are at greater risk of myocardial infarction than non-diabetic individuals. In addition to the underlying metabolic disturbance, the cardiovascular influence of antidiabetic therapy has also been a subject of clinical interest. The present study evaluated the association between oral and parenteral antidiabetic treatment and myocardial infarction in diabetic patients.

A comparative analysis was performed among control subjects and diabetic patients with acute myocardial infarction receiving either oral or parenteral antidiabetic therapy. Statistical evaluation demonstrated significant differences among the study groups ($P < 0.001$). Higher mean values were observed in diabetic patients receiving oral antidiabetic treatment (534.0 ± 2.27) compared with control individuals (293.4 ± 2.71). Patients receiving parenteral antidiabetic therapy also showed elevated values (532.0 ± 4.33). These findings indicate that diabetic patients with myocardial infarction exhibited marked biochemical alterations irrespective of treatment modality.

The study suggests a possible association between antidiabetic therapy and myocardial infarction-related biochemical changes in diabetic patients. However, because treatment history, disease duration, and clinical variables may influence cardiovascular outcomes, further well-designed studies are needed to better define this relationship.

Keywords: Diabetes mellitus; Acute myocardial infarction; Oral antidiabetic drugs; Parenteral antidiabetic therapy; Cardiovascular risk; Biochemical markers

THE HEALTH–LABOUR NEXUS: A CRITICAL REVIEW OF OCCUPATIONAL HEALTH CHALLENGES, THEORETICAL FRAMEWORKS, AND MULTILEVEL STRATEGIES FOR SUSTAINABLE WORKER WELL-BEING

Zahra ORDUDARI,

(PhD, Isfahan University of Medical Science)

ABSTRACT

The intricate relationship between health sciences and labour constitutes a foundational pillar of sustainable socioeconomic development, yet it remains systematically underaddressed in both public health policy and workplace practice. This paper synthesises current epidemiological evidence, theoretical frameworks, and intervention strategies at the intersection of occupational health and the modern world of work. Drawing upon recent Global Burden of Disease data (Zong et al., 2026), International Labour Organization reports (ILO, 2019), and World Health Organization guidelines (WHO, 2022), the analysis demonstrates that occupational accidents and work-related diseases claim approximately 2.78 million lives annually, while productivity losses due to absenteeism and presenteeism amount to 3–4% of global gross domestic product. The paper critically examines four major theoretical frameworks—the Job Demand-Control model (Karasek, 1979), the Effort-Reward Imbalance model (Siegrist, 1996), the Psychosocial Safety Climate theory (Loh & Dollard, 2019), and the Total Worker Health® approach (NIOSH, 2015)—each of which offers distinct insights into how work organisation, psychosocial exposures, and workplace policies shape health outcomes. The results and discussion section integrates empirical findings across six domains: cardiovascular and metabolic consequences of shift work (Nabeel et al., 2024), the mental health crisis in contemporary workplaces (WHO, 2022), occupational health inequalities (Schulte & Chun, 2022), the economic burden of lost productivity, the role of precarious employment (ILO, 2019), and the efficacy of workplace interventions (Driscoll et al., 2025). The paper concludes that advancing worker health requires a paradigm shift from reactive, individual-level risk management to proactive, systems-level strategies that integrate occupational safety with health promotion, address structural determinants of health inequalities, and embed safe and healthy working conditions as a fundamental right at work.

Keywords: occupational health; decent work, psychosocial safety climate; work-related stress; health inequalities, Total Worker Health

THERAPEUTIC IMPACT OF SOCIAL SKILLS-BASED INTERVENTION ON HIV SELF-STIGMA AMONG NEWLY DIAGNOSED PATIENTS IN OYO STATE, NIGERIA

Ndidi M, Ofole Ph. D

Department of Counselling and Human Development Studies, Faculty of Education University of Ibadan, Nigeria

OKESIJI L.A Ph. D

Department of Counselling and Human Development Studies, Faculty of Education University of Ibadan, Nigeria.

ABSTRACT

HIV/AIDS related Self-stigma results into feelings of shame, ignominy and worthlessness, thereby reduce the eudaemonic well-being in Persons Living With HIV and AIDS. This study therefore, investigated the therapeutic effects of Social Skills Training (SST) on Self-stigma among persons newly diagnosed of HIV in Oyo State, Nigeria. Pretest-posttest control group quasi-experimental design with 2x5 factorial matrix was adopted. Forty-two persons (male=14; female=28) newly diagnosed of HIV with age range between 20-45 years were purposively selected from Antiretroviral therapy (ART) centres in two Hospitals in Oyo State, Nigeria. The centres were randomly assigned to SST (23) and control groups (19). Instruments used were Internalized Stigma of Mental Illness Scale-Adapted for HIV (ISMI-HIV) ($r = 0.90$) and Internalized AIDS-Related Stigma Scale (IA-RSS) ($r = 0.78$). The results of the study revealed that social skills training had a significant main effect on the reduction of self-stigma among persons newly diagnosed with HIV in Oyo State, Nigeria, $F(2, 33) = 711.644$, $p < .05$, $\eta^2 = .979$, indicating a very large effect size and showing that the intervention accounted for a substantial proportion of the variance in post-test self-stigma scores. In addition, there was a significant interaction effect between treatment group and age on self-stigma reduction, $F(2, 33) = 6.528$, $p < .05$, $\eta^2 = .296$, demonstrating that age significantly moderated the effectiveness of the intervention. Further post hoc analysis using Scheffé tests indicated that younger participants (20–29 years) experienced greater reductions in self-stigma compared to older participants (35 years and above), with the largest difference observed between the 20–24 and 40+ age groups. However, differences among older age groups were not statistically significant. Hence, the findings suggest that social skills training is highly effective in reducing self-stigma, with stronger benefits observed among younger participants.

Keywords: People living with HIV, HIV self-stigma, Well-being, Social Skills Training, age.

THE RELATIONSHIP BETWEEN ENDOMETRIAL CANCER AND LYNCH SYNDROME

Loichita Mihai

Doctoral School, "Victor Babes" University of Medicine and Pharmacy Timisoara, Eftimie Murgu Square 2, 300041 Timisoara, Romania

Petre Ion

Department of Functional Sciences, Medical Informatics and Biostatistics Discipline, "Victor Babes" University of Medicine and Pharmacy, 300041 Timisoara

Furau Marius

Vasile Goldiș" Western University of Arad, Romania, Address: B-dul Revoluției nr. 94, Arad, Arad County, Romania, Postal Code: 310130

Faur Ionut

X Department of General Surgery, "Victor Babeș" University of Medicine and Pharmacy Timisoara, 300041 Timisoara, Romania

Bobora Razvan

Doctoral School, "Victor Babes" University of Medicine and Pharmacy Timisoara, Eftimie Murgu Square 2, 300041 Timisoara, Romania

Mirica Nicoleta

Department of Kinetotherapy and Motor Skills, Faculty of Physical Education and Sport, West University of 14 Timișoara, 300223 Timișoara, Romania

Voinea Oana

Carol Davila Univ Med & Pharm, Pathol, Bucharest, Romania

Petre Izabella

Dept Obstet & Gynaecol, "Victor Babes "University of Medicine and Pharmacy, 300041 Timisoara, Romania

ABSTRACT

Background and Objectives: Endometrial cancer is the most common malignant tumor of the female genital tract in developed countries. Although the majority of cases are sporadic, approximately 2–5% are associated with hereditary cancer syndromes, most commonly Lynch syndrome. Identifying patients with Lynch syndrome is essential not only for optimal oncologic management, but also for family screening and prevention of associated malignancies. Lynch syndrome, also known as hereditary nonpolyposis colorectal cancer (HNPCC), is an autosomal dominant genetic disorder caused by germline mutations in DNA mismatch repair (MMR) genes. The most frequently involved genes are MLH1, MSH2, MSH6, PMS2, and EPCAM through secondary inactivation of MSH2. Deficiency of the MMR system leads to the accumulation of DNA replication errors and the development of microsatellite instability (MSI), a key mechanism involved in carcinogenesis. Endometrial cancer is one of the most common extracolonic manifestations of Lynch syndrome and may represent the first clinical manifestation of the disease. Epidemiological studies indicate that women with Lynch syndrome have an estimated 40–60% lifetime risk of developing endometrial cancer. Compared with sporadic cases, the disease occurs at a younger age, frequently before 50 years, and in some families the risk of endometrial cancer may exceed that of colorectal cancer.

Conclusions: The diagnosis of Lynch syndrome enables periodic surveillance, individualized preventive strategies, prophylactic surgery in selected cases, and family screening. Lynch syndrome remains one of the most important hereditary causes of endometrial cancer. The integration of immunohistochemistry and molecular testing into modern oncologic practice facilitates the early identification of patients with MMR deficiency, confirmation of the genetic diagnosis, and

implementation of personalized therapeutic approaches. Universal screening of endometrial cancer for MMR protein expression is becoming increasingly important in contemporary cancer prevention and management.

Keywords: endometrial cancer, Lynch syndrome, oncologic management

THE IMPACT OF ESTROGEN DEFICIENCY DURING PERIMENOPAUSE ON ARTERIAL STIFFNESS: A CLINICAL STUDY

Burlica Sorin

Doctoral School, "Victor Babes" University of Medicine and Pharmacy Timisoara, Eftimie Murgu Square 2, 300041 Timisoara, Romania

Petre Izabella

Dept Obstet & Gynaecol, "Victor Babes "University of Medicine and Pharmacy, 300041 Timisoara, Romania

Iurciuc Mircea

Department of Clinic Nursing, "Victor Babes" University of Medicine and Pharmacy, Eftimie Murgu Square 28 2, 300041 Timisoara, Romania

Buleu Tiberiu

Faculty of General Medicine, "Victor Babes" University of Medicine and Pharmacy, 300041 Timisoara, Romania

Burlica Adela

"Victor Babes" University of Medicine and Pharmacy Timisoara, Eftimie Murgu Square 2, 300041 Timisoara, Romania

Mercioni Marina

"Victor Babes" University of Medicine and Pharmacy Timisoara, 300041 Timisoara, Romania; Applied Electronics Department, Faculty of Electronics, Telecommunications and Information Technologies, Politehnica University Timis, oara, 300223 Timisoara, Romania

Iurciuc Stela

Department of Cardiology, "Victor Babes" University of Medicine and Pharmacy, E. Murgu Square No. 2, 300041 Timisoara, Romania

Petre Ion

Department of Functional Sciences, Medical Informatics and Biostatistics Discipline, "Victor Babes" University of Medicine and Pharmacy, 300041 Timisoara, Romania

ABSTRACT

Background and Objectives: Arterial stiffness is closely correlated with the presence of cardiovascular risk factors and with the atherosclerotic process. The elastic properties of arteries are increasingly used for cardiovascular risk stratification across various populations. In this context, the guidelines of the European Society of Hypertension and the European Society of Cardiology recommend the use of pulse wave velocity (PWV) in the monitoring of hypertensive patients, as it is considered the gold standard for the assessment of arterial stiffness. Arterial stiffness reflects a reduction in vascular elasticity and is recognized as an important marker of cardiovascular risk. In females, estrogen has a protective effect on the cardiovascular system, contributing to the maintenance of vascular elasticity. A decrease in estrogen levels, which may occur before the onset of menopause, as in cases of premature ovarian insufficiency, is associated with accelerated vascular changes and an increased cardiovascular risk. **Materials and Methods:** The study included 211 women, divided into two groups: Group A (n=105), consisting of perimenopausal women, and Group B (n=105), consisting of postmenopausal women. Group A included women aged between 40 and 44 years. Perimenopausal status was defined in women aged 40 to 55 years with irregular menstrual cycles. Participants were further classified as early perimenopausal if they experienced two or more menstrual cycles with a variation in cycle length of at least 7 days, or as late perimenopausal if they had amenorrhea lasting 2 months or more.

Group B included postmenopausal women aged between 45 and 48 years, with the overall postmenopausal age range extending from 45 to 70 years, defined by the presence of amenorrhea for at least 12 consecutive months. Menopausal status was established based on clinical evaluation, medical history, and the presence of symptom clusters according to the Stages of Reproductive Aging Workshop (STRAW) criteria. These symptom clusters included sweating, hot flashes, insomnia, cognitive impairment, weight gain, appetite changes, mood swings, reduced libido, difficulties in concentration, and short-term memory complaints.

Conclusions: Pulse wave velocity (PWV) is regarded as the gold standard method for assessing arterial stiffness, providing valuable information on early vascular aging and helping to predict cardiovascular events. Due to its simple methodology, high reproducibility, and non-invasive nature, PWV is increasingly applicable in routine clinical practice worldwide for evaluating peripheral arterial stiffness. Overall, PWV represents a useful and reliable tool for the diagnosis and risk stratification of cardiovascular disease.

Keywords: rigiditatea arteriala, deficit de estrogen, perimenopauza, menopauza

THE EMERGING ROLE OF GLP-1 ANALOGS IN NUTRITION AND OBESITY MANAGEMENT: CURRENT PERSPECTIVES AND NUTRITIONAL CONSIDERATIONS

Melike Postallı

Department of Nutrition and Dietetics, Faculty of Health Sciences, Nuh Naci Yazgan University

Yusuf AYKEMAT

Department of Nutrition and Dietetics, Faculty of Health Sciences, Nuh Naci Yazgan University

ABSTRACT

Glucagon-like peptide-1 (GLP-1) analogs have recently gained substantial attention due to their remarkable efficacy in obesity treatment and metabolic disease management. Initially developed for the treatment of type 2 diabetes mellitus, these agents are now increasingly utilized for weight reduction through mechanisms involving appetite suppression, delayed gastric emptying, improved glycemic control, and enhanced satiety signaling. The rapid expansion of GLP-1 analog use has also generated growing interest regarding their nutritional implications and long-term dietary management strategies.

This literature-based presentation aims to evaluate the current evidence concerning the relationship between GLP-1 analog therapy and nutrition. Particular emphasis will be placed on changes in appetite regulation, dietary intake, body composition, micronutrient adequacy, gastrointestinal side effects, and the importance of individualized nutritional counseling during treatment. Furthermore, recent findings regarding muscle mass preservation, protein intake optimization, and sustainable dietary approaches during pharmacological weight loss will be discussed. The presentation will also address potential risks associated with inadequate nutrient intake and highlight the critical role of dietitians in multidisciplinary obesity management. In conclusion, GLP-1 analogs represent a promising advancement in obesity therapeutics; however, effective outcomes require comprehensive nutritional monitoring and personalized dietary interventions to maximize benefits while minimizing adverse nutritional consequences.

Keywords: GLP-1 analogs; obesity, nutrition therapy; weight management, appetite regulation; dietary intake

FOOD NOISE: NEUROBEHAVIORAL MECHANISMS, APPETITE REGULATION, AND NUTRITIONAL PERSPECTIVES

Ümit Enes Ünsal

Department of Nutrition and Dietetics, Faculty of Health Sciences, Nuh Naci Yazgan University

Yusuf AYKEMAT

Department of Nutrition and Dietetics, Faculty of Health Sciences, Nuh Naci Yazgan University

ABSTRACT

The term “food noise” has recently emerged to describe persistent and intrusive thoughts about food, eating, cravings, and meal planning that may significantly affect eating behaviors and quality of life. Although not yet formally recognized as a clinical diagnosis, food noise has gained increasing attention in obesity research and nutritional sciences due to its potential relationship with appetite dysregulation, emotional eating, and overeating behaviors. Individuals experiencing food noise often report difficulty controlling food-related thoughts, which may contribute to excessive energy intake and challenges in long-term weight management.

This literature-based presentation aims to evaluate the current evidence regarding food noise and its potential neurobehavioral and nutritional mechanisms. Particular emphasis will be placed on the role of appetite-regulating hormones, reward pathways, stress, emotional triggers, hedonic hunger, and highly processed foods in the development of persistent food-related thoughts. Furthermore, recent findings concerning the effects of dietary patterns, behavioral interventions, mindful eating approaches, and GLP-1 receptor agonists on food noise reduction will be discussed. The presentation will also address the relationship between food noise, obesity, eating behaviors, and psychological well-being.

In conclusion, food noise represents an emerging concept that may help explain complex eating behaviors and difficulties associated with appetite control. Better understanding of its underlying mechanisms may contribute to the development of more effective nutritional and behavioral strategies for obesity management and long-term dietary adherence.

Keywords: food noise; appetite regulation; obesity; eating behavior; hedonic hunger; nutrition therapy

MINDFUL EATING: CURRENT PERSPECTIVES ON EATING AWARENESS AND NUTRITIONAL BEHAVIOR

Rabia Çiçek

Department of Nutrition and Dietetics, Faculty of Health Sciences, Nuh Naci Yazgan University

Yusuf AYKEMAT

Department of Nutrition and Dietetics, Faculty of Health Sciences, Nuh Naci Yazgan University

ABSTRACT

Mindful eating has gained increasing attention as a behavioral and nutritional approach that promotes awareness during food consumption and encourages healthier eating habits. Derived from the broader concept of mindfulness, mindful eating focuses on paying deliberate attention to hunger and satiety cues, emotional triggers, sensory experiences, and eating behaviors without judgment. This approach has been associated with improved dietary quality, reduced emotional eating, and better weight management outcomes.

This literature-based presentation aims to evaluate the current evidence regarding mindful eating and its potential effects on nutritional behavior and metabolic health. Particular emphasis will be placed on the psychological and physiological mechanisms underlying mindful eating practices, including appetite awareness, emotional regulation, stress reduction, and eating control. Furthermore, recent findings related to mindful eating and obesity prevention, binge eating behaviors, dietary adherence, and body weight management will be discussed. The presentation will also address the practical applications of mindful eating strategies within nutrition counseling and multidisciplinary health interventions.

In conclusion, mindful eating represents a promising behavioral strategy that may contribute to healthier dietary habits and improved relationships with food. However, sustainable outcomes require individualized approaches and integration with comprehensive nutrition and lifestyle interventions.

Keywords: mindful eating; eating behavior; obesity; appetite regulation; nutrition counseling; dietary awareness

ULTRA-PROCESSED FOODS AND APPETITE REGULATION: CURRENT EVIDENCE AND NUTRITIONAL PERSPECTIVES

Rümeysa Karapınar

Department of Nutrition and Dietetics, Faculty of Health Sciences, Nuh Naci Yazgan University

Yusuf AYKEMAT

Department of Nutrition and Dietetics, Faculty of Health Sciences, Nuh Naci Yazgan University

ABSTRACT

Ultra-processed foods (UPFs) have become increasingly prevalent in modern dietary patterns and are considered a major contributor to the global rise in obesity and metabolic disorders. Characterized by high levels of added sugar, fat, salt, flavor enhancers, and industrial additives, these foods are often designed to be highly palatable and convenient. Growing scientific evidence suggests that excessive consumption of ultra-processed foods may disrupt appetite regulation mechanisms, promote overeating behaviors, and negatively affect metabolic health.

This literature-based presentation aims to evaluate the current evidence regarding the relationship between ultra-processed food consumption and appetite regulation. Particular emphasis will be placed on the physiological and neurobehavioral mechanisms associated with hyper-palatability, reward pathways, satiety signaling, glycemic responses, and hedonic hunger. Furthermore, recent findings concerning the effects of ultra-processed foods on energy intake, body weight regulation, gut microbiota, and eating behaviors will be discussed. The presentation will also address the potential role of food additives, texture modification, and rapid digestibility in altering hunger and satiety responses.

In conclusion, ultra-processed foods may significantly impair appetite control and contribute to obesity development through multiple biological and behavioral pathways. Increasing awareness regarding food processing levels and promoting healthier dietary patterns may represent important strategies for improving long-term metabolic health and obesity prevention.

Keywords: ultra-processed foods; appetite regulation; obesity; eating behavior; hedonic hunger; nutrition therapy

FOOD ADDICTION: CURRENT APPROACHES, NEUROBIOLOGICAL MECHANISMS, AND NUTRITIONAL PERSPECTIVES

Hümeyra Çorakçı

Department of Nutrition and Dietetics, Faculty of Health Sciences, Nuh Naci Yazgan University

Yusuf AYKEMAT

Department of Nutrition and Dietetics, Faculty of Health Sciences, Nuh Naci Yazgan University

ABSTRACT

Food addiction has emerged as an increasingly discussed concept in recent years due to the rising prevalence of obesity, overeating behaviors, and highly processed food consumption. Defined as a pattern of compulsive eating behavior characterized by impaired control over food intake despite negative consequences, food addiction shares several behavioral and neurobiological similarities with substance use disorders. Particularly, foods rich in sugar, fat, and salt are believed to stimulate reward-related pathways in the brain, potentially contributing to addictive-like eating behaviors.

This literature-based presentation aims to evaluate the current evidence regarding food addiction from nutritional and neurobiological perspectives. Particular emphasis will be placed on the underlying mechanisms involving dopamine-mediated reward systems, appetite regulation, emotional eating, stress-related eating behaviors, and the role of ultra-processed foods. Furthermore, the relationship between food addiction and obesity, metabolic disorders, psychological well-being, and eating disorders will be discussed. The presentation will also address current nutritional approaches, behavioral strategies, and multidisciplinary interventions that may support the management of addictive eating behaviors.

In conclusion, food addiction represents a complex and multifactorial phenomenon influenced by biological, psychological, and environmental factors. Understanding the mechanisms underlying addictive eating behaviors may contribute to the development of more effective nutritional and behavioral interventions for obesity prevention and long-term dietary management.

Keywords: food addiction; obesity; eating behavior; ultra-processed foods; appetite regulation; nutrition therapy

THE POTENTIAL ROLE OF BITTER HOP EXTRACT IN OBESITY MANAGEMENT: CURRENT EVIDENCE AND NUTRITIONAL PERSPECTIVES

Merve Nur Demir

Department of Nutrition and Dietetics, Faculty of Health Sciences, Nuh Naci Yazgan University

Yusuf AYKEMAT

Department of Nutrition and Dietetics, Faculty of Health Sciences, Nuh Naci Yazgan University

ABSTRACT

Obesity is a complex chronic disease associated with metabolic disturbances, excessive energy intake, and impaired appetite regulation. In recent years, increasing scientific interest has focused on natural bioactive compounds that may contribute to body weight management and metabolic health improvement. Among these compounds, bitter hop extract derived from *Humulus lupulus* has attracted attention due to its potential effects on appetite control, energy metabolism, and gastrointestinal signaling pathways.

This literature-based presentation aims to evaluate the current evidence regarding the effects of bitter hop extract on obesity management and metabolic regulation. Particular emphasis will be placed on the activation of bitter taste receptors, modulation of gut hormones such as glucagon-like peptide-1 (GLP-1), peptide YY (PYY), and ghrelin, as well as potential impacts on satiety, gastric emptying, and energy intake. Furthermore, recent findings concerning the anti-inflammatory, antioxidant, and metabolic effects of hop-derived bioactive compounds will be discussed. The presentation will also address current limitations, safety considerations, and the potential role of bitter hop extract within evidence-based nutritional interventions for obesity management.

In conclusion, bitter hop extract may represent a promising nutritional approach for appetite regulation and obesity management through multiple physiological mechanisms. However, further human clinical studies are needed to clarify its long-term efficacy, safety profile, and practical applications in personalized nutrition strategies.

Keywords: bitter hop extract; obesity, appetite regulation; GLP-1; satiety; nutrition therapy

THE EFFECTS OF WHEY PROTEIN SUPPLEMENTATION ON APPETITE CONTROL: CURRENT EVIDENCE AND NUTRITIONAL PERSPECTIVES

Yusuf Erdoğan

Department of Nutrition and Dietetics, Faculty of Health Sciences, Nuh Naci Yazgan University

Yusuf AYKEMAT

Department of Nutrition and Dietetics, Faculty of Health Sciences, Nuh Naci Yazgan University

ABSTRACT

Whey protein has become one of the most widely utilized nutritional supplements due to its high biological value, rapid digestibility, and potential metabolic benefits. Beyond its established role in muscle protein synthesis and sports nutrition, increasing scientific evidence suggests that whey protein supplementation may contribute significantly to appetite regulation and energy intake control. These effects have generated considerable interest in the context of obesity management, weight control, and metabolic health improvement.

This literature-based presentation aims to examine the current evidence regarding the effects of whey protein on appetite control and satiety mechanisms. Particular focus will be placed on the physiological pathways involved in hunger regulation, including gastric emptying, gut hormone responses such as glucagon-like peptide-1 (GLP-1), peptide YY (PYY), and ghrelin, as well as postprandial glycemic responses. Additionally, the influence of whey protein on short-term satiety, daily energy intake, body weight regulation, and dietary adherence will be discussed. The presentation will further address the practical applications of whey protein supplementation in clinical nutrition and weight management strategies.

In conclusion, whey protein supplementation appears to have beneficial effects on appetite control and satiety regulation through multiple physiological mechanisms. However, individualized nutritional planning and evidence-based supplementation approaches remain essential to optimize health outcomes and ensure sustainable dietary management.

Keywords: whey protein; appetite control; satiety; obesity; nutrition therapy; dietary supplementation

THE ROLE OF *AKKERMANSIA MUCINIPHILA* IN OBESITY MANAGEMENT: CURRENT INSIGHTS AND NUTRITIONAL PERSPECTIVES

Fatma Aybike Bozoklu

Department of Nutrition and Dietetics, Faculty of Health Sciences, Nuh Naci Yazgan University

Yusuf AYKEMAT

Department of Nutrition and Dietetics, Faculty of Health Sciences, Nuh Naci Yazgan University

ABSTRACT

Obesity is a multifactorial chronic disease associated with metabolic disorders, low-grade inflammation, and alterations in gut microbiota composition. In recent years, growing scientific evidence has highlighted the significant role of intestinal microbiota in energy metabolism and obesity pathogenesis. Among the microbial species investigated, *Akkermansia muciniphila*, a mucin-degrading bacterium naturally present in the human gastrointestinal tract, has emerged as a promising target in obesity management and metabolic health improvement.

This literature-based presentation aims to evaluate the current evidence regarding the relationship between *Akkermansia muciniphila* and obesity management. Particular emphasis will be placed on the mechanisms through which this microorganism may influence body weight regulation, intestinal barrier integrity, glucose metabolism, lipid metabolism, inflammatory pathways, and insulin sensitivity. Furthermore, recent studies investigating the effects of dietary patterns, prebiotics, probiotics, polyphenols, and lifestyle interventions on *Akkermansia muciniphila* abundance will be discussed. The presentation will also address the potential clinical applications and limitations of microbiota-targeted nutritional strategies in obesity treatment.

In conclusion, *Akkermansia muciniphila* represents a promising microbial candidate for obesity management due to its potential beneficial effects on metabolic health and gut barrier function. However, further large-scale human studies are needed to better understand its therapeutic potential and long-term clinical efficacy within personalized nutrition approaches.

Keywords: *Akkermansia muciniphila*; obesity; gut microbiota; metabolic health; nutrition therapy; probiotics

DETERMINATION OF THE FATTY ACID COMPOSITION OF THE HEXANE EXTRACT OF COLD-PRESSED BLACK CUMIN WASTE BY GC-MS

Mesut GÖK

Dr., Siirt University, Science and Technology Application and Research Center, Siirt-Türkiye, ORCID ID: 0000-0001-9217-8022

İbrahim TEĞİN

Prof. Dr., Siirt University, Faculty of Arts and Science, Department of Chemistry, Siirt, Türkiye, ORCID ID: 0000-0002-5661-7195

ABSTRACT

Black cumin (Nigella sativa) is a plant that bears black seeds beneath its delicate flowers. While black cumin oil is used for conditions such as nasal ulcers, boils, eczema, joint swelling, and orchitis, it is also used today for cosmetic purposes in skin care, anti-aging, and hair loss prevention, and its sun-protective effects have been identified.

When seeds are exposed to high heat (hot pressing), the delicate natural compounds within them may be damaged. For this reason, temperature is strictly controlled in cold-pressing machines. The seeds are separated drop by drop in their most natural state without being scorched. This method ensures that the oil retains its characteristic aroma and biological value in their freshest form. After cold pressing, the pomace may still contain (15–25%) oil.

In this study, the hexane extract of black cumin (Nigella sativa) waste remaining after oil extraction by the cold-press method was analyzed by gas chromatography–mass spectrometry (GC-MS). Upon examination of the fatty acid methyl ester (FAME) profile of the extract, it was observed that the most predominant component was 8,11-octadecadienoic acid methyl ester (linoleic acid methyl ester) at a rate of 45.08%. This was followed by 9-octadecenoic acid (Z)-methyl ester (oleic acid methyl ester) at 22.42% and hexadecanoic acid methyl ester (palmitic acid methyl ester) at 20.83%. Additionally, octadecanoic acid methyl ester (stearic acid methyl ester) was detected at 5.06%, along with low levels of 11,13-eicosadienoic acid methyl ester (3.93%) and 11-eicosenoic acid methyl ester (0.61%). In total, phenolic derivatives and other bioactive compounds (e.g., 3,6-bis(t-butyl) fluorenone, 18,19-secoyohimban-19-oic acid) were identified in varying proportions ranging from 0.21% to 0.46%. The results indicate that cold-pressed black cumin seed waste is particularly rich in linoleic and oleic acids, and that the utilization of this waste could serve as an economical resource for food, cosmetic, and pharmaceutical applications.

Keywords: Black cumin waste, hexane extract, GC-MS, Fatty acids, bioactive compounds

1. INTRODUCTION

Nigella sativa L. (Ranunculaceae), commonly known as black cumin or black seed, is one of the most revered medicinal plants in traditional medicine systems across the Middle East, South Asia, and the Mediterranean region (Thani et al., 2025; Kizil et al., 2008). The seeds of this annual herb have been extensively utilized for over two millennia for their therapeutic and nutritional properties, with documented applications ranging from respiratory disorders and inflammatory conditions to metabolic dysfunctions and infectious diseases (Deniz, 2023). The growing body of modern pharmacological evidence has largely validated these traditional uses, attributing the biological activities of N. sativa to a diverse array of phytochemicals, including thymoquinone, sterols, saponins, and various fatty acid derivatives (Vatansev et al., 2013; Ahmad et al., 2013).

The fixed oil of N. sativa seeds, typically comprising 30–38% of the seed mass, has been the primary focus of commercial and research interest (Hannan et al., 2021). Cold pressing, a mechanical extraction

method devoid of organic solvents and high temperatures, is widely preferred for producing high grade Nigella oil, as it preserves heat labile bioactive constituents and yields an oil with superior antiradical properties and characteristic organoleptic profiles (Kiralan et al., 2014; Abedinzadeh et al., 2024). However, this extraction process generates a substantial quantity of solid residue, often referred to as press cake or extraction waste, which remains underexplored despite representing a significant portion of the original biomass (Łopusiewicz et al., 2022).

The valorisation of agricultural and food processing by products has become a critical imperative within the framework of circular economy and sustainable development (Makris & Şahin, 2019). Recent studies have begun to challenge the perception of N. sativa press residue as mere waste. For instance, Barkah et al. (2021) reported that cold press residue of black seed retains considerable nutritional value, including 27.78% crude protein and 350 ppm thymoquinone, the latter being the primary bioactive marker of N. sativa (Barkah et al., 2021). Furthermore, Thani et al. (2025) demonstrated that significant proportions of health benefiting phytoconstituents, including total phenolic content (78.1–85.9%) and antioxidant capacity (65.4–90.4%), are transferred into the solid residue rather than the oil phase during screw pressing (Thani et al., 2025). These findings underscore the potential for repurposing this by product for value added applications in nutraceutical, cosmetic, or environmental remediation sectors (Makris & Şahin, 2019).

Despite this growing recognition, detailed characterization of the lipophilic fraction of cold press N. sativa residue remains limited. Gas chromatography mass spectrometry (GC MS) analysis of non-polar extracts provides critical insight into the residual fatty acid methyl esters, hydrocarbons, and other lipophilic compounds that persist in the press cake after oil extraction. Such analyses are essential for comprehensive mass balance studies, for evaluating the potential for sequential extraction processes, and for identifying unique marker compounds that may confer biological properties distinct from those of the expressed oil. Therefore, this study presents a detailed GC MS based compositional analysis of the hexane extract of Nigella sativa cold press residue, aiming to characterize the remaining lipophilic profile and contribute to the scientific foundation for the effective utilization of this underappreciated agricultural by product.

2. EXPERIMENTAL RESEARCH

Five grams of Black cumin waste were placed in a 50 mL falcon tube and completed to 50 mL with hexane solvent, then left to stand for 1 hour in a 70 °C water bath. 2 milliliters of this hexane extract was taken tube and transferred to a 2 mL GC-MS vial using a syringe and a 0.22 µm PVDF filter, ready for analysis. Biolubricant raw material and cold press Nigella sativa residue are shown in Figure 1.



Figure 1. Biolubricant raw material and cold press Nigella sativa residue

Pine resin hexane extract were analysed using ISQ mass spectrometry (Thermo Fisher Scientific, Austin, TX) and Trace 1310 gas chromatography. The procedure was held at an initial temperature of 80°C for 2 minutes, then heated to 300°C at 3°C/minute and held at 300°C for 1 minutes, reheated to 310°C at 5°C/minute, and finally held at 310°C for 10 minutes. The ion source and detector temperatures were 250°C, respectively. The sample injection volume was 1.0 mL, and separation was performed using a Thermo TG-5MS GC column (30 m x 0.25 mm ID x 0.25 µm) with helium as the carrier gas at 2 mL/min. The mass spectral scan range was set to 55–550 (amu). Components were identified in the NIST Demo, Wiley7, Wiley9, redlip, mainlip, and WinRI libraries (Sırma et al. 2025).

3. RESULTS AND DISCUSSION

The hexane extract of cold press Nigella sativa residue was analyzed by gas chromatography mass spectrometry (GC MS), and a total of 13 compounds were identified, accounting for nearly 100% of the chromatographic peak area (Table 1 and Figure 2). The extract was overwhelmingly dominated by fatty acid methyl esters (FAMEs), which constituted approximately 99% of the total ion current, indicating that the non-polar fraction of the press cake consists almost entirely of residual neutral lipids.

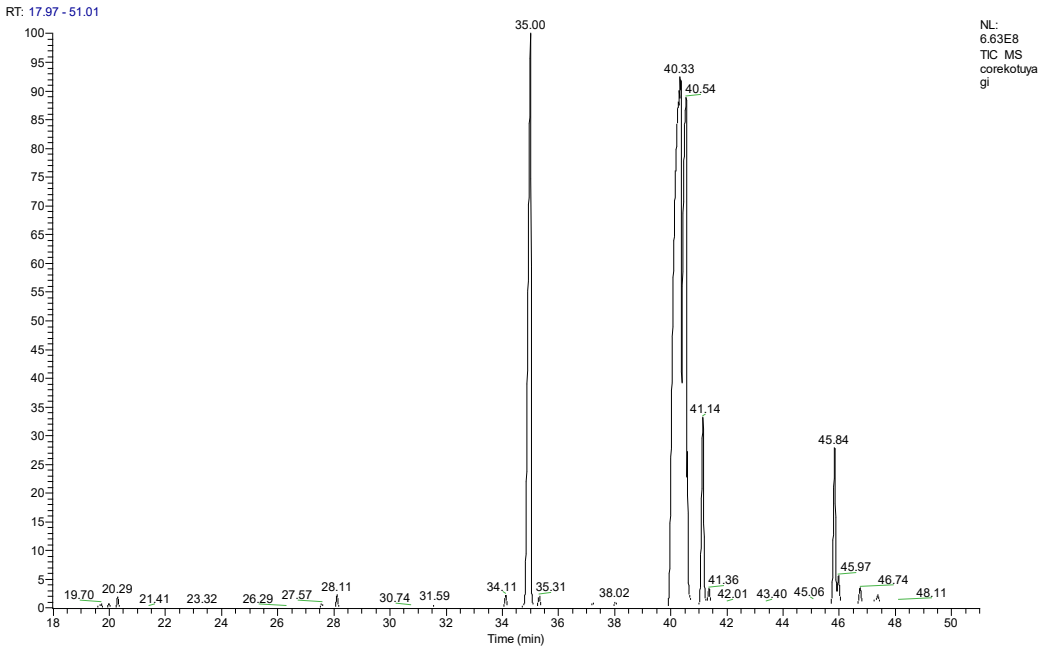


Figure 2. GC-MS chromatogram of the hexane extract of cold press Nigella sativa residue

Table 1. GC-MS results for the hexane extract of cold press Nigella sativa residue

	Compound Name	RT	%AREA	CasNumber
1	Phenol,2,4-bis(1,1-dimethylethyl)-	20.30	0.21	96-76-4
2	Methyl tetradecanoate	28.11	0.26	124-10-7
3	7-Hexadecenoic acid, methylester, (Z)-	34.12	0.29	56875-67-3
4	Hexadecanoicacid, methylester	35.00	20.83	112-39-0
5	3,6-bis(t-Butyl)fluorenone	35.31	0.25	NA
6	8,11-Octadecadienoic acid,methyl ester	40.33	45.08	56599-58-7
7	9-Octadecenoicacid (Z)-,methyl ester	40.54	22.42	112-62-9
8	Octadecanoicacid, methylester	41.14	5.06	112-61-8
9	Oleic Acid	41.36	0.46	112-80-1
10	11,13-Eicosadienoic acid,methyl ester	45.84	3.93	56599-57-6
11	11-Eicosenoicacid, methylester	45.97	0.61	3946-08-5
12	Eicosanoicacid, methylester (CAS)	46.74	0.38	1120-28-1
13	18,19-Secoyohimban-19-oicacid	47.37	0.23	5523-49-9

The most abundant compound was 8,11 Octadecadienoic acid methyl ester (linoleic acid methyl ester, C18:2n 6), comprising 45.08% of the total peak area (RT 40.33 min), followed closely by 9

Octadecenoic acid (Z) methyl ester (oleic acid methyl ester, C18:1n 9) at 22.42% (RT 40.54 min). Together, these two unsaturated fatty acid derivatives accounted for over 67% of the entire extract. Linoleic acid is an essential polyunsaturated fatty acid (PUFA) that plays a critical role in human health, including anti inflammatory, cardioprotective, and dermatological effects (Marangoni et al., 2020; Simopoulos, 2016). Oleic acid, a monounsaturated fatty acid (MUFA), is known for its hypocholesterolemic properties and oxidative stability (Lopez et al., 2011). The predominance of linoleic and oleic acid in the cold press residue is consistent with the fatty acid profile of whole Nigella sativa seed oil, where linoleic acid (50–60%) and oleic acid (20–25%) are also the two major constituents (Cheikh-Rouhou et al., 2008; Tiruppur Venkatachallam et al., 2010). The fact that these compounds remain in substantial quantities (together >67%) after mechanical oil extraction suggests that the cold pressing process leaves behind a significant fraction of the original lipid content. This observation aligns with Thani et al. (2025), who reported that screw pressing transfers only 65–80% of the total oil into the liquid phase, leaving a considerable residue in the press cake (Thani et al., 2025).

The third most abundant compound was hexadecanoic acid methyl ester (palmitic acid methyl ester, C16:0) at 20.83% (RT 35.00 min). This saturated fatty acid is a common component of seed oils and has been associated with both pro inflammatory and pro apoptotic effects depending on context (Agostoni, Moreno & Shamir, 2016). Octadecanoic acid methyl ester (stearic acid methyl ester, C18:0) was present at 5.06% (RT 41.14 min), while a smaller amount of methyl tetradecanoate (myristic acid methyl ester, C14:0) was also detected at 0.26% (RT 28.11 min). The saturated/unsaturated ratio calculated from the data is approximately 1:3.3, which reflects a health beneficial profile dominated by unsaturated fatty acids. Notably, the presence of eicosanoic acid methyl ester (arachidic acid methyl ester, C20:0) at 0.38% (RT 46.74 min) and 11 eicosenoic acid methyl ester (C20:1) at 0.61% (RT 45.97 min) indicates that long chain fatty acids also survive the cold pressing process. These minor components have been previously reported in N. sativa seed oil, albeit at low concentrations (Hassanien & Moersel, 2003). The extract also contained 11,13 eicosadienoic acid methyl ester (C20:2) at 3.93% (RT 45.84 min) and 7 hexadecenoic acid methyl ester (C16:1) at 0.29% (RT 34.12 min). While C20:2 PUFAs are relatively uncommon in plant seeds, their presence has been documented in Ranunculaceae species and may contribute to unique biological activities such as anti proliferative effects on cancer cell lines (Terzioğlu et al., 2008). The detection of oleic acid (free fatty acid form) at 0.46% (RT 41.36 min) suggests partial hydrolysis of triglycerides during storage or processing, which is a common phenomenon in cold pressed oil residues (Castejón et al., 2014).

Although the extract was predominantly lipidic, several non fatty acid compounds were identified at lower abundances. Phenol, 2,4 bis(1,1 dimethylethyl) (2,4 di tert butylphenol) was detected at 0.21% (RT 20.30 min). This compound is not a natural product of N. sativa but is widely recognized as a contaminant or an antioxidant additive originating from plastic materials, laboratory solvents, or chromatographic column bleed (Zhao et al., 2020). Its presence at very low concentration (0.21%) is unlikely to affect biological interpretations. Similarly, 3,6 bis(t butyl)fluorenone (RT 35.31 min, 0.25%) is another non typical plant metabolite. Fluorenone derivatives have been reported as oxidation products or artifacts formed during GC MS analysis, particularly when samples are exposed to high temperatures (Shi & Gao, 2016). Most intriguingly, 18,19 secoyohimban 19 oic acid (RT 47.37 min, 0.23%) was identified. This compound belongs to the yohimbane type indole alkaloid family, which is known to occur in Nigella sativa seeds. Previous studies have reported the presence of indazole alkaloids such as nigellidine and nigellicine in N. sativa (Atta-ur-Rahman et al., 1995; Yuan et al., 2014). The detection of a seco yohimbane derivative in the press residue indicates that some alkaloids, being less soluble in the cold pressed oil, remain concentrated in the solid fraction. This finding supports the hypothesis that press cake may be enriched in polar or amphiphilic bioactives compared to the expressed oil (Thani et al., 2025).

The GC MS data demonstrate that cold press Nigella sativa residue retains a complex and quantitatively significant lipophilic fraction, dominated by nutritionally valuable unsaturated fatty acids (linoleic and oleic acids) but also containing minor bioactive alkaloids. From a circular economy perspective, this residue should not be regarded as waste but rather as a co product suitable for second stage extraction or direct valorization (Makris & Şahin, 2019; Saini et al., 2025). The high residual linoleic acid content (45%) suggests potential applications in animal feed formulations as an omega 6 source, in cosmetic

emollients, or in bio based lubricants (Uppar, Dinesha & Kumar, 2022). Furthermore, the presence of the alkaloid 18,19 secoyohimban 19 oic acid, albeit minor, warrants further investigation for potential CNS or antimicrobial activities, as yohimbane alkaloids are known to interact with adrenergic receptors (Lambert et al., 1978). A limitation of this study is the use of hexane extraction, which recovers only non polar to moderately polar compounds. Press cake also contains water soluble phenolics, proteins, and polysaccharides that are not captured in this analysis (Barkah et al., 2021). Future studies should employ sequential extraction with solvents of increasing polarity (e.g., ethyl acetate, methanol, water) to achieve a complete mass balance.

4. CONCLUSION

Cold-pressed black cumin seed cake contains a total of approximately 73% beneficial unsaturated fatty acids, consisting of 45% linoleic acid and 22% oleic acid. This byproduct can be utilized as a low-cost raw material source in the food, cosmetics, animal feed, or biolubricant industries. Cold-pressed sesame seed cake should be viewed not as “waste” but as a co-product. The presence of the alkaloid 18,19-Secoyohimban-19-oic acid in the cake indicates that this material also has pharmaceutical potential. Black cumin can be subjected to sequential extraction using solvents such as hexane (non-polar), ethyl acetate, methanol, and water, allowing for the analysis of phenolics, proteins, and polysaccharides (total mass balance). Bioactivity tests, such as those for antimicrobial, anticancer, or CNS effects, should be conducted on fractions containing alkaloids. Formulation studies, such as the integration of waste fatty acids into emulsions, creams, or animal feed rations, can be performed.

Process optimization can be performed by testing green solvents (supercritical CO_2) to achieve maximum yield of fatty acids from the waste.

REFERENCES

Abedinzadeh, S., Torbati, M., Azadmard-Damirchi, S., & Hashempour-Baltork, F. (2024). Changes in the quality of oil extracted by hot pressing from black cumin (Nigella sativa) seeds and by solvent from the obtained cake during refining. Food science & nutrition, 12(5), 3563–3573. https://doi.org/10.1002/fsn3.4025

Agostoni, C., Moreno, L., & Shamir, R. (2016). Palmitic Acid and Health: Introduction. Critical reviews in food science and nutrition, 56(12), 1941–1942. https://doi.org/10.1080/10408398.2015.1017435

Ahmad, A., Husain, A., Mujeeb, M., Khan, S. A., Najmi, A. K., Siddique, N. A., & Anwar, F. (2013). A review on therapeutic potential of Nigella sativa : A miracle herb. Asian Pacific Journal of Tropical Biomedicine , 3(5), 337–352.

Atta-ur-Rahman, Malik, S., Hasan, S. S., Choudhary, M. I., Choudhary, M. I., Ni, C.-Z., & Clardy, J. (1995). Nigellidine — A new indazole alkaloid from the seeds of Nigella sativa. Tetrahedron Letters, 36(12), 1993–1996. https://doi.org/10.1016/0040-4039(95)00210-4

Barkah, N.N., Wiryawan, K.G., Retnani, Y., Wibawan, W.T., & Wina, E. (2021). Physicochemical properties of products and waste of black seed produced by cold press method. IOP Conference Series: Earth and Environmental Science, 756.

Castejón, David & Mateos-Aparicio, Inmaculada & Molero, M. & Cambero, Isabel & Herrera, Antonio. (2014). Evaluation and Optimization of the Analysis of Fatty Acid Types in Edible Oils by 1H-NMR. Food Analytical Methods. 7. 10.1007/s12161-013-9747-9.

Cheikh-Rouhou, Salma & Besbes, Souhail & Lognay, Georges & Blecker, Christophe & Deroanne, Claude & Attia, Hamadi. (2008). Sterol composition of black cumin (Nigella sativa L.) and Aleppo pine (Pinus halpensis Mill.) seed oils. Journal of Food Composition and Analysis. 162-168. 10.1016/j.jfca.2007.09.001.

Deniz, F. (2023). Application of biorefinery by product of Nigella sativa L. herb for green treatment of synthetic dye impurity in aquatic environment: a circular economy based approach to water purification. International Journal of Phytoremediation , 25(1).

Hannan, M. A., Rahman, M. A., Sohag, A. A. M., Uddin, M. J., Dash, R., Sikder, M. H., Rahman, M. S., Timalsina, B., Munni, Y. A., Sarker, P. P., Alam, M., Mohibbullah, M., Haque, M. N., Jahan, I., Hossain, M. T., Afrin, T., Rahman, M. M., Tahjib-Ul-Arif, M., Mitra, S., Oktaviani, D. F., … Kim, B. (2021). Black Cumin (Nigella sativa L.): A Comprehensive Review on Phytochemistry, Health Benefits, Molecular Pharmacology, and Safety. Nutrients, 13(6), 1784. https://doi.org/10.3390/nu13061784

Hassanien, Mohamed & Moersel, Joerg-Th. (2003). Analysis of glycolipids from black cumin (Nigella sativa L.), coriander (Coriandrum sativum L.) and niger (Guizotia abyssinica Cass.) oilseeds. Food Chemistry. 197-204. 10.1016/S0308-8146(02)00254-6.

Kiralan, M., Özkan, G., Bayrak, A., & Ramadan, M. F. (2014). Physicochemical properties and stability of black cumin (Nigella sativa) seed oil as affected by different extraction methods. Industrial Crops and Products , 57, 52–58.

Kizil, S., KIRICI, S., Çakmak, Ö., & KHAVAR, K. M., (2008). Effects of sowing periods and P application rates on yield and oil composition of black cumin (Nigella sativa L.). Journal of Food, Agriculture and Environment , vol.6, no.2, 242-246.

Lambert, G. A., Lang, W. J., Friedman, E., Meller, E., & Gershon, S. (1978). Pharmacological and biochemical properties of isomeric yohimbine alkaloids. European journal of pharmacology, 49(1), 39–48. https://doi.org/10.1016/0014-2999(78)90220-0

Lopez, S., Bermudez, B., Ortega, A., Varela, L. M., Pacheco, Y. M., Villar, J., Abia, R., & Muriana, F. J. (2011). Effects of meals rich in either monounsaturated or saturated fat on lipid concentrations and on insulin secretion and action in subjects with high fasting triglyceride concentrations. The American journal of clinical nutrition, 93(3), 494–499. https://doi.org/10.3945/ajcn.110.003251

Łopusiewicz, Ł., Śmietana, N., Paradowska, D., & Drozłowska, E. (2022). Black Cumin (Nigella sativa L.) Seed Press Cake as a Novel Material for the Development of New Non-Dairy Beverage Fermented with Kefir Grains. Microorganisms, 10(2), 300. https://doi.org/10.3390/microorganisms10020300

Makris, D. P., & Şahin, S. (2019). Polyphenolic Antioxidants from Agri-Food Waste Biomass. Antioxidants (Basel, Switzerland), 8(12), 624. https://doi.org/10.3390/antiox8120624

Marangoni, F., Agostoni, C., Borghi, C., Catapano, A. L., Cena, H., Ghiselli, A., La Vecchia, C., Lercker, G., Manzato, E., Pirillo, A., Riccardi, G., Risé, P., Visioli, F., & Poli, A. (2020). Dietary linoleic acid and human health: Focus on cardiovascular and cardiometabolic effects. Atherosclerosis, 292, 90–98. https://doi.org/10.1016/j.atherosclerosis.2019.11.018

Saini, R. K., Khan, M. I., Kumar, V., Shang, X., Lee, J.-H., & Ko, E.-Y. (2025). Bioactive Compounds of Agro-Industrial By-Products: Current Trends, Recovery, and Possible Utilization. Antioxidants, 14(6), 650. https://doi.org/10.3390/antiox14060650

Shi, Yingbo & Gao, Shuanhu. (2016). Recent Advances of Synthesis of Fluorenone and Fluorene Containing Natural Products. Tetrahedron. 47. 10.1016/j.tet.2016.02.022.

Simopoulos, A. P. (2016). An increase in the omega 6/omega 3 fatty acid ratio increases the risk for obesity. Nutrients , 8(3), 128.

Terzioğlu, S., Yaşar, A., Yayli, N., Yilmaz, N., Karaoglu, S., & Yayli, N., (2008). Antimicrobial activity and essential oil compositions of two Ranunculus species from Turkey: R-constantinopolitanus and R-arvensis. ASIAN JOURNAL OF CHEMISTRY , vol.20, no.4, 3277-3283.

Thani, P. R., Johnson, J. B., Bhattarai, S., Trotter, T., Walsh, K., Broszczak, D., & Naiker, M. (2025). Profiling Key Phytoconstituents in Screw Pressed Nigella Solid Residue and Their Distribution in Products and Byproducts During Oil Processing. Applied Sciences , 15(2), 986.

Tiruppur Venkatachallam, S. K., Pattekhan, H., Divakar, S., & Kadimi, U. S. (2010). Chemical composition of Nigella sativa L. seed extracts obtained by supercritical carbon dioxide. Journal of food science and technology, 47(6), 598–605. https://doi.org/10.1007/s13197-010-0109-y

Uppar, Rajendra & Dinesha, P. & Kumar, Shiva. (2022). A critical review on vegetable oil-based bio-lubricants: preparation, characterization, and challenges. Environment, Development and Sustainability. 25. 1-36. 10.1007/s10668-022-02669-w.

Vatansev, H., Ciftci, H., Ozkaya, A., Ozturk, B., Evliyaoglu, N., & Kiyici, A. (2013). Chemical Composition of Nigella sativa L. Seeds Used as a Medical Aromatic Plant from East Anatolia Region, Turkey. Asian Journal of Chemistry , 25.

Yuan, T., Nahar, P., Sharma, M., Liu, K., Slitt, A., Aisa, H. A., & Seeram, N. P. (2014). Indazole-type alkaloids from Nigella sativa seeds exhibit antihyperglycemic effects via AMPK activation in vitro. Journal of natural products, 77(10), 2316–2320. https://doi.org/10.1021/np500398m

[21] Zhao, F., Wang, P., Lucardi, R. D., Su, Z., & Li, S. (2020). Natural Sources and Bioactivities of 2,4-Di-Tert-Butylphenol and Its Analogs. Toxins, 12(1), 35. https://doi.org/10.3390/toxins12010035

GC-MS ANALYSIS OF HEXANE-EXTRACTED PINE GUM (Pinus spp.): CHEMICAL COMPOSITION AND BIOACTIVE POTENTIAL

İbrahim TEĞİN

Prof. Dr., Siirt University, Faculty of Arts and Science, Department of Chemistry, Siirt, Türkiye, ORCID ID: 0000-0002-5661-7195

Mesut GÖK

Dr., Siirt University, Science and Technology Application and Research Center, Siirt-Türkiye, ORCID ID: 0000-0001-9217-8022

ABSTRACT

Pine resin is a sticky substance secreted by pine trees when they are damaged. This natural healing response protects the tree in various ways. First and foremost, resin possesses antiseptic, astringent, anti-inflammatory, and antibacterial properties. Pine resin has been used for thousands of years to aid in wound healing and treat other skin conditions.

Just as pine resin repairs and heals the tree's damaged bark, it works in a similar way on human skin to support wound healing. Thanks to its powerful antiseptic, antibacterial, and anti-inflammatory properties, pine resin helps scrapes on the skin heal quickly. It supports the body's natural healing process and reduces the risk of infection. While doing all this, it also soothes irritation. This makes it an excellent ingredient in natural ointments for minor wounds, cuts, scrapes, burns, and skin irritations.

Believed by many to be particularly beneficial for the respiratory and digestive systems, pine resin purifies and cleanses the air when burned, reducing the amount of pathogens in the atmosphere thanks to its antiseptic properties. The pine tree is also thought to have energetically cleansing, grounding, and purifying qualities.

In this study, a sample of pine resin (Pinus spp. resin) was extracted using hexane as a solvent and analyzed by gas chromatography-mass spectrometry (GC-MS). The obtained components were identified based on their retention times (RT) and area percentage (%AREA) values. The analysis revealed that the major components were pimaric acid (19.32%), abietic acid (16.22%), androstan-17-one, 3-ethyl-3-hydroxy (15.72%), 6-octadecenoic acid (Z) (16.93%), and 1-phenanthrenecarboxylic acid derivative (12.54%). Additionally, palmitic acid, stearic acid, junipene, (S)-cis-verbenol, podocarp-7-en-3-one derivative, and various methyl ester structures were also detected.

These results demonstrate that pine resin exhibits a rich chemical profile in terms of resin acids (particularly pimaric and abietic acids), long-chain fatty acids, and steroid derivatives. The findings highlight the potential of pine resin as a raw material in the pharmaceutical, cosmetic, or polymer industries.

Keywords: Pine gum, hexane extract, GC-MS, abietic acid, bioactive compounds

1. INTRODUCTION

Pine resin (Pinus spp.) is a viscous, sticky substance produced as a natural defense mechanism by pine trees in response to mechanical damage or pathogen attacks on their bark (Phillips & Croteau, 1999). For centuries, it has been used in traditional medicine in Anatolia and various parts of the world for its antiseptic, anti-inflammatory, and wound-healing properties (Baytop, 2021; Phillips & Croteau, 1999). This natural product, which is widely used for a wide range of conditions from respiratory illnesses to skin disorders also stands out for its chemical composition, which is rich in resin acids, terpenoids, and essential oil components (Keeling & Bohlmann, 2006).

In terms of chemical composition, pine resin consists primarily of two main fractions: volatile turpentine oil (monoterpenes) and non-volatile resin (diterpene acids) (Harman Ware et al., 2016; Luan et al., 2021). Diterpene resin acids particularly abietic acid, dehydroabietic acid, palustric acid, pimaric acid, and

isopimaric acid are the primary compounds responsible for the biological activity of pine resin (Harman Ware et al., 2016; Ottavioli et al., 2019; Parihar et al., 2006; Ulukanli et al., 2014). Studies conducted on various Pinus species in the literature have shown that abietic acid is typically present in resin at concentrations ranging from 9% to 24% and that it possesses antimicrobial, anti-inflammatory, and antitumor activities, as well as potential as an industrial raw material (Harman Ware et al., 2016; Luan et al., 2021; Ottavioli et al., 2019; Parihar et al., 2006; Ulukanli et al., 2014).

Species belonging to the genus Pinus are widely distributed throughout the world, including in Turkey, and there are only a limited number of studies on the chemical composition and bioactive potential of resins obtained from pine species growing in the Eruh region of Siirt Province. Therefore, a detailed chemical characterization of the region's native pine resins is of great importance from both scientific and commercial perspectives.

In this study, resin samples collected from pine trees (Pinus spp.) growing in the Eruh region of Siirt were extracted using hexane, and the chemical composition of the resulting extract was analyzed using gas chromatography–mass spectrometry (GC-MS). The findings aim to elucidate the chemical profile of regional pine resin, thereby contributing to the evaluation of this natural product as a potential raw material for the pharmaceutical, cosmetic, and polymer industries.

2. EXPERIMENTAL RESEARCH

Five grams of Pine resin were placed in a 50 mL falcon tube and completed to 50 mL with hexane solvent, then left to stand for 1 hour in a 70 °C water bath. 2 milliliters of this hexane extract was taken tube and transferred to a 2 mL GC-MS vial using a syringe and a 0.22 µm PVDF filter, ready for analysis.

Pine resin hexane extract were analyzed using ISQ mass spectrometry (Thermo Fisher Scientific, Austin, TX) and Trace 1310 gas chromatography. The procedure was held at an initial temperature of 80°C for 2 minutes, then heated to 300°C at 3°C/minute and held at 300°C for 1 minutes, reheated to 310°C at 5°C/minute, and finally held at 310°C for 10 minutes. The ion source and detector temperatures were 250°C, respectively. The sample injection volume was 1.0 mL, and separation was performed using a Thermo TG-5MS GC column (30 m x 0.25 mm ID x 0.25 µm) with helium as the carrier gas at 2 mL/min. The mass spectral scan range was set to 55–550 (amu). Components were identified in the NIST Demo, Wiley7, Wiley9, redlip, mainlip, and WinRI libraries (Sırma et al. 2025).

3. RESULTS AND DISCUSSION

In this study, the chemical composition of a hexane extract from a pine resin (Pinus spp.) sample collected from the Eruh region of Siirt was elucidated using GC-MS analysis Table 1 and Figure 1-2). The results indicate that the resin exhibits a rich profile in terms of di terpene resin acids (pimaric acid and abietic acid), long-chain fatty acids, steroid derivatives, and phenanthrene carboxylic acid derivatives.

The most notable compound identified in the analysis was pimaric acid (RT: 48.84, 19.32%). In the literature, pimaric acid is described as an important resin acid found particularly in the oleoresins of Pinus species and exhibiting antimicrobial and anti-inflammatory properties (Keeling & Bohlmann, 2006; Ottavioli et al., 2019). It has been reported that the content of pimaric acid in different pine species generally ranges from 5% to 15% (Harman Ware et al., 2016; Ottavioli et al., 2019). The fact that the percentage obtained in this study (~19.32%) is higher than many values reported in the literature suggests that the pine species native to the Siirt Eruh region may be a rich source of pinamaric acid. Abietic acid (RT: 50.72, 16.22%) was identified as the second major resin acid. Abietic acid is one of the most common diterpenes found in pine resins and is known for its potent antimicrobial, anti-inflammatory, antitumor, and wound-healing properties (Harman Ware et al., 2016; Parihar et al., 2006; Ulukanli et al., 2014). The combined concentration of these two major resin acids (~35.54%) contributes significantly to the resin's biological activity. It is believed that the synergistic effects of pimaric and abietic acids may explain the resin's traditional uses as an antiseptic, astringent, and wound-healing agent (Baytop, 2021; Phillips & Croteau, 1999). In addition, the presence of an abietic acid derivative

such as methyl 8,12-abietadiene-18-oate (0.62%) indicates that partial esterification reactions may have occurred within the resin.

1. Phenanthrene carboxylic acid derivative (RT: 49.74, 12.54%) is another major compound. This compound may arise as a product of the oxidation or rearrangement of resin acids (Keeling & Bohlmann, 2006; Luan et al., 2021). The antioxidant and antimicrobial potential of fenanthrene derivatives has been reported in the literature (Ulukanli et al., 2014).

Steroid derivatives are also quite notable. 17-one, 3-ethyl-3-hydroxy (5α)-androstan (RT: 46.72, 15.72%) was identified as the steroid compound with the highest concentration. Additionally, other steroid derivatives such as podocarp-7-en-3-one, 13α-methyl-13-vinyl (0.34%), androst-4-en-3-one, 17-hydroxy-17-methyl (0.44%), and 19-di-torulosol (0.44%) have also been detected. The presence of steroid-based compounds in such high concentrations in pine resin (15.72% for a single compound) is a rare occurrence in the literature (Keeling & Bohlmann, 2006). Since steroid derivatives are known for their anti-inflammatory, immunomodulatory, and wound-healing effects, it is believed that these compounds significantly contribute to the resin's traditional properties of soothing irritation and promoting tissue repair (Baytop, 2021; Phillips & Croteau, 1999).

Long-chain fatty acids and their methyl esters also constitute an important group of components. 6 Octadecenoic acid (Z) (RT: 41.70, 16.93%) stands out as the most abundant fatty acid. This is followed by hexadecanoic acid (palmitic acid) (4.81%), octadecanoic acid (stearic acid) (2.60%), 10,13-octadecadienoic acid methyl ester (total 3.33%), and 10,12-tricosadienoic acid methyl ester (2.11%). These long-chain fatty acids and their methyl esters not only contribute to the resin's hydrophobic structure but also hold potential in cosmetic and dermatological formulations due to their skin-barrier-supporting, emollient, and moisturizing properties (Luan et al., 2021). In particular, 6-octadecenoic acid (petroselinic acid), an unsaturated fatty acid, is known for its anti-inflammatory properties.

In addition, monoterpene and sesquiterpene derivatives such as (S)-cis-verbenol (1.03%), junipene (1.99%), and bicycle [3.1.1] heptane-3-ol (0.48%) were also detected. These volatile compounds contribute to the resin's characteristic odor and its antimicrobial and antioxidant activities (Keeling & Bohlmann, 2006; Ulukanli et al., 2014). In particular, verbenol derivatives play a significant role in traditional use due to their bronchodilatory and antiseptic effects (Baytop, 2021).

These findings have demonstrated that pine resin from the Eruh region of Siirt is rich in diterpene resin acids primarily pimaric acid and abietic acid—as well as androstane-derived steroids and unsaturated fatty acids. This chemical profile scientifically supports the resin's traditional uses for its antiseptic, anti-inflammatory, wound-healing, and bronchodilatory effects (Baytop, 2021; Parihar et al., 2006; Phillips & Croteau, 1999; Ulukanli et al., 2014).

Table 1. GC-MS results for the pine resin sample

	Compound Name	**RT**	**%AREA**	**CasNumber**
1	Bicyclo[3.1.1]Heptan-3-Ol	6.85	0.48	547-61-5
2	(S)-cis-Verbenol	7.01	1.03	18881-04-4
3	Junipene	16.06	1.99	475-20-7
4	Hexadecanoicacid	36.25	4.81	57-10-3
5	6-Octadecenoicacid, (Z)	41.70	16.93	593-39-5
6	Octadecanoicacid	42.27	2.60	57-11-4
7	Podocarp-7-en-3-one,13á-methyl-13-vinyl-	43.17	0.34	57344-99-7

8	19-DI-TORULOSOL	44.01	0.44	1438-63-7
9	10,13-Octadecadiynoic acid,methyl ester	45.03	2.24	18202-24-9
10	Methyl8,12-abietadien-18-oate	45.18	0.62	33892-22-7
11	10,13-Octadecadiynoic acid,methyl ester	45.25	1.09	18202-24-9
12	8(2,6Dimethyl1,5heptadienyl)3,7,7trimethylbicyclo[4.2.0]oct2ene	45.94	0.98	113725-567
13	Androstan-17-one,3-ethyl-3-hydroxy (5à)	46.72	15.72	57344-99-7
14	10,12-Tricosadiynoic acid,methyl ester	47.11	2.11	NA
15	Androst-4-en-3-one,17-hydroxy-17-methyl-, (17á)-(CAS)	48.12	0.44	58-18-4
16	Pimaric acid	48.84	19.32	79-54-9
17	1-Phenanthrenecarboxylic acid,1,2,3,4,4a,9,10,10a-octahydro- 1,4a-dimethyl-7-(1-methylethyl)-,[1R-(1à,4aá,10aà)]- (CAS)	49.74	12.54	1740-19-8
18	Abietic acid	50.72	16.22	514-10-3

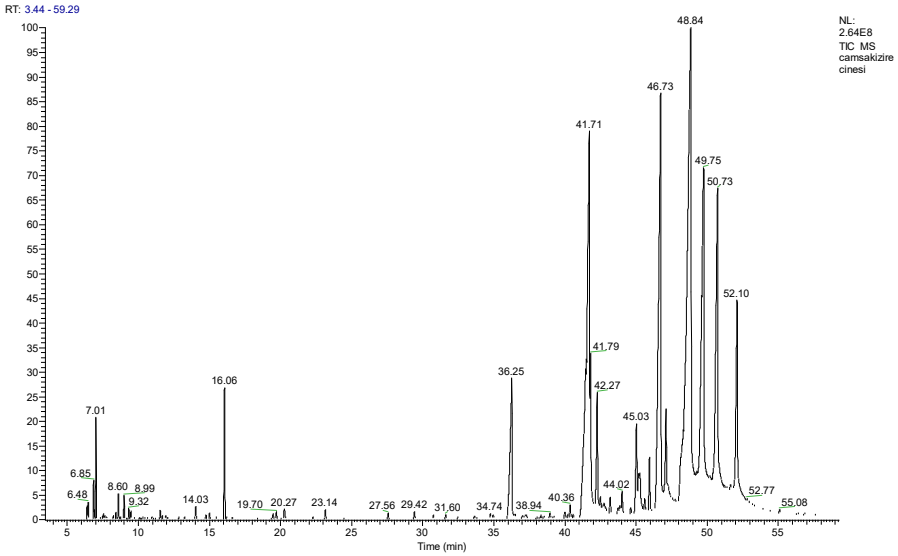


Figure 1. GC-MS chromatogram of the pine resin sample

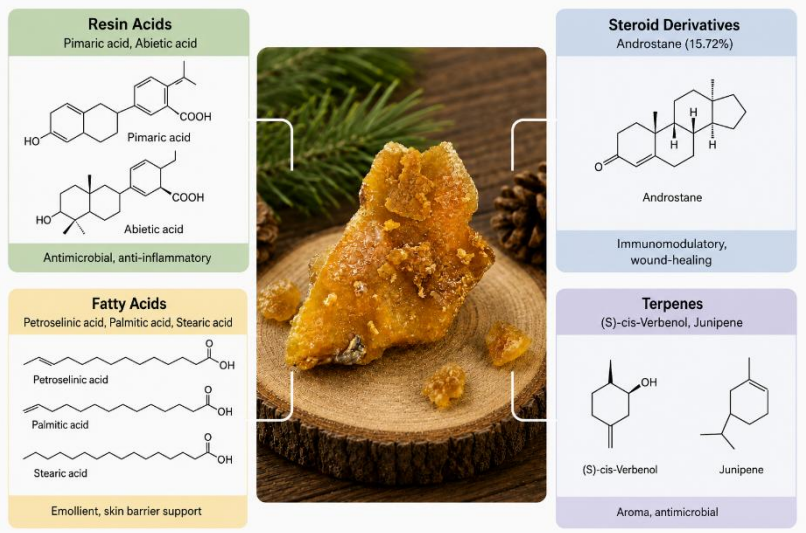


Figure 2. Results of the pine resin sample

4. CONCLUSION

In conclusion, this study conducted a detailed chemical characterization of a regional pine resin sample and demonstrated that pimaric acid (19.32%) is more prevalent than abietic acid (16.22%). Additionally, the presence of a 17-one derivative of androstane (15.72%) at a notably high concentration has been reported for the first time. The data obtained indicate that this natural product has the potential to be utilized not only in traditional medicine but also in the pharmaceutical, cosmetic, and polymer industries. In future studies, it is recommended to test the biological activities of these components (antimicrobial, antioxidant, cytotoxic, wound-healing) using in vitro and in vivo methods, to conduct a comparative analysis of different solvent extracts (ethanol, methanol, acetone, etc.), investigating the synergistic effects of pimaric acid and androstane derivatives, and comparing the resin profiles of different Pinus species in the region.

REFERENCES

Baytop, T. (2021). Türkiye'de Bitkiler ile Tedavi: Geçmişte ve Bugün. Ankara: Nobel Tıp Kitabevleri, 451-501.

Harman Ware, A. E., Sykes, R., Peter, G. F., & Davis, M. (2016). Determination of terpenoid content in pine by organic solvent extraction and fast GC analysis. Frontiers in Energy Research , 4, 2.

Keeling, C. I., & Bohlmann, J. (2006). Diterpene resin acids in conifers. Phytochemistry , 67(22), 2415 2423.

Luan, Qifu & Tao, Xue-yu & Diao, Shu & Ding, Xian-yin & Jiang, Jing-min. (2021). Methods, characteristics, variance, and genetics of pine oleoresin components, and their potential for renewable and sustainable energy. 10.1016/B978-0-12-819485-0.00018-9

Ottavioli, J., Paoli, M., Casanova, J., Tomi, F., & Bighelli, A. (2019). Identification and Quantitative Determination of Resin Acids from Corsican Pinus pinaster Aiton Oleoresin Using 13 C-NMR Spectroscopy. Chemistry & biodiversity, 16(1), e1800482. https://doi.org/10.1002/cbdv.201800482

Parihar, P. & Parihar, Leena & Bohra, A.. (2006). Antibacterial activity of extracts of Pinus roxburghii Sarg. Bangladesh Journal of Botany. 35. 85-86.

Phillips, M. A., & Croteau, R. B. (1999). Resin based defenses in conifers. Trends in Plant Science , 4(5), 184 190.

Sırma, E., Fidan, M., Gök, M., Tegin, İ., Yılmaz, M. A., & Yabalak, E. (2026). Chemical profiling and antioxidant potential of propolis from Pervari, Siirt: discovery of tannic acid and key bioactive compounds. Natural Product Research, 40(11), 3169–3182. https://doi.org/10.1080/14786419.2025.2456677

Ulukanli, Z., Karabörklü, S., Bozok, F., Ates, B., Erdogan, S., Cenet, M., & Karaaslan, M. G. (2014). Chemical composition, antimicrobial, insecticidal, phytotoxic and antioxidant activities of Mediterranean Pinus brutia and Pinus pinea resin essential oils. Chinese journal of natural medicines, 12(12), 901–910. https://doi.org/10.1016/S1875-5364(14)60133-3

EFFECT OF CANNABIDIOL DERIVED FROM *CANNABIS INDICA* LAM. CALLUS CULTURE ON SERUM OXIDATIVE STRESS PARAMETERS IN DMBA-INDUCED RATS

Tuba OKUTAN,

Lect. Dr., Fırat University, Faculty of Science, Department of Biology, ORCID NO: 0000-0001-8745-0343

Ökkeş YILMAZ

Prof. Dr., Fırat University, Faculty of Science, Department of Biology, ORCID NO: 0000-0002-8276-4498

ABSTRACT

Cannabidiol (CBD) is a non-psychoactive phytocannabinoid that has attracted considerable attention because of its antioxidant and cytoprotective properties. In the present study, the effects of CBD isolated from *Cannabis indica* Lam. callus culture on serum oxidative stress parameters in a DMBA-induced rat model were investigated. Sprague Dawley rats received DMBA (25 mg/rat, oral gavage) on days 1 and 4, while CBD was administered intraperitoneally at doses of 5 mg/kg and 10 mg/kg for eight weeks. At the end of the experimental period, serum malondialdehyde (MDA), total protein levels, and antioxidant enzyme activities including glutathione S-transferase (GST), glutathione peroxidase (GPx), glutathione reductase (GR), superoxide dismutase (SOD), and catalase (CAT) were determined.

DMBA administration markedly increased serum MDA levels and reduced total protein concentration together with GPx, GR, SOD, CAT, and GST activities compared with the control group. CBD treatment significantly attenuated lipid peroxidation, particularly in the C1, DC1, and DC2 groups, where MDA values approached those of the control animals. Total protein levels increased from 29,03 ± 0,64 mg/mL in the DMBA group to 36,44 ± 0,39 mg/mL and 36,45 ± 0,42 mg/mL in the C2 and DC2 groups, respectively. GPx activity reached its highest value in the C1 group (13,82 ± 1,33 µmol/mL/min), whereas SOD activity was maximally elevated in the DC2 group (4,36 ± 0,10 U/mL/min). Overall, the findings indicate that callus-derived CBD effectively improves systemic antioxidant defense and reduces oxidative damage induced by DMBA, suggesting its potential as a promising biotechnological antioxidant agent.

Key Words: CBD, oxidative stress, antioxidant enzymes, MDA

1. INTRODUCTION

7,12-Dimethylbenz[a]anthracene is a potent carcinogenic agent that is metabolized via cytochrome P450 enzymes, leading to an increase in reactive oxygen species and suppression of cellular antioxidant defense mechanisms. This DMBA-induced oxidative process triggers macromolecular damage by causing an increase in malondialdehyde levels, an indicator of lipid peroxidation, and disruption of cellular redox balance (1,2). This biochemical disruption can compromise the integrity of the membrane structure, leading to irreversible losses in cell function (3). Plant sources rich in secondary metabolites, such as cannabis species, stand out as natural agents with the potential to mitigate this DMBA-induced oxidative damage thanks to the cannabinoids and phenolic compounds they contain (4). Cannabidiol, in particular, is noteworthy for its potential to support antioxidant enzyme activities by modulating free radical formation (5). In this context, standardized cannabinoid production by callus culture methods enhances the pharmacological efficacy of plant material and exhibits ameliorative effects on DMBA-induced oxidative stress parameters (6). Plant callus culture technology offers an innovative approach in pharmacological research in terms of controlled production of secondary metabolites and standardization of bioactive components (6). This research aims to evaluate the hepatoprotective and antioxidant effects of cannabidiol obtained by biotechnological approaches in an experimentally created oxidative stress model through serum biochemical parameters. The study also investigated the protective role of cannabidiol on oxidative damage caused by DMBA application; in particular, the changes it causes in the activities of key antioxidant enzymes such as catalase and superoxide dismutase were analyzed in a dose-dependent manner. Based on the data obtained, the aim was to comprehensively

reveal the chemopreventive properties of cannabidiol produced by biotechnological methods and its possible regulatory effects on the antioxidant defense system.

2. MATERIALS- METHODS

In this study, cannabidiol (CBD) isolated from *Cannabis indica* Lam. callus culture was evaluated in a Sprague Dawley rat model of DMBA-induced oxidative stress. The experimental procedures were carried out in accordance with the Regulation on Cannabis Cultivation and Control**,** published in the Official Gazette of the Republic of Türkiye (No. 29842, dated 29 September 2016). All animal experiments were reviewed and approved by the Fırat University Local Ethics Committee for Animal Experiments (Session No: 2022/18-04, Approval Date: 16 November 2022). Animal housing, care, and experimental procedures were performed at the Fırat University Experimental Research Center (FÜDAM) under standard laboratory conditions.

Oxidative stress was induced by oral administration of DMBA at a dose of 25 mg/rat on the 1st and 4th days of the experiment, whereas CBD was administered intraperitoneally at doses of 5 mg/kg (C1) and 10 mg/kg (C2) for eight consecutive weeks. At the end of the experimental period, serum samples were collected and analyzed for malondialdehyde (MDA), total protein, and the antioxidant enzymes glutathione S-transferase (GST), glutathione peroxidase (GPx), glutathione reductase (GR), superoxide dismutase (SOD), and catalase (CAT) to evaluate the effects of biotechnologically derived CBD on systemic oxidative status and antioxidant defense mechanisms.

2.1. Measurement of Protein Content

The protein content of the samples was measured spectrophotometrically according to the method presented by Lowry et al. (1951) (7). Lowry solution was added to the collected sample and left for 10 minutes. At the end of this time, folin reagent diluted 1/1 (v/v) with water was added. After 30 minutes, the absorbances of the samples were read against the blank under UV light at a wavelength of 660 nm. Bovine serum albumin was used as a standard. Results are expressed in mg/mL.

2.2. Analysis of MDA Content

For this procedure, 1 ml of the supernatant was taken from the samples and 10% perchloric acid (PCA) was added to precipitate the proteins. This mixture was centrifuged again at 5000 rpm for 5 minutes. The resulting supernatant was transferred to autosampler vials and analyzed using a Shimadzu (Kyoto, Japan) brand HPLC instrument. The mobile phase was a mixture of 30 mmol KH2PO4 and methanol (82%-18%, H3PO4 with pH=3.6). The ODS-3 column (150 mm x 4.6, 5 µm) was used as the column. The mobile phase flow rate was determined as 1.0 ml/min and the wavelength of the DAD detector was 254 nm (8).

2.3. Glutathione Peroxidase Activity (GPx)

2.9 mL K-Na buffer (pH= 7.0), 100 µl cell homogenate, and 200 µl 4 mM GSH were added and left to stand for 1 minute. 200 µl 2 mM H2O2 was added to the mixture and the reaction was started at 37°C. After 10 minutes, 8% MPA was added to the mixture and the reaction was stopped. 100 µl DTNB was added, and the reaction of GSH with DTNB (5,5'-dithiobis-2-nitrobenzoic acid) resulted in the formation of yellow colored products, GSTNB and TNB, which were measured at 412 nm using a spectrophotometer. The results were calculated using a calibration curve created with the GSH standard and found in µmol/ml/min (9-11).

2.4. Glutathione Reductase Activity (GR)

The enzyme activity was tested according to Smith et al. (1988) (12). 2.9 mL of K-Na buffer (pH= 7.2), 100 µl of cell homogenate, and 200 µl of 4 mM GSSG were added and left to stand for 1 minute. 200 µl of 3 mM NADPH was added to the mixture and the reaction was started at 37°C. After 10 minutes, 8% MPA was added to the mixture and the reaction was stopped. Finally, 100 µl of DTNB was added and the yellow colored products GSTNB and TNB formed as a result of the reaction of DTNB with GSH in the medium were measured at 412 nm in a spectrophotometer. The results were calculated with

a calibration graph created according to the GR enzyme concentration and the GR enzyme amount was found in units/ml/min.

2.5. Catalase Activity (CAT)

CAT activity was tested according to the method of Korolyuk et al. (13). 20 mM H2O2 was diluted in 50 mM/L Na-K phosphate buffer (pH= 7.4) and the reaction was started by adding it to 100 µl of homogenate taken into tubes. It was incubated at 37°C for 3 minutes. Then, 4 mL of 32.4 mmol/L ammonium molybdate was added to stop the enzyme activity. Absorbances were read at 374 nm against blank. The results were calculated in units/ml/min by using the calibration curve created with H2O2 concentrations.

2.6. Superoxide Dismutase Activity (SOD)

SOD activity was determined using the method presented by Sun et al. (1988) (14). The reagent, prepared by combining 0.3 mM xanthine, 0.6 mM EDTA, 150 µg/L NBT, 400 mM Na2CO3, and 1 g/L bovine serum albumin, was mixed with 100 µl of homogenate and 50 µl of 167 U/ml xanthine oxidase (XO) enzyme. It was incubated at 25°C for 20 minutes. After this time, 100 µl of 10 mmol CuCl2 was added, and then the reaction was stopped by adding 8% MPA. Absorbances were read at 560 nm against the blank. The following formula was used to calculate enzyme activity in IU.ml-1:

Activity = (A1-A2) /A1 x 100.

2.7. Glutathione-S-Transferase Activity

2.9 mL of K-Na buffer (pH= 6.5), 100 µl of cell homogenate, and 200 µl of 4 mM GSH were added and allowed to stand for 1 minute. 50 µl of 100 mM CDNB was added to the mixture and the reaction was started at 37°C. After 10 minutes, 8% MPA was added to the mixture and the reaction was stopped. The amount of GSH that did not form a CDNB conjugate was measured at 412 nm using a spectrophotometer as GSTNB and TNB yellow products formed as a result of the reaction of DTNB (5,5'-dithiobis-2-nitrobenzoic acid). The results were calculated using a calibration curve created with the GSH standard and found in µmol/ml/min (15).

2.8. Statistical Analysis

Statistical analyses were performed using one-way analysis of variance (ANOVA) to evaluate differences among the experimental groups. When a significant overall effect was detected, Duncan's multiple range test was employed for pairwise group comparisons, while Fisher's least significant difference (LSD) test was applied to assess differences between the treatment groups and the control group. Statistical significance was established at $p < 0,05$, and all data are presented as mean ± standard error (Mean ± SE).

3. RESULTS AND DISCUSSION

When serum malondialdehyde (MDA) levels were evaluated, it was observed that DMBA administration significantly increased lipid peroxidation. Compared to the control group, MDA levels were significantly higher in the DMBA group, and this increase was statistically highly significant ($p<0,001$). This finding clearly demonstrates that DMBAcauses oxidative stress in the serum (Figure 3.1).

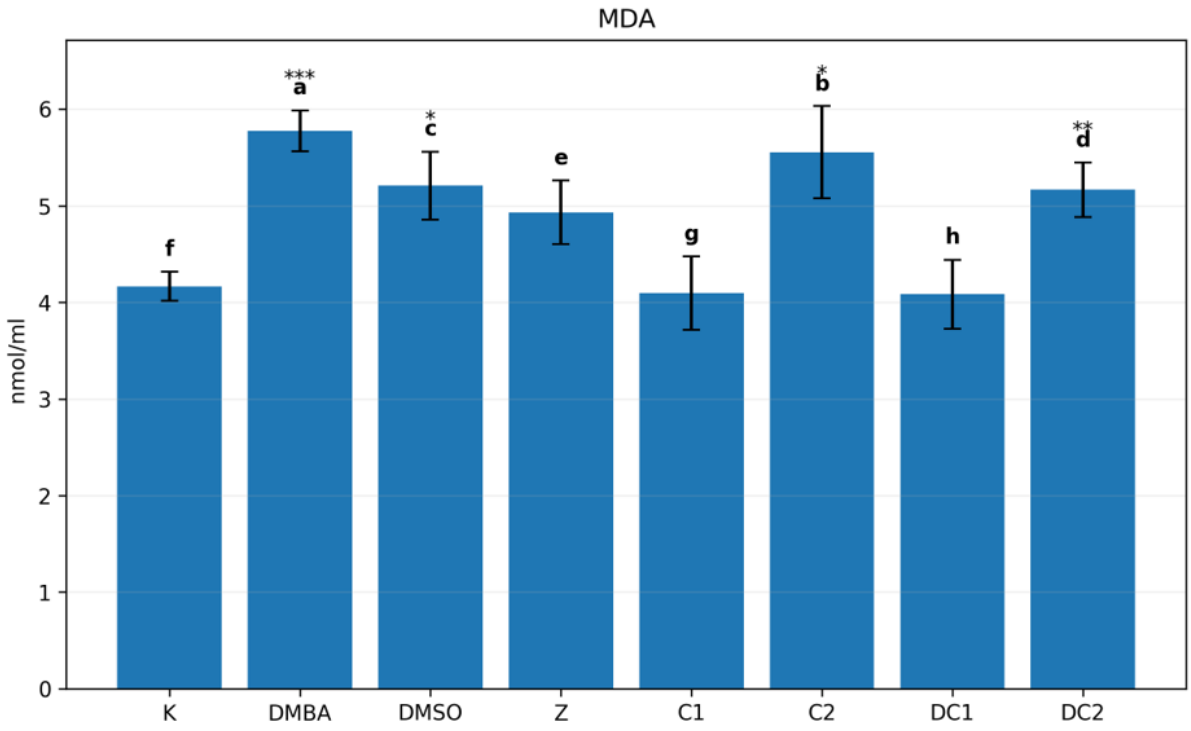


Figure 3.1. Serum Malondialdehyde (MDA) Levels in Experimental Groups Following Treatment

Values are expressed as mean ± SE. Different letters indicate significant differences according to Duncan's multiple comparison test. Asterisks indicate significant differences compared with the control group according to Fisher's LSD test (*p < 0,05, p < 0,01, *p < 0,001).

As illustrated in Figure 3.1**,** CBD-treated groups exhibited an overall reduction in serum MDA levels compared with the DMBA group. The most pronounced decreases were observed in the low-dose CBD group (C1) and in the combined treatment groups (DC1 and DC2). In these groups, MDA values tended to approach those of the control group, suggesting that callus-derived CBD may alleviate oxidative damage by limiting lipid peroxidation.

Serum total protein levels presented in Table 3.1 demonstrated a significant effect of DMBA administration on protein metabolism. While the control group exhibited a total protein level of 33,71 ± 0,17 mg/mL, this value decreased to 29,03 ± 0,64 mg/mL in the DMBA group, representing a highly significant reduction **(**p < 0,001**).** These findings indicate that DMBA induces a marked impairment in systemic protein homeostasis. In contrast, CBD-treated groups showed an overall increase in total protein concentrations, suggesting that CBD administration contributes to the preservation of protein metabolism under oxidative stress conditions.

Table 3.1. Effect of Cannabidiol Treatment on Serum Total Protein Levels in DMBA-Induced Rats

Group	Total protein (mg/mL)
K	$33,71 \pm 0,17^{e}$
DMBA	$29,03 \pm 0,64^{h***}$
DMSO	$32,99 \pm 0,30^{f}$
Z	$33,97 \pm 0,29^{d}$
C1	$35,32 \pm 0,45^{c**}$

C2	36,44 ± 0,39^{b***}
DC1	31,18 ± 0,40^{g***}
DC2	36,45 ± 0,42^{a***}

Values are expressed as mean ± SE. Different letters indicate significant differences according to Duncan's multiple comparison test. Asterisks indicate significant differences compared with the control group according to Fisher's LSD test (*p < 0,05, p < 0,01, *p < 0,001).

In the CBD-treated groups, a general trend of increasing total protein levels was observed. Total protein levels were determined as 35,32 ± 0,45 mg/mL in the C1 group (p<0,01), 36,44 ± 0,39 mg/mL in the C2 group (p<0,001), 31,18 ± 0,40 mg/mL in the DC1 group (p<0,001), and 36,45 ± 0,42 mg/mL in the DC2 group (p<0,001). The highest total protein values were found in the C2 and DC2 groups, and the results obtained in these groups exceeded those of the control group. These findings suggest that high-dose CBD administration, in particular, contributes to the preservation of protein metabolism by increasing total protein levels (Table 3.1).

When serum antioxidant enzyme activities were examined, statistically significant differences were observed between the experimental groups (p<0,05). GST activity was determined as 9,38±0,40 µmol/mL/min in the control group, while DMBA application caused this value to decrease to 7,45 ± 0,47 µmol/mL/min (p<0,05). The most significant decrease in GST activity was observed in the DC1 group with 1,67±0,52 µmol/mL/min. These findings indicate that glutathione dependent detoxification capacity changed significantly, especially in some application groups (Table 3.2).

Table 3.2. Effects of Experimental Treatments on Serum Antioxidant Enzyme Activities

Group	GST (µmol/mL/dk)	GPx (µmol/mL/dk)	GR (unit/mL/dk)	SOD (unit/mL/dk)	CAT (unit/mL/dk)
K	9,38 ± 0,40^{a}	11,03 ± 0,70^{d}	30,31 ± 1,34^{b}	3,43 ± 0,05^{f}	4487,36 ± 3,74^{a}
DMBA	7,45 ± 0,47^{c*}	4,31± 0,56^{h***}	22,65±0,58^{g***}	3,04±0,02^{h***}	4404,45 ± 45,99^{e}
DMSO	7,49 ± 0,36^{b**}	7,34 ± 0,46^{g**}	28,55 ± 0,93^{c}	3,66 ± 0,06^{d*}	4352,99± 25,33^{g***}
Z	5,39 ± 0,41^{d***}	7,60 ± 0,75^{f**}	31,27 ± 1,53^{a}	3,46 ± 0,07^{e}	4337,36 ± 36,99^{h**}
C1	3,76 ± 0,41^{e***}	13,82 ± 1,33^{a}	23,87±1,20^{e**}	3,41 ± 0,06^{g}	4361,49 ± 24,26^{f***}
C2	2,94 ± 0,27^{f***}	11,03 ± 0,94^{e}	25,37 ± 1,22^{d*}	4,19 ±0,21^{b**}	4441,53 ± 9,22^{c***}
DC1	1,67 ± 0,52^{h***}	11,43 ± 0,37^{c}	17,99±0,71^{h***}	4,05±0,06^{c***}	4457,60 ± 21,71^{b}
DC2	1,93 ± 0,05^{g***}	12,20 ± 0,78^{b}	23,82 ± 1,96^{f*}	4,36±0,10^{a***}	4418,02 ± 34,69^{d}

Values are expressed as mean ± SE. Different letters indicate significant differences according to Duncan's multiple comparison test. Asterisks indicate significant differences compared with the control group according to Fisher's LSD test (*p < 0,05, p < 0,01, *p < 0,001).

GPx activity decreased from 11,03 ± 0,70 µmol/mL/min in the control group to 4,31 ± 0,56 µmol/mL/min in the DMBA group, and this decrease was found to be highly significant ($p<0,001$). In contrast, a significant increase in GPx activity was observed in the CBD treated groups. The highest value was determined in the C1 group as 13,82 ± 1,33 µmol/mL/min, while in the DC2 group, an activity exceeding that of the control group was detected with 12,20 ± 0,78 µmol/mL/min. This suggests that CBD supports this enzyme, which is involved in the removal of hydroperoxides (Table 3.2).

GR activity was also negatively affected by DMBA treatment. The activity, which was 30,31 ± 1,34 units/mL/min in the control group, decreased to 22,65 ± 0,58 units/mL/min in the DMBA group ($p<0,001$). The lowest value was observed in the DC1 group with 17,99 ± 0,71 units/mL/min, while the olive oil group obtained results quite close to the control group with 31,27 ± 1,53 units/mL/min. This finding shows that some applications can support the re-reduction of glutathione (Table 3.2).

When evaluated in terms of SOD activity, the value measured as 3,43 ± 0,05 units/mL/min in the control group decreased to 3,04 ± 0,02 units/mL/min in the DMBA group, and this decrease was found to be statistically significant ($p<0,001$). In contrast, the C2, DC1, and DC2 groups obtained values of 4,19 ± 0,21, 4,05 ± 0,06, and 4,36 ± 0,10 units/mL/min, respectively, indicating that the activity in these groups exceeded the control level. The highest SOD activity was detected in the DC2 group (Table 3.2).

CAT activity was determined as 4487,36 ± 3,74 units/mL/min in the control group. In the DMBA group, this value decreased to 4404,45 ± 45,99 units/mL/min, while lower values were also observed in the DMSO and olive oil groups. In contrast, in the DC1 group, CAT activity was significantly preserved with a value of 4457,60 ± 21,71 units/mL/min. In the C2 group, a value of 4441,53 ± 9,22 units/mL/min was obtained (Table 3.2).

When the numerical data given in Table 3.2 and the multi-panel boxplot graphs presented in Figure 3.2 are evaluated together, it is understood that DMBA application leads to significant changes in the antioxidant defense system, and CBD obtained from callus culture shows a protective effect against oxidative stress, especially by increasing GPx and SOD activities. Duncan's multiple comparison test revealed differences between groups, while Fisher's LSD test showed significant differences compared

to the control group.

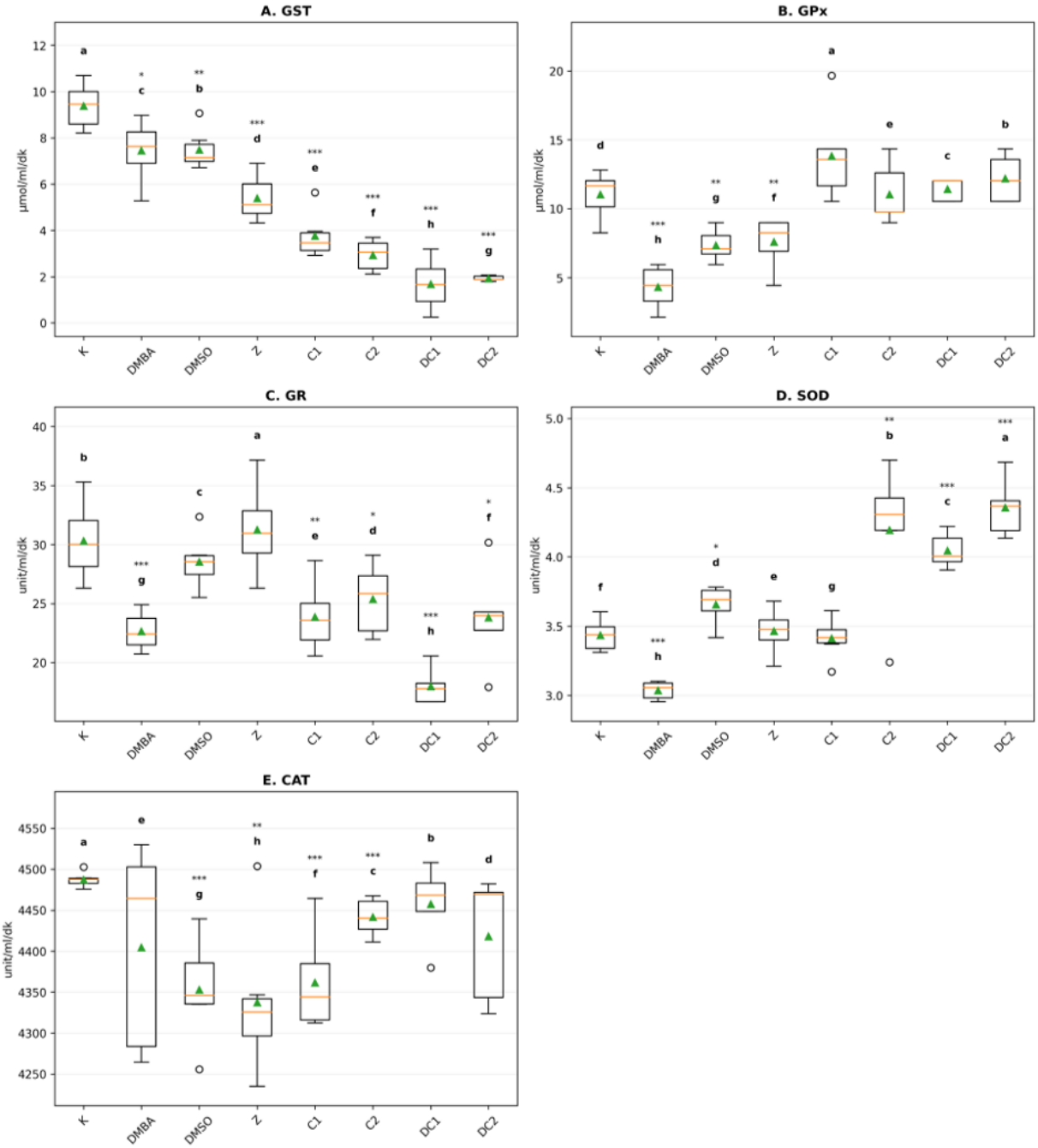


Figure 3.2. Multi-panel boxplots of serum antioxidant enzyme activities. **(**A) GST, (B) GPx, (C) GR, (D) SOD, and (E) CAT. Data are presented as mean ± SE. Different lowercase letters indicate significant differences among experimental groups according to Duncan's multiple range test. Asterisks denote significant differences compared with the control group according to Fisher's LSD test (*p < 0,05, **p < 0,01, ***p < 0,001).

Figure 3.2 presents multi-panel boxplot graphs of serum GST, GPx, GR, SOD, and CAT activities. The graphs visually support the numerical results given in Table 3.2 and clearly demonstrate the changes caused by DMBA application on the antioxidant defense system. At the same time, the direction and magnitude of the effects of CBD obtained from callus culture on different enzymes become clearer.

Examining the graph of GST activity, it is seen that the high activity observed in the control group decreased with DMBA application, and this decrease became more pronounced, especially in the DC1 and DC2 groups. In contrast, the GPx graph shows that the activity, which was significantly suppressed in the DMBA group, increased again with CBD application. The highest GPx activity was obtained in the C1 group, and the values in the DC2 group exceeded the control level, suggesting that CBD supports this enzyme, which is involved in the removal of hydroperoxides.

The distributions of GR activity show that DMBA application negatively affects this enzyme, which is involved in the re-reduction of glutathione. It is noteworthy that the median value is significantly lower, especially in the DC1 group. In contrast, the values observed in the olive oil group are close to the control group, indicating that the carrier solution does not have a negative effect on this parameter. Box plots related to SOD activity reveal one of the most significant effects of CBD application. The decreased activity in the DMBA group increased significantly, especially in the C2, DC1, and DC2 groups; reaching its highest level in the DC2 group. Similarly, the CAT graph shows more limited changes between groups, but the activity in the DC1 and C2 groups is closer to the control values.

Overall, the findings obtained in Figure 3.2 show that DMBA application causes significant changes in the serum antioxidant defense system. In contrast, it is understood that CBD obtained from callus culture significantly reduces oxidative stress-related deterioration, especially by increasing GPx and SOD activities. Duncan letters used in the graphs indicate statistical differences between groups, while asterisks indicate whether the relevant groups are significantly different from the control group. These visual indicators allow for a clearer and more understandable evaluation of numerical data.

MDA is one of the end products of oxidative degradation of cell membrane lipids and is considered a reliable biomarker of oxidative stress. Reactive oxygen species formed during the metabolism of DMBA via the cytochrome P450 enzyme increase lipid peroxidation and cause an increase in MDA levels. The results show that CBD can reduce lipid peroxidation by suppressing free radical formation (16). Similarly, it has been observed that CBD administration restores cellular redox balance by restoring the levels of antioxidant enzymes such as glutathione and catalase, which are reduced under DMBA-induced oxidative stress (4, 17). These restorative effects support the idea that CBD plays a central role in redox regulation by stimulating critical enzyme activities such as glutathione peroxidase and glutathione reductase (18, 19). Furthermore, cannabidiol is thought to stabilize Nrf2 protein levels and stimulate the transcription of genes such as HMOX-1 and SOD via antioxidant response elements, thereby suppressing inflammatory processes associated with oxidative stress (20,21). As observed in diabetic models, CBD's ability to increase endogenous glutathione reserves and restrict lipid peroxidation confirms its protective mechanisms against DMBA-induced toxicity (22). In particular, modulation of the Nrf2/HMOX1 axis plays a crucial role in preventing membrane phospholipid damage caused by oxidative stimuli and maintaining intracellular redox homeostasis (23,24). These molecular interactions of CBD allow for the mitigation of oxidative-induced pathological processes by restricting the interaction of reactive oxygen species with their intracellular targets (25,26). Furthermore, this compound is reported to suppress inflammatory cytokine release and stabilize the cytoprotective response by regulating the cross-interaction between Nrf2 and NF-κB transcription factors (27). Through these mechanisms, CBD provides strong protection against cellular damage caused by oxidative agents, such as under UVA and UVB-induced stress conditions, by increasing antioxidant enzyme activities (28). This cytoprotective capacity of CBD supports the continuity of enzymatic functions by preventing oxidative modification of proteins thanks to its high affinity with cysteine and selenocysteine residues (29). In addition, CBD's activation of cellular defense pathways by promoting nuclear pNRF2 translocation proves that it directly or indirectly suppresses oxidative stress triggered by reactive oxygen species (30).

4. CONCLUSION

The findings suggest that the bioactive compound obtained from callus culture may contribute to the preservation of serum antioxidant capacity and mitigate the negative effects of oxidative stress. In particular, the observed improvements in antioxidant enzyme activities and the decrease in oxidative damage markers indicate that CBD application may support the maintenance of cellular redox balance. Although no molecular-level investigation was conducted in this study, biochemical data reveal that

CBD has a supportive effect on the antioxidant defense system and, consequently, may contribute to limiting damage caused by reactive oxygen species.

REFERENCES

1. Allam, A. M., AbuBakr, H. O., Yassin, A. M., Abdel-Razek, A. S., Khattab, M. S., Gouda, E. M., & Mousa, S. Z. (2023). Potential chemopreventive effects of Broccoli extract supplementation against 7, 12 dimethyl Benz(a)anthracene (DMBA) -induced toxicity in female rats. *Scientific Reports*, *13*(1), 17234–17234. https://doi.org/10.1038/s41598-023-43629-2

2. Shaban, N. Z., El-Rashidy, F. H., Adam, A. H., Beltagy, D. M., Ali, A. E., Abde-Alaziz, A. A., & Talaat, I. M. (2023). Anticancer role of mango (Mangifera indica L.) peel and seed kernel extracts against 7,12- dimethylbenz[a]anthracene-induced mammary carcinogenesis in female rats. *Scientific Reports*, *13*(1), 7703–7703. https://doi.org/10.1038/s41598-023-34626-6

3. B, Muh. R., Syamsu, R. F., Karim, M., Gani, A. B., & Hasbi, B. E. (2023). Toksısıtas Senyawa Dmba (7,12 Dımethylbenz[A]Anthracene) Sebagaı Larutan Karsınogenesıs Kanker Kolorektal Pada Tıkus Putıh (Rattus Novergıcus). Jurnal Kesehatan Tambusai, 4(4), 6524–6530. https://doi.org/10.31004/Jkt.V4i4.22209

4. Kubilienė, A., Mickutė, K., Baranauskaitė, J., Marksa, M., Liekis, A., & Sadauskienė, I. (2021). The Effects of Cannabis sativa L. Extract on Oxidative Stress Markers In Vivo. Life, 11(7), 647–647. https://doi.org/10.3390/life11070647

5. Atalay, S., Jarocka-Karpowicz, I., & Skrzydlewska, E. (2019). Antioxidative and Anti-Inflammatory Properties of Cannabidiol. Antioxidants, 9(1), 21–21. https://doi.org/10.3390/antiox9010021

6. Yu, G., Kim, D.-H., Kim, H., & Lim, D. (2025). Evaluation of Cannabis sativa L. Callus Extract as a Novel Cosmetic Ingredient with Dual Anti-Inflammatory and Antioxidant Effects. Plants, 14(7), 1148–1148. https://doi.org/10.3390/plants14071148

7. Lowry, O.H., Rosenbrough, N.J., Farr, A.L. and Randall, R.J., (1951). Protein measurement with the Folin-phenol reagent. The Journal of Biochemistry, 193, 265-277.

8. Karatepe, M. (2004). Simultaneous determination of ascorbic acid and free malondialdehyde in human serum by HPLC-UV. LC-GC North America, 22(6), S104-S104.

9. Rotruck, J. T. ӊ., Pope, A. L., Ganther, H. E., Swanson, A. B., Hafeman, D. G., & Hoekstra, W. (1973). Selenium: biochemical role as a component of glutathione peroxidase. Science, 179(4073), 588-590.

10. Dileepkumar, H. V., & Ritesh, K. R. (2018). Dichlorvos induces differential oxidative stress in the brain regions of rat. Adv Pharmac J, 3(5), 150-156.

11. Ahmed, A. Y., Aowda, S. A., & Hadwan, M. H. (2021). A validated method to assess glutathione peroxidase enzyme activity. Chemical Papers, 75, 6625-6637.

12. Smith, I. K., Vierheller, T. L., & Thorne, C. A. (1988). Assay of glutathione reductase in crude tissue homogenates using 5, 5′-dithiobis (2-nitrobenzoic acid). Analytical biochemistry, 175(2), 408-413.

13. Korolyuk, M. A., Ivanova, L. I., & Majorova, I. T. (1988). Methods of definition of catalase activity. Lab Manuals, 1, 16-19.

14. Sun, Y. I., Oberley, L. W., & Li, Y. (1988). A simple method for clinical assay of superoxide dismutase. Clinical chemistry, 34(3), 497-500.

15. Habig, W. H., Pabst, M. J., & Jakoby, W. B. (1974). Glutathione S-transferases: the first enzymatic step in mercapturic acid formation. Journal of biological Chemistry, 249(22), 7130-7139.

16. Kajero, J. A., Seedat, S., Ohaeri, J. U., Akindele, A. J., & Aina, O. (2022). Effects of cannabidiol on vacuous chewing movements, plasma glucose and oxidative stress indices in rats administered high dose risperidone. Scientific Reports, 12(1), 19718–19718. https://doi.org/10.1038/s41598-022-24235-0

17. Comelli, F., Bettoni, I., Colleoni, M., Giagnoni, G., & Costa, B. (2009). Beneficial effects of aCannabis sativaextract treatment on diabetes-induced neuropathy and oxidative stress. Phytotherapy Research, 23(12), 1678–1684. https://doi.org/10.1002/ptr.2806

18. Bih, C. I., Chen, T., Nunn, A. V. W., Bazelot, M., Dallas, M., & Whalley, B. J. (2015). Molecular Targets of Cannabidiol in Neurological Disorders [Review of Molecular Targets of Cannabidiol in Neurological Disorders]. Neurotherapeutics, 12(4), 699–730. Springer Science+Business Media. https://doi.org/10.1007/s13311-015-0377-3

19.Şahin, S., Türksoy, V. A., & Azarkan, S. Y. (2025). Investigating the Efficacy of Cannabidiol Against Arsenic-Induced Liver Cell Damage. Cumhuriyet Science Journal, 46(1), 55–61. https://doi.org/10.17776/csj.1616411
20.Reagan, A. (2024). Investigating the Potential Effects of CBD in Vitro. The Boller Review, 7. https://doi.org/10.18776/tcu/br/7/173
21.Yan, G., Zhang, X., Li, H., Guo, Y., Yong, V. W., & Xue, M. (2023). Anti-oxidant effects of cannabidiol relevant to intracerebral hemorrhage. Frontiers in Pharmacology, 14, 1247550–1247550. https://doi.org/10.3389/fphar.2023.1247550
22. Çalışkan, U. K., & YILDIRIM, S. (2020). HEMP AND ITS USE IN HEALTH. Ankara Universitesi Eczacilik Fakultesi Dergisi, 112–136. https://doi.org/10.33483/jfpau.559665
23. Ferreira, B. P., Costa, G., Mascarenhas-Melo, F., Pires, P. C., Heidarizadeh, F., Giram, P., Mazzola, P. G., Cabral, C., Veiga, F., & Paiva-Santos, A. C. (2023). Skin applications of cannabidiol: sources, effects, delivery systems, marketed formulations and safety. Phytochemistry Reviews, 22(3), 781–828. https://doi.org/10.1007/s11101-023-09860-5
24.Juknat, A., Pietr, M., Kozela, E., Rimmerman, N., Levy, R., Coppola, G., Geschwind, D. H., & Vogel, Z. (2011). Differential transcriptional profiles mediated by exposure to the cannabinoids cannabidiol and Δ9-tetrahydrocannabinol in BV-2 microglial cells. British Journal of Pharmacology, 165(8), 2512–2528. https://doi.org/10.1111/j.1476-5381.2011.01461.x
25. Mukhopadhyay, P., Rajesh, M., Horváth, B., Bátkai, S., Park, O., Tanchian, G., Gao, R. Y., Patel, V., Wink, D. A., Liaudet, L., Haskó, G., Mechoulam, R., & Pacher, P. (2011). Cannabidiol protects against hepatic ischemia/reperfusion injury by attenuating inflammatory signaling and response, oxidative/nitrative stress, and cell death. IRIS, 50(10), 1368–1381. https://doi.org/10.1016/j.freeradbiomed.2011.02.021
26.Río, C. del, Ruíz-Pino, F., Prados, M. E., Fiebich, B. L., Tena-Sempere, M., & Muñóz, E. (2022). Cannabidiol markedly alleviates skin and liver fibrosis. Frontiers in Pharmacology, 13. https://doi.org/10.3389/fphar.2022.981817
27. Louisa, M., Putera, A. M., Sidqi, A. A., Mahaputra, D. K., Firmansyah, E. R., Ammar, M. F., Talya, N., Aryadevi, N. N. B., Sandhiutami, N. M. D., Sukmawati, D., & Soetikno, V. (2022). Attenuation of cisplatin-induced hepatotoxicity by nanocurcumin through modulation of antioxidative and anti-inflammatory pathways. Journal of Applied Pharmaceutical Science. https://doi.org/10.7324/japs.2023.44149
28.Jastrząb, A., Gęgotek, A., & Skrzydlewska, E. (2019). Cannabidiol Regulates the Expression of Keratinocyte Proteins Involved in the Inflammation Process through Transcriptional Regulation. Cells, 8(8), 827–827. https://doi.org/10.3390/cells8080827
29. Panzella, L. (2020). Natural Phenolic Compounds for Health, Food and Cosmetic Applications. https://doi.org/10.3390/books978-3-03936-735-1
30. Tripson, M., Litwa, K., & Soderstrom, K. (2023). Cannabidiol inhibits neuroinflammatory responses and circuit-associated synaptic loss following damage to a songbird vocal pre-motor cortical-like region. Scientific Reports, 13(1), 7907–7907. https://doi.org/10.1038/s41598-023-34924-z

MODULATORY EFFECTS OF CANNABİDİOL ISOLATED FROM CANNABİS İNDİCA LAM. CALLUS CULTURE ON SERUM LİPOPHİLİC COMPOUNDS AND FATTY ACİD COMPOSİTİON İN A DMBA-INDUCED RAT MODEL

Tuba OKUTAN

Lect. Dr., Fırat University, Faculty of Science, Department of Biology, ORCID NO: 0000-0001-8745-0343

Ökkeş YILMAZ

Prof. Dr., Fırat University, Faculty of Science, Department of Biology, ORCID NO: 0000-0002-8276-4498

ABSTRACT

This study evaluated the effects of cannabidiol (CBD), biotechnologically obtained from *Cannabis indica* Lam. callus culture, on serum lipophilic compounds and fatty acid composition in a DMBA-induced rat model. Sprague Dawley rats received DMBA orally at a dose of 25 mg/rat on the 1st and 4th days of the experiment, while CBD was administered intraperitoneally at doses of 5 mg/kg and 10 mg/kg for eight weeks. At the end of the experimental period, serum fat-soluble vitamins, sterols, and fatty acid profiles were determined using HPLC and GC analyses.

CBD administration altered the serum lipophilic profile, particularly vitamin D3, α-tocopherol, retinol, and sterol levels. The C2 group exhibited a broader distribution of α-tocopherol and ergosterol, whereas the DC1 group showed comparatively higher retinol and cholesterol levels. Among saturated fatty acids, palmitic acid represented the predominant fraction (32,25–36,44%), while capric acid levels increased significantly in the C1 (0,77± 0,05) and C2 (0,78± 0,13) groups compared with the control group ($p < 0,05$). Palmitoleic acid differed significantly in the C1 and DC2 groups, whereas docosahexaenoic acid (DHA) was significantly elevated in the C1, DC1, and DC2 groups. Saturated fatty acids constituted the major lipid fraction in all experimental groups, while the highest proportion of polyunsaturated fatty acids was observed in the C2 group (27,63%).

Overall, callus-derived CBD contributed to the preservation of serum lipophilic compounds and polyunsaturated fatty acids, suggesting a modulatory role in maintaining lipid homeostasis under oxidative stress conditions. These findings indicate that biotechnologically produced CBD may represent a promising bioactive agent for preventing oxidative stress-associated metabolic alterations.

Keywords: CBD, fatty acid, lipophilic molecules, DMBA

1. INTRODUCTION

Oxidative stress is a significant biological process resulting from an imbalance between reactive oxygen species (ROS) and the organism's antioxidant defense system, which can cause irreversible damage to proteins, lipids, and nucleic acids. Polyunsaturated fatty acids (PUFAs), which form the basic components of cell membranes, are particularly susceptible to free radical attacks due to their double bonds and are the main targets of the lipid peroxidation process (1,2). As lipid peroxidation progresses, membrane integrity is compromised, cellular signaling mechanisms are altered, and the development of various metabolic diseases is accelerated (3).

7,12-dimethylbenz[a]anthracene (DMBA), commonly used in experimental studies to induce oxidative stress, is converted into reactive intermediates via the cytochrome P450 enzyme system during its metabolic activation, leading to the formation of high amounts of free radicals. This process is not limited to DNA damage but also leads to significant changes in lipid metabolism, fatty acid composition, and the cellular antioxidant system (4,5). Therefore, experimental models created with DMBA are considered reliable systems in investigating the biological effects of natural antioxidant compounds.

Cannabis indica Lam. is one of the medicinal plants that has attracted intense pharmacological interest in recent years due to its phytocannabinoids. Among these compounds, cannabidiol (CBD) stands out because it does not exhibit psychoactive properties and has antioxidant, anti-inflammatory, and neuroprotective effects. Studies show that CBD can reduce free radical formation, suppress lipid

peroxidation, and support endogenous antioxidant enzyme systems (6,7). In addition, it is reported that CBD contributes to the maintenance of cellular homeostasis by easily interacting with biological membranes thanks to its high lipophilicity (8).Plant tissue culture techniques are among the important biotechnological methods that allow the sustainable production of secondary metabolites under controlled conditions. Callus cultures, in particular, allow for standardized biomass production independent of environmental variables and constitute an alternative source for obtaining pharmaceutically valuable compounds (9). This approach offers significant advantages in terms of conserving natural plant populations and ensuring the production of standardized phytochemicals.

Fat-soluble vitamins, sterols, and fatty acids are essential components of cell membranes and play a critical role in regulating oxidative stress. α-Tocopherol and retinol protect membrane lipids from oxidative damage, while vitamin D contributes to maintaining redox balance (10,11). Phytosterols and cholesterol are involved in maintaining membrane fluidity and lipid homeostasis, and changes in serum levels provide important information about metabolic status (12). Similarly, changes in serum fatty acid composition are considered reliable biochemical indicators of the organism's oxidative status and lipid metabolism (13).

In light of this information, evaluating the effects of cannabidiol isolated from Cannabis indica Lam. callus culture on serum lipophilic compounds and fatty acid composition in a DMBA-induced rat model is important both for elucidating the biological activity of biotechnologically derived CBD and for understanding oxidative stress-related metabolic changes. This study is expected to contribute to the literature on the modulatory effects of callus-derived CBD on serum lipid homeostasis.

2. MATERIALS- METHODS

In this study, the effects of cannabidiol (CBD), obtained from Cannabis indica Lam. callus culture using biotechnological methods, on serum lipophilic compounds and fatty acid composition in an oxidative stress model induced by DMBA were investigated. The research process was carried out in accordance with the provisions of the "Regulation on Hemp Cultivation and Control," published in the Official Gazette dated September 29, 2016, and numbered 29842. The experimental protocol was ethically evaluated and approved by the Fırat University Animal Experiments Local Ethics Committee at its session on November 16, 2022 (Session No: 2022/18-04) (Appendix 2). The care, feeding, and all application processes of the experimental animals were carried out under standard laboratory conditions within the Fırat University Experimental Research Center (FÜDAM). In the experimental model, DMBA was administered orally via gavage at a dose of 25 mg/rat on days 1 and 4 of the experiment to induce oxidative stress in Sprague Dawley rats, while CBD was administered intraperitoneally at doses of 5 mg/kg (C1) and 10 mg/kg (C2) for eight weeks. Serum samples obtained at the end of the experiment were analyzed for fat-soluble vitamins (K1, D3, α-tocopherol, and retinol), sterols (ergosterol, sitosterol, β-sitosterol, and cholesterol), and saturated, monounsaturated, and polyunsaturated fatty acid profiles. Based on the findings, the potential modulatory effects of CBD obtained from callus culture on serum lipophilic components and fatty acid composition were evaluated biochemically.

2.1. Analysis of Lipophilic Vitamins and Ergosterol Amounts

For the analysis of serum lipophilic compounds, samples were added to a 10% KOH solution, vortexed, and incubated at 85 °C for 15 minutes. The samples, cooled to room temperature, were diluted with pure water, and the lipophilic compounds were separated by hexane extraction. The resulting organic phase was evaporated under nitrogen gas, and the remaining residue was dissolved in an acetonitrile/methanol (60%/40%, v/v) mixture and transferred to vials for analysis. Analyses were performed using a Shimadzu HPLC system on a Cosmosil AR II column (150 mm, 4.6, 5 µm USA). An acetonitrile/methanol (88%/12%, v/v) mixture was used as the mobile phase, and the flow rate was set to 1 mL/min. Vitamin A was determined at 326 nm, and vitamins D, E, K, and phytosterols at 202 nm using a PDA-UV detector. The analyses were carried out based on the methods described by Katsanidis and Addis (1999) and Lopez-Cervantes et al. (2006) (14,15).

2.2. Preparation of Fatty Acid Methyl Esters

To determine the serum fatty acid composition, 2% methanolic sulfuric acid was added to the samples and vortexed for homogenization. The methylation process was carried out at 55 °C for 15 hours, after which the samples were cooled to room temperature. Then, 5% NaCl solution was added, and the resulting fatty acid methyl esters were extracted with hexane. The methyl ester preparation process was carried out according to the method described by Christie (1988) (16). Phase separation was achieved by adding 2% $KHCO_3$ to the obtained hexane phase, and the mixtures were allowed to stand for approximately 16 hours. After removing the solvent from the organic phase under nitrogen gas at 45 °C, the remaining residue was dissolved in 1 mL of chloroform. The prepared fatty acid methyl esters were analyzed using Shimadzu GC 2010 Plus gas chromatography and an Rtx 2330 GC capillary column (30 µm, 0.25 mm ID, 0.20 µm, USA).

2.3. Analysis of Fatty Acids by GC

In gas chromatography analyses, the column temperature was set to 138–222 °C, the injection port to 245 °C, and the detector temperature to 280 °C. The temperature program was initially increased from 138 °C to 200 °C at a rate of 5 °C/min, then from 200 °C to 222 °C at a rate of 4 °C/min, and kept constant at the final temperature for 8 minutes. The total analysis time was 28 minutes, and helium was used as the carrier gas. Before proceeding with sample analyses, standard fatty acid methyl ester mixtures were injected into the instrument to determine the retention times for each compound in order to accurately identify fatty acid methyl esters. In line with the obtained standard data, the instrument parameters were optimized, and fatty acid methyl esters of serum samples were analyzed under the same conditions (16).

2.4. Statistical Analysis

One-way analysis of variance (ANOVA) was applied to the statistical evaluation of the experimental data. Duncan's multiple comparison test was used to determine differences between groups, and Fisher's least significant difference (LSD) test was used for comparisons with the control group. The statistical significance level was accepted as $p<0.05$, and the results were expressed as arithmetic mean ± standard error (Mean ± SE).

3. RESULTS AND DISCUSSION

Figure 3.1 presents multi-panel boxplot graphs of serum vitamin K1, vitamin D3, α-tocopherol, ergosterol, cholesterol, stigmasterol, β-sitosterol, and retinol levels. The graphs visually reveal the distribution, median values, and individual differences among the experimental groups.

In terms of vitamin K1, the DMBA group showed a wider distribution and higher values compared to the control group. In the CBD-treated groups, K1 levels generally showed lower variability and exhibited a distribution close to the control group.

When vitamin D3 levels were examined, it was noteworthy that the widest distribution was observed in the C1 group. While the median value was observed to be higher in the DC1 group compared to other groups, a narrower distribution was observed in the control, DMSO, olive oil, and DC2 groups.

In α-tocopherol levels, a significant variability was found in the C2 group, and it was determined that the maximum values were observed in this group. In the control, DMSO, olive oil, DC1, and DC2 groups, a more homogeneous distribution of values is observed.

When ergosterol levels are evaluated, both the mean value and individual variability are higher in the C2 group compared to the other groups. Lower and more limited distributions were observed in the control and DC1 groups.

In terms of cholesterol levels, a wide distribution is observed in the DMBA and DMSO groups, while higher median and mean values are noteworthy in the DC1 group. In the olive oil and C1 groups, cholesterol levels are seen to be lower and more balanced.

In the stigmasterol graph, it was determined that group C2 had a significantly wider distribution and reached higher values compared to other groups. In the control group, although there was a single high outlier value, the overall distribution was at lower levels. When β-sitosterol levels were examined, a

distinct outlier value was observed in group C1, while the values were observed to be distributed within a narrower range in other groups. In particular, the median values were close to each other in the control, DMSO, olive oil, and DC2 groups.

In retinol levels, the highest distribution and widest variability were determined in the DC1 group. While higher values were observed in the DMBA and C1 groups compared to the control group, it was determined that retinol levels showed a more limited distribution in the C2 and DC2 groups.

When the boxplot graphs in Figure 3.1 are evaluated together, it is seen that the serum levels of lipophilic molecules differ depending on the applications, and especially in some CBD application groups, wider distributions and higher values were observed in vitamins and sterol compounds. The extreme values and variability observed in the graphs support the idea that individual biological responses can differ between experimental groups.

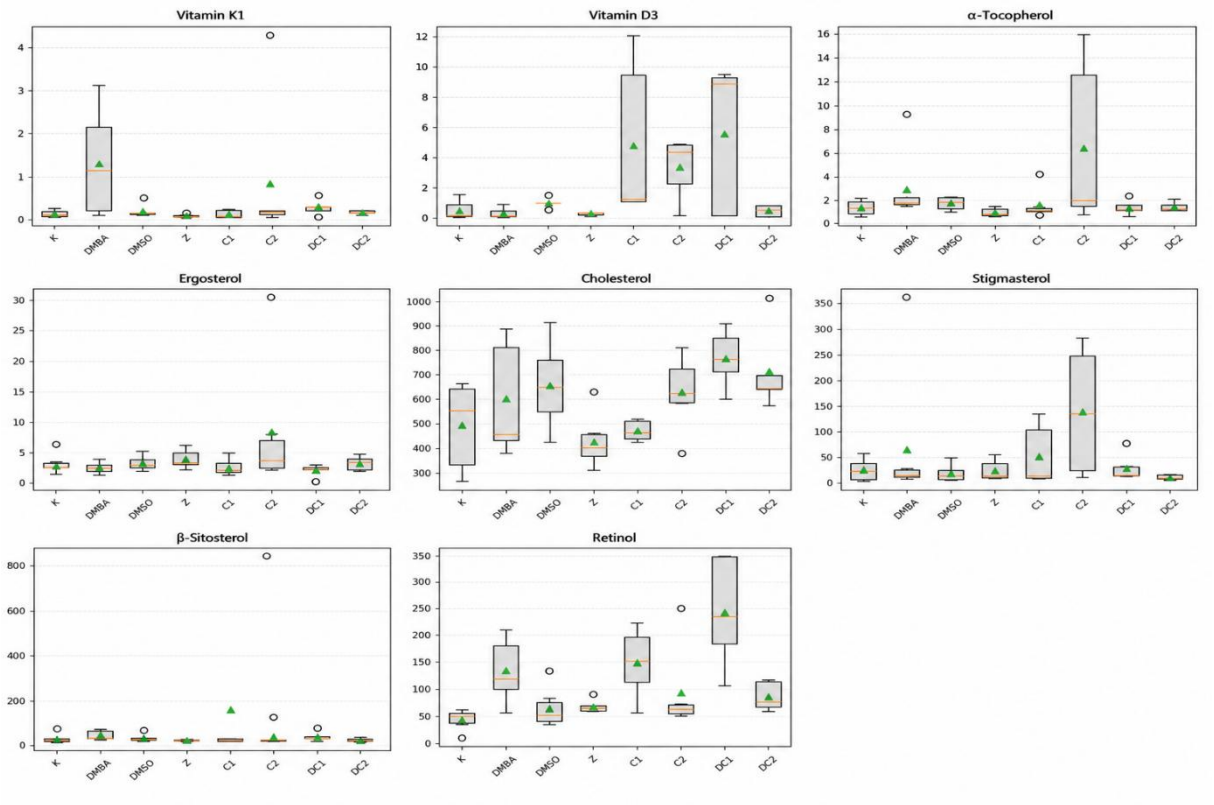


Figure 3.1. Serum Lipophilic Molecule Profile Following Experimental Treatments (µg/mL)

When the serum lipophilic molecule profile was evaluated, significant differences in distribution were observed among the experimental groups, especially in vitamin D3, α-tocopherol, retinol, and phytosterol levels. Fat-soluble vitamins and sterols play an important role in maintaining cellular membrane integrity and limiting oxidative damage. α-tocopherol, in particular, is considered one of the key antioxidants that protect membrane lipids from free radical attacks (17).

In the present study, the wider distribution of α-tocopherol levels in the C2 group and the high levels of retinol and vitamin D3 in some CBD application groups suggest that CBD obtained by biotechnological methods may contribute to the preservation of the serum lipophilic antioxidant profile. Similarly, the effects of CBD in reducing oxidative stress and supporting endogenous antioxidant systems have been reported in different experimental models (18).

Among the functions of vitamin D, besides classical calcium metabolism, are the reduction of oxidative stress and the maintenance of cellular redox balance. Recent studies have shown that adequate vitamin D levels can limit the formation of reactive oxygen species and support antioxidant defense (19).

Cholesterol and phytosterols are essential structural components of the cell membrane and play an important role in maintaining membrane fluidity and lipid homeostasis (20). The changes observed in

serum cholesterol and sterol profiles in our study show that experimental applications can affect serum lipid composition. However, since the current research is limited to biochemical analyses, it is not possible to make a definitive comment about the molecular effects of the observed changes on sterol metabolism or lipoprotein transport.

Table 3.1 shows that when serum saturated fatty acid profiles were evaluated, capric acid (10:0) levels were determined as 0,57± 0,02 in the control group, while the lowest average was found in the DMBA group (0,43 ± 0.04) and the highest average was found in the C2 group (0,78 ± 0,13). According to Duncan's multiple comparison test, groups C1 and C2 were in different letter groups than the DMBA group, while Fisher's LSD test showed a significant difference between groups C1 and C2 compared to the control group ($p<0,05$).

Lauric acid (12:0) values ranged from 0,68± 0,06 to 1,01 ± 0,55, with all groups in the same Duncan letter group and no significant difference compared to the control group. Similarly, although there were numerical differences between groups in the levels of myristic acid (14:0), pentadecanoic acid (15:0), palmitic acid (16:0), margaric acid (17:0), and stearic acid (18:0), all groups were in the same letter group according to the Duncan test, and no significant change was observed compared to the control group according to Fisher's LSD test (Table 3.1).

Palmitic acid (16:0) was determined to be the fatty acid with the highest proportion among all groups, with values ranging from 32,25 ± 0,97 to 36,44 ± 0,59. The highest average was found in the DMSO group, and the lowest average was found in the DC2 group. Stearic acid (18:0) levels ranged from 13,62 ± 1,13 to 17,17 ± 1,22, with the highest value determined in the DC1 group. Although numerical changes were observed in the serum saturated fatty acid profile depending on the treatments, statistically significant differences were found only for capric acid (10:0) in groups C1 and C2 (Table 3.1).

Table 3.1. Saturated fatty acid levels in serum (%)

Fatty acid	K	DMBA	DMSO	Z	C1	C2	DC1	DC2
10:0	0,57± 0,02^{ab}	0,43 ± 0,04^{b}	0,58 ± 0,04^{ab}	0,60± 0,07^{ab}	0,77± 0,05^{a*}	0,78± 0,13^{a*}	0,73± 0,09^{ab}	0,66± 0,05^{ab}
12:0	0,78 ± 0,06^{a}	1,01± 0,55^{a}	0,69± 0,09^{a}	0,68± 0,06^{a}	0,85± 0,13^{a}	0,93± 0,16^{a}	0,69± 0,05^{a}	0,83± 0,15^{a}
14:0	1,68 ± 0,32^{a}	3,87± 0,38^{a}	5,23± 0,28^{a}	2,33± 0,27^{a}	2,23± 0,27^{a}	2,29 ± 0,35^{a}	2,50± 0,27^{a}	2,00± 0,11^{a}
15:0	0,82± 0,14^{a}	0,88± 0,15^{a}	0,90± 0,22^{a}	0,71± 0,03^{a}	0,68± 0,03^{a}	0,72± 0,03^{a}	0,64± 0,01^{a}	0,67± 0,03^{a}
16:0	35,70± 2,26^{a}	36,08± 0,65^{a}	36,44± 0,59^{a}	33,75± 1,95^{a}	32,66± 1,42^{a}	32,43± 0,60^{a}	33,22± 1,58^{a}	32,25± 0,97^{a}
17:0	0,80 ± 0,22^{a}	0,76± 0,03^{a}	0,69± 0,02^{a}	0,60± 0,04^{a}	0,56± 0,03^{a}	0,67± 0,05^{a}	0,67± 0,03^{a}	0,69± 0,06^{a}
18:0	16,15± 1,72^{a}	14,03± 1,01^{a}	13,92± 1,49^{a}	13,62± 1,13^{a}	14,17± 0,99^{a}	15,78± 0,64^{a}	17,17± 1,22^{a}	15,60± 1,48^{a}

Values are expressed as mean ± SE. Different superscript letters indicate significant differences among groups according to Duncan multiple range test. Asterisks indicate significant differences compared with the control group according to Fisher LSD test (*$p<0.05$, **$p<0.01$, ***$p<0.001$).

When serum unsaturated fatty acids were examined, pentadekenoic acid (15:1) levels ranged from 1,18 ± 0,10 to 1,71 ± 0,21, and all groups were in the same Duncan letter group. Palmitoleic acid (16:1 n-7) levels were determined as 1,39 ± 0,20 in the control group, while the highest average was found in the DC2 group (3,05 ± 0,97). Although all groups were in the same letter group in the Duncan test, according to Fisher's LSD test, a significant difference was observed in the C1 ($p<0,05$) and DC2 ($p<0,01$) groups compared to the control group (Table 3.2).

Table 3.2. Unsaturated fatty acid levels in serum **(%)**

Fatty acid	K	DMBA	DMSO	Z	C1	C2	DC1	DC2
15:1	1,44± 0,13^{a}	1,18± 0,10^{a}	1,47± 0,18^{a}	1,54± 0,18^{a}	1,61± 0,11^{a}	1,68± 0,09^{a}	1,55± 0,10^{a}	1,71± 0,21^{a}
16:1 n-7	1,39± 0,20^{a}	1,55± 0,10^{a}	2,10± 0,16^{a}	2,12± 0,29^{a}	2,63± 0,26^{a*}	2,33± 0,36^{a}	1,98± 0,16^{a}	3,05± 0,97^{a**}
18:1 n-9	10,66±1,15^{a}	13,52± 1,38^{a}	10,94± 0,51^{a}	13,01±1,56^{a}	12,47±1,68^{a}	10,61±0,82^{a}	11,06± 0,56^{a}	11,99± 1,05^{a}
18:1 n-11	1,57± 0,13^{a}	2,42± 0,16^{a}	5,81± 3,80^{a*}	1,80± 0,13^{a}	2,01± 0,35^{a}	1,83± 0,06^{a}	2,35± 0,26^{a}	2,49± 0,31^{a}
18:2 n-6	12,47±1,02^{a}	13,08± 1,65^{a}	12,34± 1,78^{a}	15,40±2,49^{a}	12,98±0,53^{a}	12,91±0,36^{a}	12,78± 0,83^{a}	14,53± 0,80^{a}
18:3 n-3	0,61± 0,10^{a}	0,63± 0,05^{a}	0,91± 0,35^{a}	1,03± 0,24^{a}	0,65± 0,04^{a}	0,67± 0,06^{a}	0,81± 0,09^{a}	0,63 ± 0,03^{a}
20:4 n-6	10,69±1,61^{a}	7,60± 1,38^{a}	6,66± 1,29^{a*}	8,99± 1,41^{a}	10,70±1,10^{a}	10,92±1,32^{a}	9,12± 0,73^{a}	9,82± 0,71^{a}
24:1	0,63± 0,07^{a}	0,60± 0,07^{a}	0,50± 0,04^{a}	0,77± 0,13^{a}	0,49± 0,05^{a}	0,57± 0,05^{a}	0,58± 0,08^{a}	0,52± 0,04^{a}
22:6 n-3	1,85± 0,21^{b}	1,84± 0,13^{b}	1,55± 0,31^{b}	1,78± 0,18^{b}	2,57± 0,24^{a*}	2,48± 0,15^{ab}	3,07± 0,36^{a**}	2,58 ±0,30^{ab*}

Values are expressed as mean ± SE. Different superscript letters indicate significant differences among groups according to Duncan multiple range test. Asterisks indicate significant differences compared with the control group according to Fisher LSD test (*$p<0.05$, **$p<0.01$, ***$p<0.001$).

Oleic acid (18:1 n9) levels ranged from 10,61 ± 0,82 to 13,52 ± 1,38, and no significant difference was found between the groups. The highest mean vaccenic acid (18:1 n11) level was observed in the DMSO group (5,81 ± 3,80), and this group was significantly different from the control group according to Fisher's LSD test ($p<0,05$). While numerical variations were observed between the groups in linoleic acid (18:2 n-6c) and α-linolenic acid (18:3 n3 LNA) levels, no significant difference was found in Duncan's and LSD tests (Table 3.2).

Arachidonic acid (20:4 n6) levels were determined as 10,69 ± 1,61 in the control group, while the lowest value was obtained in the DMSO group (6,66± 1,29), and this group was found to be significantly different from the control group according to Fisher's LSD test ($p<0,05$). Nervonic acid (24:1) values showed a similar distribution in all groups. Docosahexaenoic acid (22:6 n3) levels ranged from 1,55 ± 0,31 to 3,07 ± 0,36, with the highest average determined in the DC1 group. In the Duncan multiple comparison test, the control, DMBA, DMSO, and Z groups were in letter group b, the C1 and DC1 groups in a, and the C2 and DC2 groups in ab. According to Fisher's LSD test, significant differences

were found in groups C1 (p<0,05), DC1 (p<0,01), and DC2 (p<0,05) compared to the control group (Table 3.2).

Figure 3.2 shows the percentage distribution of serum fatty acid classes (SFA, MUFA, and PUFA) in the experimental groups. In all groups, saturated fatty acids (SFA) constituted the majority of the serum fatty acid profile, with percentages ranging from 52,67% to 58,01%. The highest SFA percentage was found in the DMSO group (58,01%), while the lowest percentage was found in the DC2 group (52,67%).

When monounsaturated fatty acids (MUFA) were examined, more limited variations were observed between the groups, with percentages ranging from 16,05% to 20,68%. The lowest MUFA rate was obtained in the control group (16,05%), while the highest rate was obtained in the DMSO group (20,68%).

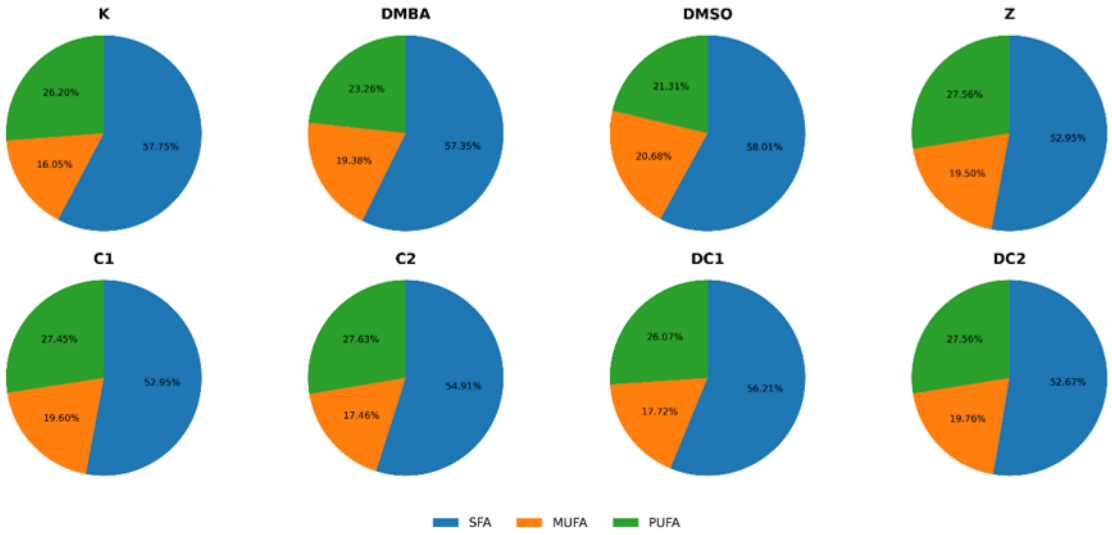


Figure 3.2. Serum Fatty Acid Composition of Experimental Groups Following Experimental Treatments (%)

Polyunsaturated fatty acids (PUFAs) constituted 21,31–27,63% of the total fatty acid profile. The lowest PUFA ratio was observed in the DMSO group (21,31%), while the highest ratio was determined in the C2 group (27,63%). Similar PUFA distributions were observed in the Z (27,56%) and DC2 (27,56%) groups. Overall, it was observed that the SFA fraction was dominant in all experimental groups, the MUFA ratios were within a narrower range, and the PUFA fraction reached higher percentages, especially in some groups treated with CBD. However, it is noteworthy that there were significant but limited changes in the distribution of serum fatty acid classes among the experimental groups. When serum fatty acid classes were evaluated together, it was observed that saturated fatty acids constituted the dominant fraction in all groups, the MUFA ratios varied more limitedly, and the PUFA ratios differed depending on the treatments. The highest SFA ratio and the lowest PUFA ratio in the DMSO group suggest that the fatty acid composition in this group has shifted towards a more saturated profile. In contrast, the higher PUFA ratios in the C2, Z, and DC2 groups indicate that polyunsaturated fatty acids, in particular, are more significantly conserved in the serum lipid profile. Under oxidative stress conditions, fatty acids, especially polyunsaturated fatty acids, are more susceptible to free radical attack due to their double bond content. Therefore, changes in PUFA levels are considered important in terms of lipid peroxidation and membrane integrity. The literature reports that PUFAs are the main substrates susceptible to lipid peroxidation and that these fatty acids are structurally more easily affected under oxidative stress (21). In this study, the low PUFA ratio in the DMSO group may reflect a change in serum lipid composition related to oxidative balance. However, this finding should not be considered as a mechanistic result alone, but should be interpreted together with the MDA and antioxidant enzyme results. The higher levels of PUFAs in the CBD-treated groups, particularly in the C2 and DC2 groups, suggest that callus-derived CBD may contribute to the maintenance of the serum lipid profile. Similarly, previous studies have reported that CBD can exert regulatory effects on lipid metabolism, oxidative stress, and inflammation; and that it can create changes in favor of n-3 PUFAs in some experimental

models (22). This seems consistent with the increasing trend in PUFA levels observed in our study. However, since the current study does not include gene expression or enzyme levels related to lipid metabolism, no definitive conclusion should be drawn about which molecular mechanisms CBD creates these changes through.

4. CONCLUSION

In serum lipophilic molecule analyses, treatment-dependent changes were observed, particularly in vitamin D3, α-tocopherol, retinol, and phytosterol levels. The higher levels of these compounds in some CBD treatment groups suggested that this could contribute to the preservation of serum antioxidant capacity. Similarly, when the serum fatty acid profile was examined, it was determined that saturated fatty acids constituted the dominant fraction in all groups, while the preservation of higher proportions of polyunsaturated fatty acids (PUFA) in the CBD-treated groups indicated that the lipid composition may become more resistant to oxidative stress.

The changes observed in the fatty acid fractions, especially in palmitoleic acid (16:1 n-7) and docosahexaenoic acid (22:6 n3) levels, along with the preservation of PUFA ratios, reveal that callus-derived CBD may contribute to the sustainability of the serum lipid profile. However, the combined evaluation of observed changes in serum sterols, vitamins, and fatty acids suggests that CBD administration may simultaneously affect not just a single biochemical parameter, but multiple processes related to lipid metabolism and the antioxidant defense system. Consequently, it can be said that CBD obtained from callus tissue using biotechnological methods is a potential bioactive compound that contributes to the maintenance of serum biochemical homeostasis and supports the serum lipid profile under experimental oxidative stress conditions. However, since this study is limited to biochemical analyses, it is considered necessary to support further studies at the lipidomic, metabolomic, gene expression, and protein levels to elucidate the underlying mechanisms of the observed effects in more detail. The results obtained reveal that biotechnologically derived CBD has significant research potential in terms of preventing oxidative stress-related diseases and developing supportive treatment strategies.

REFERENCES

1. Ayala, A., Muñoz, M. F., & Argüelles, S. (2014). Lipid peroxidation: Production, metabolism, and signaling mechanisms of malondialdehyde and 4-hydroxy-2-nonenal. *Oxidative Medicine and Cellular Longevity, 2014*, 360438. https://doi.org/10.1155/2014/360438
2. Mortensen, M. S., Ruiz, J., & Watts, J. L. (2023). Polyunsaturated fatty acids drive lipid peroxidation during ferroptosis. *Cells*, *12*(5), 804.
3. Halliwell, B., & Gutteridge, J. M. (2015). *Free radicals in biology and medicine*. Oxford university press.
4. Miyata, M., Furukawa, M., Takahashi, K., Gonzalez, F. J., & Yamazoe, Y. (2001). Mechanism of 7, 12-dimethylbenz [a] anthracene-induced immunotoxicity: role of metabolic activation at the target organ. The Japanese Journal of Pharmacology, 86(3), 302-309.
5. Klaunig, J. E., & Kamendulis, L. M. (2004). The role of oxidative stress in carcinogenesis. Annu. Rev. Pharmacol. Toxicol., 44(1), 239-267.
6. Atalay, S., Jarocka-Karpowicz, I., & Skrzydlewska, E. (2019). Antioxidative and anti-inflammatory properties of cannabidiol. *Antioxidants*, *9*(1), 21.
7. Jîtcă, G., Ősz, B. E., Vari, C. E., Rusz, C. M., Tero-Vescan, A., & Pușcaș, A. (2023). Cannabidiol: Bridge between antioxidant effect, cellular protection, and cognitive and physical performance. *Antioxidants, 12*(2), 485. https://doi.org/10.3390/antiox12020485
8. Pereira, S. R., Hackett, B., O'Driscoll, D. N., Sun, D., & Downer, E. J. (2021). Cannabidiol modulation of oxidative stress and signalling. *Neuronal Signalling, 5*(3), NS20200080. https://doi.org/10.1042/NS20200080
9. Murthy, H. N., Lee, E. J., & Paek, K. Y. (2014). Production of secondary metabolites from cell and organ cultures: Strategies and approaches for biomass improvement and metabolite accumulation. *Plant Cell, Tissue and Organ Culture, 118*(1), 1–16. https://doi.org/10.1007/s11240-014-0467-7
10. Vázquez-Lorente, H., Herrera-Quintana, L., Jiménez-Sánchez, L., Fernández-Perea, B., & Plaza-Diaz, J. (2024). Antioxidant functions of vitamin D and CYP11A1-derived vitamin D, tachysterol, and lumisterol metabolites: Mechanisms, clinical implications, and future directions. *Antioxidants, 13*(8), 996. https://doi.org/10.3390/antiox13080996
11. Brigelius-Flohé, R., & Traber, M. G. (1999). Vitamin E: Function and metabolism. *The FASEB Journal, 13*(10), 1145–1155. https://doi.org/10.1096/fasebj.13.10.1145
12. Catani, M. V., Gasperi, V., Bisogno, T., & Maccarrone, M. (2018). Essential dietary bioactive lipids in neuroinflammatory diseases. *Antioxidants & Redox Signaling*, *29*(1), 37-60.
13. Ferreri, C., Masi, A., Sansone, A., Giacometti, G., Larocca, A. V., Menounou, G., ... & Chatgilialoglu, C. (2016). Fatty acids in membranes as homeostatic, metabolic and nutritional biomarkers: recent advancements in analytics and diagnostics. *Diagnostics*, *7*(1), 1.
14. Katsanidis, E., & Addis, P. B. (1999). Novel HPLC analysis of tocopherols, tocotrienols, and cholesterol in tissue. *Free Radical Biology and Medicine*, *27*(11-12), 1137-1140.
15. Lopez-Cervantes, J., Sanchez-Machado, D. I., & Rios-Vazquez, N. J. (2006). High-performance liquid chromatography method for the simultaneous quantification of retinol, α-tocopherol, and cholesterol in shrimp waste hydrolysate. *Journal of Chromatography A*, *1105*(1-2), 135-139.
16. Christie, W. W. (1989). Gas chromatography and lipids.
17. Nau, R., Sörgel, F., & Prange, H. W. (1994). Lipophilicity at pH 7.4 and molecular size govern the entry of the free serum fraction of drugs into the cerebrospinal fluid in humans with uninflamed meninges. *Journal of the neurological sciences*, *122*(1), 61-65.
18. Jîtcă, G., Ősz, B. E., Vari, C. E., Rusz, C. M., Tero-Vescan, A., & Pușcaș, A. (2023). Cannabidiol: bridge between antioxidant effect, cellular protection, and cognitive and physical performance. *Antioxidants*, *12*(2), 485.
19. Vázquez-Lorente, H., Herrera-Quintana, L., Jiménez-Sánchez, L., Fernández-Perea, B., & Plaza-Diaz, J. (2024). Antioxidant functions of vitamin D and CYP11A1-derived vitamin D, tachysterol, and lumisterol metabolites: mechanisms, clinical implications, and future directions. *Antioxidants*, *13*(8), 996.
20. Luo, J., Yang, H., & Song, B. L. (2020). Mechanisms and regulation of cholesterol homeostasis. *Nature reviews Molecular cell biology*, *21*(4), 225-245.

21.Ayala, A., Muñoz, M. F., & Argüelles, S. (2014). Lipid peroxidation: production, metabolism, and signaling mechanisms of malondialdehyde and 4-hydroxy-2-nonenal. *Oxidative medicine and cellular longevity*, *2014*(1), 360438.
22.Bielawiec, P., Harasim-Symbor, E., Sztolsztener, K., Konstantynowicz-Nowicka, K., & Chabowski, A. (2021). Attenuation of oxidative stress and inflammatory response by chronic cannabidiol administration is associated with improved n-6/n-3 PUFA ratio in the white and red skeletal muscle in a rat model of high-fat diet-induced obesity. *Nutrients*, *13*(5), 1603.

FENİLKETONÜRİDE BESLENME TEDAVİSİ

Berra BAYRAKTAR
Bezmialem Vakıf Üniversitesi, Sağlık Bilimleri Fakültesi, Beslenme ve Diyetetik Bölümü
ORCID: 0009-0006-8559-1242

Beyza MENDEŞ
Bezmialem Vakıf Üniversitesi, Sağlık Bilimleri Fakültesi, Beslenme ve Diyetetik Bölümü,
ORCID: 0000-0002-4182-1273

ÖZET

Fenilketonüri, fenilalanin hidroksilaz enziminin yetersizliği sonucu fenilalanin metabolizmasının bozulmasıyla ortaya çıkan kalıtsal bir metabolik hastalıktır. Fenilalanin hidroksilaz enziminin aktivitesindeki azalma, fenilalaninin tirozine dönüşümünü engelleyerek kanda fenilalanin birikimine yol açmaktadır. Yüksek fenilalanin düzeyleri beyinde nörotoksik etki göstererek bilişsel gerilik, yürütücü işlev bozuklukları ve nöropsikiyatrik sorunlara neden olabilmektedir. Yenidoğan tarama programları ile erken tanı mümkün olmakta; ancak hastalığın etkin yönetimi yaşam boyu sürdürülen tıbbi beslenme tedavisine dayanmaktadır. Güncel yaklaşımlar yalnızca fenilalanin kısıtlamasını değil, yeterli enerji ve protein alımının sağlanmasını, tirozin desteğini, mikro besin ögesi yeterliliğini ve multidisipliner izlem süreçlerini kapsamaktadır.

Literatür, erken tanı ve yaşamın ilk haftalarında başlanan düşük fenilalaninli diyetin nörogelişimsel prognoz açısından belirleyici olduğunu göstermektedir. Aminoasit karışımları, yeterli protein alımının sağlanması ve tirozin eksikliğinin önlenmesi açısından önemlidir. Bununla birlikte uzun süreli diyet kısıtlamalarının mikro besin ögesi eksiklikleri, kemik mineral yoğunluğunda azalma ve diyet uyum sorunları ile ilişkili olabileceği bildirilmektedir. Büyük nötral aminoasitler gibi destekleyici yaklaşımlar bazı hasta gruplarında fenilalanin düzeylerinin kontrolüne katkı sağlayabilmektedir. Ergenlik ve yetişkinlik döneminde diyet uyumunun azalabildiği, metabolik kontrol bozulduğunda yürütücü işlevlerde gerileme ve psikososyal sorunların artabildiği bildirilmiştir. Maternal fenilketonüri olgularında gebelik öncesi ve gebelik süresince sıkı metabolik kontrol sağlanmadığında fetal mikrosefali, konjenital kalp hastalıkları ve intrauterin büyüme geriliği riskinin arttığı gösterilmiştir.

Sonuç olarak, fenilketonüride tıbbi beslenme tedavisi nörogelişimsel hasarın önlenmesinde temel yaklaşımdır. Etkin metabolik kontrol; bireyselleştirilmiş diyet planlaması, düzenli biyokimyasal izlem ve yaşa özgü beslenme stratejileri ile sağlanabilmektedir. Bu derlemenin amacı, fenilketonüride uygulanan tıbbi beslenme tedavisinin metabolik temellerini ve güncel tedavi seçeneklerini sistematik bir çerçevede değerlendirmektir.

Anahtar Kelimeler: Aminoasit, Beslenme, Fenilalanin, Fenilketonüri

GİRİŞ

Fenilketonüri, fenilalanin hidroksilaz enziminin yetersizliği sonucunda fenilalaninin tirozine dönüşümünün bozulmasıyla ortaya çıkan kalıtsal bir aminoasit metabolizması bozukluğudur. Fenilalanin, insan vücudunda sentezlenemeyen ve besinlerle alınması zorunlu olan esansiyel bir aminoasittir. Sağlıklı bireylerde fenilalanin, karaciğerde fenilalanin hidroksilaz enzimi ve tetrahidrobiopterin kofaktörü yardımıyla tirozine dönüştürülür. Fenilketonürili bireylerde ise bu metabolik yolakta meydana gelen bozukluk nedeniyle fenilalanin kanda birikmekte ve yüksek fenilalanin düzeyleri özellikle beyin gelişimi üzerinde olumsuz etkilere neden olmaktadır. [1]

Tedavi edilmeyen fenilketonüri olgularında zihinsel gelişme geriliği, nörolojik bozukluklar, mikrosefali, davranış problemleri, öğrenme güçlüğü, pigmentasyon bozuklukları, egzama benzeri deri bulguları ve idrar ile terde karakteristik koku görülebilmektedir. Hastalığın etkileri özellikle bebeklik ve erken çocukluk döneminde belirgindir. Çünkü bu dönem beyin gelişiminin hızlı olduğu, miyelinizasyonun devam ettiği ve nörogelişimsel süreçlerin yoğun şekilde ilerlediği bir dönemdir. Bu nedenle

fenilketonüride erken tanı ve erken tedavi nörolojik hasarın önlenmesi açısından kritik öneme sahiptir. [2]

Yenidoğan tarama programlarının yaygınlaşması, fenilketonürinin erken dönemde saptanmasını mümkün hale getirmiştir. Tarama sonucunda yüksek fenilalanin düzeyi saptanan bebeklerde tanı doğrulanmakta ve vakit kaybetmeden beslenme tedavisine başlanmaktadır. Tedavinin temel amacı, kan fenilalanin düzeylerini hedef aralıkta tutarak nörolojik hasarı önlemek ve aynı zamanda bebeğin büyüme-gelişmesini desteklemektir. Bu nedenle fenilketonüride tedavi yalnızca bir diyet kısıtlaması olarak görülmemeli; yaşam boyu izlem, aile eğitimi, metabolik kontrol, psikososyal destek ve multidisipliner yaklaşım gerektiren kapsamlı bir süreç olarak değerlendirilmelidir. [3]

Fenilketonüride tıbbi beslenme tedavisi hastalığın en temel tedavi yaklaşımıdır. Düşük fenilalaninli diyet, fenilalanin içermeyen aminoasit karışımları, düşük proteinli özel tıbbi ürünler, düzenli biyokimyasal izlem ve bireyselleştirilmiş beslenme planı tedavinin ana bileşenleridir. Bununla birlikte, beslenme tedavisinin sürdürülebilir olması hastanın yaşına, yaşam tarzına, aile desteğine, ekonomik koşullara, özel ürünlere erişimine ve psikolojik durumuna bağlıdır. Özellikle ergenlik ve erişkinlik dönemlerinde diyet uyumunun azalması metabolik kontrolü olumsuz etkileyebilir. Bu nedenle fenilketonüride yaşam boyu tedavi yaklaşımı benimsenmeli ve hasta merkezli bir izlem planı oluşturulmalıdır. [4]

Bu derleme çalışmasının amacı, fenilketonüride tıbbi beslenme tedavisinin temel ilkelerini, fenilalanin kısıtlamasının önemini, aminoasit karışımlarının kullanımını, yaşa göre beslenme yönetimini, mikro besin ögesi gereksinimlerini, diyet uyumunu, maternal fenilketonüriyi ve güncel destekleyici tedavi yaklaşımlarını literatür doğrultusunda değerlendirmektir.

GELİŞME

Fenilketonürinin Metabolik ve Genetik Temeli

Fenilketonüri, fenilalanin hidroksilaz enzim aktivitesindeki bozukluk sonucunda ortaya çıkar. Fenilalanin hidroksilaz enzimi, fenilalaninin tirozine hidroksilasyonunu sağlar. Bu reaksiyonun gerçekleşebilmesi için tetrahidrobiopterin kofaktörüne ihtiyaç vardır. Fenilalanin hidroksilaz enzimindeki eksiklik ya da tetrahidrobiopterin metabolizmasındaki bozukluklar sonucunda fenilalanin yeterince metabolize edilemez ve kanda birikmeye başlar. Kandaki fenilalanin düzeyinin yükselmesi merkezi sinir sistemi üzerinde toksik etki oluşturur. Bu durum nörotransmitter sentezini, protein metabolizmasını ve beyin gelişimini olumsuz etkileyebilir. [1]

Fenilalanin metabolizmasındaki bozukluk yalnızca fenilalanin birikimiyle sınırlı değildir. Fenilalaninin tirozine dönüşümü azaldığı için tirozin düzeylerinde de düşme meydana gelebilir. Tirozin; dopamin, norepinefrin, epinefrin, melanin ve tiroit hormonlarının sentezinde görev alan önemli bir aminoasittir. Bu nedenle fenilketonüride yüksek fenilalanin düzeyleriyle birlikte tirozin yetersizliği de klinik tabloyu etkileyebilir. Özellikle nörotransmitter sentezindeki bozulmalar dikkat, öğrenme, davranış ve yürütücü işlevler üzerinde olumsuz sonuçlara yol açabilir. [2]

Fenilketonüri otozomal resesif kalıtım göstermektedir. Hastalığın ortaya çıkması için bireyin anne ve babasından hastalığa neden olan genetik varyantları alması gerekir. Fenilalanin hidroksilaz genindeki farklı mutasyonlar hastalığın klinik şiddetini etkileyebilir. Bu nedenle fenilketonüri klasik fenilketonüri, orta fenilketonüri, hafif fenilketonüri ve hafif hiperfenilalaninemi gibi farklı klinik derecelerde görülebilir. Hastalığın şiddeti genellikle bireyin fenilalanin toleransı ve kan fenilalanin düzeyi ile ilişkilidir. Klasik fenilketonüride fenilalanin toleransı oldukça düşüktür ve sıkı diyet tedavisi gereklidir. Hafif formlarda ise fenilalanin toleransı daha yüksek olabilir ve tedavi planı bireysel değerlendirme sonucunda belirlenir. [3]

Tanı ve Tarama Yöntemleri

Fenilketonüride erken tanı, tedavi başarısının en önemli belirleyicilerinden biridir. Yenidoğan döneminde yapılan tarama testleri sayesinde hastalık klinik bulgular ortaya çıkmadan saptanabilmektedir. Tarama amacıyla genellikle bebeğin topuğundan alınan kan örneği kullanılır. Bu

örnek ile fenilalanin düzeyi değerlendirilir. Fenilalanin düzeyinin yüksek bulunması durumunda tanı doğrulama testleri yapılır ve hasta metabolizma uzmanı ile diyetisyen tarafından değerlendirilir. [4]

Yenidoğan tarama programları, fenilketonürili bebeklerin erken dönemde belirlenmesini sağlayarak kalıcı nörogelişimsel hasarın önlenmesinde büyük önem taşır. Tedaviye yaşamın ilk günlerinde veya haftalarında başlanması, uzun dönem bilişsel sonuçları olumlu etkiler. Tedaviye geç başlanması ya da tedaviye uyumsuzluk durumunda ise fenilalanin düzeyleri yükselir ve merkezi sinir sistemi hasarı riski artar. Bu nedenle tanı sonrasında hızlı bir şekilde beslenme tedavisi planlanmalı ve aileye ayrıntılı eğitim verilmelidir. [2]

Tanı konulduktan sonra kan fenilalanin düzeylerinin düzenli olarak izlenmesi gerekir. İzlem sıklığı hastanın yaşına, metabolik kontrol düzeyine ve klinik durumuna göre değişir. Bebeklik döneminde daha sık izlem gerekirken, yaş ilerledikçe izlem aralıkları bireysel duruma göre düzenlenebilir. Ancak fenilketonüri yaşam boyu izlem gerektiren bir hastalık olduğu için erişkin dönemde de kan fenilalanin takibi sürdürülmelidir. Kan fenilalanin düzeyleri değerlendirilirken bireyin besin tüketimi, enfeksiyon durumu, büyüme hızı, enerji alımı ve tedaviye uyumu birlikte ele alınmalıdır. [5]

Fenilketonüride Tıbbi Beslenme Tedavisinin Temel İlkeleri

Fenilketonüride tıbbi beslenme tedavisinin temel amacı, kan fenilalanin düzeylerini güvenli aralıkta tutarken bireyin büyüme, gelişme ve sağlıklı yaşam için gerekli tüm besin ögelerini yeterli düzeyde almasını sağlamaktır. Fenilalanin vücut için tamamen zararlı bir aminoasit değildir. Aksine protein sentezi ve büyüme için belirli miktarda fenilalanine ihtiyaç vardır. Bu nedenle tedavide fenilalaninin tamamen diyetten çıkarılması değil, bireyin tolere edebileceği miktarda verilmesi esastır. [3]

Diyet tedavisinde fenilalanin içeriği yüksek olan doğal protein kaynakları kısıtlanır. Et, tavuk, balık, yumurta, süt, peynir, yoğurt, kurubaklagiller, yağlı tohumlar ve bazı tahıllar fenilalanin içerikleri nedeniyle sınırlı tüketilmesi gereken besinler arasındadır. Bu besinler sağlıklı bireyler için kaliteli protein kaynakları olmakla birlikte fenilketonürili bireylerde kan fenilalanin düzeylerini yükseltebileceği için dikkatli şekilde değerlendirilmelidir. Diyetteki doğal protein miktarı hastanın fenilalanin toleransına göre belirlenmelidir. [6]

Fenilketonüride enerji gereksiniminin yeterli düzeyde karşılanması çok önemlidir. Enerji alımı yetersiz olduğunda vücutta katabolizma gelişir ve vücut proteinlerinin yıkımı sonucunda endojen fenilalanin düzeyleri artabilir. Bu durum kan fenilalanin düzeyinin yükselmesine neden olur. Bu nedenle fenilketonürili bireylerde enerji alımı yalnızca kilo kontrolü açısından değil, metabolik kontrol açısından da önemlidir. Özellikle bebeklik, çocukluk, ergenlik, hastalık ve gebelik dönemlerinde enerji gereksinimi daha dikkatli değerlendirilmelidir. [7]

Düşük Proteinli Özel Tıbbi Ürünlerin Kullanımı

Fenilketonürili bireylerde doğal protein kaynaklarının kısıtlanması, diyet çeşitliliğini ve enerji alımını azaltabilir. Bu nedenle düşük proteinli özel tıbbi ürünler tedavide önemli yer tutar. Düşük proteinli ekmek, makarna, un, bisküvi ve benzeri ürünler, bireyin günlük enerji gereksiniminin karşılanmasına yardımcı olurken fenilalanin alımını kontrol altında tutmayı sağlar. Bu ürünler özellikle çocukluk ve ergenlik döneminde diyetin sürdürülebilirliğini artırabilir. [6]

Düşük proteinli özel ürünlerin kullanılması, bireyin sosyal yaşamını da olumlu etkileyebilir. Normal besinlere benzer ürünlerin diyette yer alması, özellikle okul çağındaki çocukların ve ergenlerin kendilerini daha az kısıtlanmış hissetmesine katkı sağlayabilir. Ancak bu ürünlerin de enerji, karbonhidrat, yağ ve katkı maddesi içerikleri dikkate alınmalıdır. Düşük proteinli olmaları, sınırsız tüketilebilecekleri anlamına gelmez. Diyet planı içinde uygun porsiyonlarda kullanılmaları gerekir.

Sebze ve meyveler fenilketonüri diyetinde kontrollü şekilde yer alabilir. Ancak her sebze ve meyvenin fenilalanin içeriği aynı değildir. Bu nedenle porsiyon miktarları ve günlük toplam fenilalanin alımı hesaplanmalıdır. Patates, bezelye gibi protein içeriği görece daha yüksek olan sebzeler daha dikkatli tüketilmelidir. Elma, armut, karpuz, çilek gibi bazı meyveler daha düşük protein içeriği nedeniyle uygun miktarlarda tercih edilebilir. Bu noktada değişim listeleri, ailelerin ve hastaların diyet yönetimini kolaylaştıran önemli araçlardır. [6]

Aminoasit Karışımlarının Rolü

Fenilketonüride doğal protein alımı kısıtlandığı için protein gereksiniminin önemli bir bölümü fenilalanin içermeyen aminoasit karışımları ile karşılanır. Bu karışımlar, fenilalanin içermeden büyüme ve doku onarımı için gerekli aminoasitleri sağlar. Ayrıca birçok formül tirozin, vitamin, mineral ve eser elementlerle zenginleştirilmiştir. Bu nedenle aminoasit karışımları yalnızca protein desteği değil, aynı zamanda genel beslenme desteği sağlar. [7]

Aminoasit karışımlarının düzenli kullanılması tedavinin başarısı açısından önemlidir. Yetersiz tüketilmesi durumunda protein alımı azalabilir, büyüme geriliği ve mikro besin ögesi yetersizlikleri görülebilir. Ayrıca yeterli protein eşdeğeri alınmadığında vücutta katabolizma artabilir ve kan fenilalanin düzeyleri yükselebilir. Bu nedenle aminoasit karışımları gün içine bölünerek, önerilen miktarda ve düzenli olarak tüketilmelidir.

Aminoasit karışımlarının tadı, kokusu ve kullanım şekli bazı hastalarda tedaviye uyumu zorlaştırabilir. Özellikle çocukluk ve ergenlik dönemlerinde bu ürünlerin düzenli tüketilmesi sorun haline gelebilir. Bu nedenle hastanın yaşına, damak tadına ve yaşam düzenine uygun ürün seçimi yapılmalıdır. Ailelerin, öğretmenlerin ve sağlık profesyonellerinin desteği tedaviye uyumu artırmada önemlidir. Ergenlik döneminde bireyin hastalığını anlaması ve tedavi sorumluluğunu aşamalı olarak üstlenmesi sağlanmalıdır.

Tirozin Desteğinin Önemi

Fenilalanin normal metabolizmada tirozine dönüştürüldüğü için fenilketonürili bireylerde tirozin düzeyleri azalabilir. Tirozin, birçok nörotransmitterin ve hormonun sentezinde rol oynayan önemli bir aminoasittir. Bu nedenle fenilketonüride tirozin yarı esansiyel hale gelir. Fenilalanin içermeyen aminoasit karışımlarının çoğunda tirozin desteği bulunur. Böylece hem protein gereksinimi karşılanır hem de tirozin yetersizliği önlenmeye çalışılır. [1]

Tirozin desteği nörotransmitter sentezi ve metabolik denge açısından önemlidir. Ancak tek başına tirozin desteği fenilketonüri tedavisi için yeterli değildir. Tedavinin temelini fenilalanin kısıtlaması, yeterli enerji alımı, aminoasit karışımlarının düzenli kullanımı ve kan fenilalanin düzeylerinin izlenmesi oluşturur. Tirozin desteği bu temel yaklaşımların tamamlayıcı bir parçası olarak değerlendirilmelidir.

Bebeklik Döneminde Beslenme Yönetimi

Bebeklik dönemi fenilketonüri tedavisinde en hassas dönemlerden biridir. Bu dönemde beyin gelişimi hızlıdır ve yüksek fenilalanin düzeyleri kalıcı nörogelişimsel hasara yol açabilir. Yenidoğan taraması ile tanı alan bebeklerde tedaviye hızlı şekilde başlanmalıdır. Tedavide amaç, bebeğin kan fenilalanin düzeylerini hedef aralıkta tutarken yeterli büyüme ve gelişmeyi sağlamaktır. [2]

Fenilketonürili bebeklerde anne sütü tamamen yasaklanmak zorunda değildir. Anne sütü fenilalanin içerir; ancak uygun miktarda ve dikkatli izlemle fenilalanin içermeyen özel formüllerle birlikte kullanılabilir. Anne sütünün bağışıklık sistemi, büyüme ve anne-bebek ilişkisi açısından önemli yararları vardır. Bu nedenle anne sütü miktarı bebeğin fenilalanin toleransına göre hesaplanmalı ve kan fenilalanin düzeyleri düzenli izlenmelidir. [6]

Ek gıdaya geçiş döneminde düşük proteinli ve düşük fenilalaninli besinler kontrollü olarak diyete eklenir. Bu dönemde aileye fenilalanin hesaplama, porsiyon kontrolü, etiket okuma ve değişim listelerini kullanma eğitimi verilmelidir. Bebeklik döneminde yapılan doğru beslenme eğitimi, ilerleyen dönemlerde diyet uyumunun temelini oluşturur. Ailenin hastalığı anlaması, tedaviye güvenmesi ve günlük yaşamda diyeti uygulayabilir hale gelmesi oldukça önemlidir.

Çocukluk ve Ergenlik Döneminde Beslenme Yönetimi

Çocukluk döneminde fenilketonüri tedavisinin temel amacı metabolik kontrolü sağlamak, normal büyüme ve gelişmeyi desteklemek, beslenme yetersizliklerini önlemek ve çocuğun sosyal yaşamını mümkün olduğunca desteklemektir. Bu dönemde çocuk okul ortamına girmekte, arkadaşlarıyla yemek yemekte ve sosyal etkinliklere katılmaktadır. Bu nedenle diyet yalnızca ev ortamında değil, okul ve sosyal çevre içinde de sürdürülebilir olmalıdır.

Okul çağındaki çocuklarda öğretmenlerin ve okul personelinin hastalık hakkında bilgilendirilmesi tedavi uyumu açısından yararlı olabilir. Çocuğun yanında düşük proteinli uygun ara öğünlerin bulunması, özel günler ve etkinlikler için alternatif yiyeceklerin hazırlanması çocuğun sosyal uyumunu kolaylaştırır. Çocuğun yaşına uygun şekilde hastalığını tanıması, hangi besinleri neden sınırlaması gerektiğini öğrenmesi ve kendi beslenme sorumluluğunu kademeli olarak kazanması önemlidir.

Ergenlik dönemi fenilketonüri tedavisinde uyum sorunlarının daha sık görüldüğü bir dönemdir. Bu dönemde bireyin bağımsızlık isteği artar, arkadaş ilişkileri önem kazanır ve diyet kısıtlamaları psikolojik baskı oluşturabilir. Ergenler özel ürünleri kullanmak istemeyebilir, aminoasit karışımlarını aksatabilir veya yüksek proteinli besinleri tüketmeye başlayabilir. Bu durum kan fenilalanin düzeylerinin yükselmesine ve metabolik kontrolün bozulmasına neden olabilir. [4]

Ergenlik döneminde tedaviye yaklaşım yalnızca uyarı ve yasaklar üzerinden yürütülmemelidir. Bireyin psikolojik durumu, beden algısı, sosyal çevresi ve motivasyonu dikkate alınmalıdır. Diyetisyen, hekim, psikolog ve aile iş birliği ile ergenin tedavi sürecine aktif katılımı sağlanmalıdır. Ergene hastalığın uzun dönem etkileri anlaşılır şekilde anlatılmalı, pratik beslenme önerileri sunulmalı ve diyetin günlük yaşama uyarlanması desteklenmelidir.

Erişkinlik Döneminde Fenilketonüri Yönetimi

Fenilketonüride güncel yaklaşım, tedavinin yaşam boyu sürdürülmesi yönündedir. Geçmişte bazı hastalarda çocukluk döneminden sonra diyetin gevşetilebileceği düşünülse de yüksek fenilalanin düzeylerinin erişkin dönemde de bilişsel işlevler, dikkat, duygu durumu ve yaşam kalitesi üzerinde olumsuz etkiler oluşturabileceği bildirilmektedir. Bu nedenle erişkin fenilketonürili bireylerde de kan fenilalanin izlemi ve beslenme tedavisi devam etmelidir. [3]

Erişkin dönemde iş yaşamı, sosyal yaşam, ekonomik koşullar ve özel ürünlere erişim tedavi uyumunu etkileyebilir. Bazı erişkin hastalar çocukluk döneminde uyguladıkları diyeti sürdürmekte zorlanabilir. Bu nedenle erişkin hastalarda diyet planı bireyin yaşam tarzına uygun şekilde yeniden düzenlenmelidir. Pratik öğün seçenekleri, düşük proteinli ürünlerin kullanımı, aminoasit karışımlarının günlük düzene uygun planlanması ve düzenli takip bu dönemde önemlidir.

Erişkin kadın hastalarda gebelik planı ayrıca değerlendirilmelidir. Fenilketonürili kadınların gebelik öncesinde metabolik kontrollerinin sağlanması gerekir. Gebelik döneminde yüksek fenilalanin düzeyleri fetüs için ciddi risk oluşturduğundan, maternal fenilketonüri ayrı bir klinik önem taşımaktadır. Bu nedenle erişkin fenilketonürili kadınlara gebelik öncesi danışmanlık verilmelidir. [8]

Mikro Besin Ögesi Gereksinimleri

Fenilketonüride doğal protein kaynaklarının kısıtlanması bazı vitamin ve mineral yetersizliklerine yol açabilir. Özellikle hayvansal kaynaklı besinlerin sınırlanması B12 vitamini, demir, çinko, kalsiyum ve D vitamini alımını olumsuz etkileyebilir. Bu besin ögeleri büyüme, bağışıklık sistemi, kemik sağlığı, kan yapımı ve nörolojik fonksiyonlar açısından önemlidir. Bu nedenle fenilketonürili bireylerde yalnızca fenilalanin düzeyi değil, genel beslenme durumu da düzenli olarak değerlendirilmelidir. [7]

Kalsiyum ve D vitamini kemik mineralizasyonu açısından kritik öneme sahiptir. Süt ve süt ürünlerinin kısıtlanması nedeniyle fenilketonürili bireylerde kalsiyum alımı yetersiz kalabilir. D vitamini yetersizliği de kemik sağlığını olumsuz etkileyebilir. Bu nedenle özellikle büyüme çağındaki çocuklarda, ergenlerde ve erişkin kadınlarda kemik sağlığı dikkatle izlenmelidir. Gerekli durumlarda kalsiyum ve D vitamini desteği sağlık profesyonelleri tarafından planlanmalıdır.

B12 vitamini çoğunlukla hayvansal kaynaklı besinlerde bulunur. Fenilketonüri diyetinde hayvansal kaynaklı besinler sınırlandırıldığı için B12 vitamini eksikliği riski ortaya çıkabilir. B12 vitamini eksikliği hematolojik bulguların yanı sıra nörolojik sorunlara da neden olabilir. Aminoasit karışımlarının düzenli kullanımı bu eksikliklerin önlenmesine katkı sağlar. Ancak ürünlerin düzensiz kullanılması durumunda mikro besin ögesi yetersizlikleri gelişebilir. [6]

Demir ve çinko da fenilketonürili bireylerde dikkat edilmesi gereken mineraller arasındadır. Demir eksikliği anemiye, halsizliğe ve bilişsel performansta azalmaya yol açabilir. Çinko ise büyüme, bağışıklık sistemi ve yara iyileşmesi açısından önemlidir. Bu nedenle beslenme tedavisi planlanırken vitamin ve mineral alımı da hesaplanmalı, laboratuvar bulguları ile desteklenmelidir.

Esansiyel Yağ Asitleri ve Nörogelişim

Fenilketonürili bireylerde balık, yumurta ve bazı hayvansal kaynaklı besinlerin sınırlanması uzun zincirli çoklu doymamış yağ asitlerinin alımını azaltabilir. Özellikle omega-3 yağ asitlerinden dokosahekzaenoik asit beyin ve retina gelişimi açısından önemlidir. Çocukluk döneminde yeterli omega-3 yağ asidi alımı nörogelişimsel süreçleri destekleyebilir. Bu nedenle fenilketonüri diyetinde yalnızca protein ve fenilalanin değil, yağ kalitesi de değerlendirilmelidir. [9]

Diyet tedavisinde enerji gereksinimini karşılamak için sıvı yağlar kullanılabilir. Ancak yağların türü ve dengesi önemlidir. Omega-3 ve omega-6 yağ asitlerinin yeterli ve dengeli alınması sağlanmalıdır. Gerekli durumlarda uygun yağ asidi desteği değerlendirilebilir. Ancak bu destekler sağlık profesyonellerinin önerisi doğrultusunda kullanılmalı ve genel beslenme tedavisinin yerine geçmemelidir.

Diyet Uyumu ve Psikososyal Destek

Fenilketonüride tedavinin başarısı büyük ölçüde diyet uyumuna bağlıdır. Tedavi yaşam boyu sürdüğü için bireyin ve ailenin tedaviye aktif katılımı gereklidir. Diyet tedavisi; besin seçimi, porsiyon kontrolü, fenilalanin hesaplama, özel ürün kullanımı, aminoasit karışımlarının düzenli tüketimi ve kan takibi gibi birçok sorumluluk içerir. Bu durum özellikle aileler ve hastalar için zaman zaman zorlayıcı olabilir.

Aile eğitimi fenilketonüri yönetiminde temel unsurlardan biridir. Tanı anından itibaren aileye hastalığın nedeni, fenilalanin kısıtlamasının önemi, hangi besinlerin sınırlanması gerektiği, özel ürünlerin kullanımı ve kan izleminin gerekliliği anlatılmalıdır. Ailenin bilgi düzeyi arttıkça tedaviye uyum da artabilir. Bunun yanında hastanın yaşı ilerledikçe bireysel eğitim ön plana çıkarılmalı ve hasta kendi tedavi sürecine hazırlanmalıdır.

Psikososyal destek, fenilketonüri tedavisinde ihmal edilmemesi gereken bir alandır. Diyet kısıtlamaları sosyal yaşamı etkileyebilir, bireyde farklılık hissi oluşturabilir ve tedaviye karşı direnç gelişmesine neden olabilir. Ergenlik ve erişkinlik dönemlerinde psikolojik destek, motivasyon görüşmeleri ve akran desteği tedavi uyumunu olumlu etkileyebilir. Multidisipliner ekip yaklaşımı bu nedenle önemlidir. Hekim, diyetisyen, psikolog, hemşire ve aile iş birliği içinde çalışmalıdır.

Maternal Fenilketonüri

Fenilketonürili kadınlarda gebelik öncesi ve gebelik sürecinde metabolik kontrolün sağlanması fetal sağlık açısından kritik öneme sahiptir. Gebelik sırasında annenin kan fenilalanin düzeylerinin yüksek olması fetüs üzerinde teratojenik etki gösterebilir. Maternal fenilketonüri sendromunda mikrosefali, intrauterin büyüme geriliği, doğumsal kalp hastalıkları, zihinsel yetersizlik ve dismorfik yüz görünümü gibi ciddi sonuçlar görülebilir. [8]

Bu nedenle fenilketonürili kadınların gebelik planlamadan önce metabolik kontrollerinin sağlanması gerekir. Gebelik öncesi dönemde kan fenilalanin düzeyleri hedef aralığa getirilmeli ve gebelik boyunca yakın izlem sürdürülmelidir. Gebelikte enerji, protein, vitamin ve mineral gereksinimleri arttığı için beslenme planı sık aralıklarla güncellenmelidir. Fenilalanin toleransı gebelik boyunca değişebilir; bu nedenle düzenli kan takibi ve diyet düzenlemesi gereklidir. [8]

Maternal fenilketonüride psikolojik durum da tedavi uyumunu etkileyebilir. Gebelik döneminde anksiyete, stres ve yaşam düzenindeki değişiklikler diyet uyumunu azaltabilir. Bu nedenle gebelik sürecinde yalnızca beslenme tedavisi değil, psikolojik destek de önemlidir. Gebelik planlayan veya gebe olan fenilketonürili kadınların metabolizma uzmanı, kadın doğum uzmanı ve diyetisyen tarafından multidisipliner olarak izlenmesi gerekir.

Alternatif ve Destekleyici Tedavi Yaklaşımları

Fenilketonüride temel tedavi düşük fenilalaninli beslenme tedavisidir. Bununla birlikte bazı hastalarda destekleyici tedavi seçenekleri kullanılabilir. Tetrahidrobiopterin tedavisi, belirli genetik özelliklere sahip ve tedaviye yanıt veren hastalarda fenilalanin toleransını artırabilir. Bu tedavi her fenilketonürili birey için uygun değildir. Yanıt durumu bireysel olarak değerlendirilmelidir. [5]

Büyük nötral aminoasit tedavisi ise özellikle bazı erişkin hastalarda kullanılan destekleyici yaklaşımlardan biridir. Bu yaklaşımın amacı, fenilalaninin kan-beyin bariyerinden geçişini azaltmaya

yardımcı olmaktır. Ancak bu tedaviler diyet tedavisinin yerine geçmez. Uygun hastalarda diyet tedavisine ek olarak değerlendirilebilir. Tedavi kararı mutlaka uzman hekim tarafından verilmelidir.

Son yıllarda fenilketonüri tedavisinde glikomakropeptit içeren ürünler, enzim replasman yaklaşımları ve yeni farmakolojik tedaviler de gündeme gelmiştir. Bu yaklaşımlar hastaların diyet yükünü azaltma, fenilalanin toleransını artırma ve yaşam kalitesini iyileştirme potansiyeline sahiptir. Ancak her hastada uygulanabilirlik, etkinlik, güvenlilik ve erişilebilirlik açısından bireysel değerlendirme yapılmalıdır. Fenilketonüri yönetiminde güncel tedaviler umut verici olsa da beslenme tedavisi temel önemini korumaktadır. [7]

SONUÇ

Fenilketonüri, erken tanı ve uygun tıbbi beslenme tedavisi ile ağır nörogelişimsel komplikasyonları büyük ölçüde önlenebilen kalıtsal bir metabolik hastalıktır. Hastalığın temelinde fenilalanin metabolizmasındaki bozukluk yer almakta ve tedavi edilmediğinde yüksek fenilalanin düzeyleri merkezi sinir sistemi üzerinde ciddi olumsuz etkiler oluşturmaktadır. Bu nedenle yenidoğan taraması, erken tedaviye başlama ve düzenli metabolik izlem hastalığın yönetiminde temel öneme sahiptir.

Fenilketonüride tıbbi beslenme tedavisinin amacı yalnızca fenilalanin alımını kısıtlamak değildir. Tedavinin asıl amacı, kan fenilalanin düzeylerini hedef aralıkta tutarken bireyin yaşına, büyüme hızına, klinik durumuna ve metabolik toleransına uygun yeterli enerji, protein, vitamin ve mineral alımını sağlamaktır. Bu nedenle beslenme tedavisi bireyselleştirilmiş, sürdürülebilir ve düzenli izlemle desteklenen bir süreç olmalıdır. Fenilalanin içeriği yüksek besinlerin kısıtlanması, fenilalanin içermeyen aminoasit karışımlarının düzenli kullanımı, düşük proteinli özel ürünlerin diyete eklenmesi ve yeterli enerji alımının sağlanması tedavinin temel bileşenleridir.

Fenilketonüri yönetiminde yaşam dönemlerine göre farklı yaklaşımlar gereklidir. Bebeklik döneminde anne sütü ve özel formüllerin dengeli kullanımı, çocukluk döneminde büyüme ve okul yaşamına uyum, ergenlik döneminde psikososyal destek ve tedavi sorumluluğunun kazanılması, erişkinlik döneminde yaşam boyu izlem ve gebelik planlaması önemlidir. Özellikle maternal fenilketonüride gebelik öncesi ve gebelik süresince metabolik kontrolün sağlanması fetal komplikasyonların önlenmesi açısından kritik öneme sahiptir.

Sonuç olarak fenilketonüri tedavisi multidisipliner yaklaşım gerektiren, yaşam boyu süren ve bireyin tüm yaşam dönemlerini etkileyen kapsamlı bir süreçtir. Başarılı bir tedavi için düzenli kan fenilalanin izlemi, bireyselleştirilmiş beslenme planı, aile ve hasta eğitimi, psikososyal destek, mikro besin ögesi izlemi ve sağlık ekibi iş birliği gereklidir. Güncel destekleyici tedavi seçenekleri diyet uyumunu ve yaşam kalitesini artırma potansiyeline sahip olmakla birlikte, tıbbi beslenme tedavisi fenilketonüri yönetiminin temelini oluşturmaya devam etmektedir.

KAYNAKÇA

1. Blau N, van Spronsen FJ, Levy HL. Phenylketonuria. *Lancet*. 2010;376(9750):1417-1427.

2. Vockley J, Andersson HC, Antshel KM, et al. Phenylalanine hydroxylase deficiency: diagnosis and management guideline. *Genet Med*. 2014;16(2):188-200.

3. van Spronsen FJ, van Wegberg AM, Ahring K, et al. Key European guidelines for the diagnosis and management of patients with phenylketonuria. *Lancet Diabetes Endocrinol*. 2017;5(9):743-756.

4. Macleod EL, Ney DM. Nutritional management of phenylketonuria. *Ann Nestle Eng*. 2010;68(2):58-69.

5. Muntau AC, Adams DJ, Bélanger-Quintana A, et al. International best practice for the evaluation of responsiveness to sapropterin dihydrochloride in patients with phenylketonuria. *Mol Genet Metab*. 2019;127(1):1-11.

6. Köksal G, Gökmen Özel H. *Çocuk Hastalıklarında Beslenme Tedavisi*. Hatiboğlu Yayınevi; 2021.

7. Elhawary NA, AlJahdali IA, Abumansour IS, et al. Genetic etiology and clinical challenges of phenylketonuria. *Hum Genomics*. 2022;16(1):22.

8. Koch R, Hanley W, Levy H, et al. Maternal phenylketonuria: an international study. *Mol Genet Metab*. 2000;71(1-2):233-239.

9. Moseley K, Koch R, Moser AB. Lipid status and long-chain polyunsaturated fatty acid concentrations in adults and adolescents with phenylketonuria on phenylalanine-restricted diet. *J Inherit Metab Dis*. 2002;25(1):56-64.

HEMŞİRELİK EĞİTİMİNDE DİJİTAL DÖNÜŞÜM: DİJİTAL İKİZ TEKNOLOJİLERİNİN CERRAHİ BECERİ ÖĞRETİMİNE YANSIMALARI

Burçin IŞIK

Doç. Dr., Gaziantep İslam Bilim ve Teknoloji Üniversitesi, Sağlık Bilimleri Fakültesi, Hemşirelik Bölümü, Gaziantep, TÜRKİYE, ORCID: 0000-0002-5469-017X

Çiğdem AKSU

Doç. Dr., Gaziantep İslam Bilim ve Teknoloji Üniversitesi, Sağlık Bilimleri Fakültesi, Hemşirelik Bölümü, Gaziantep, TÜRKİYE, ORCID: 0000-0002-7275-4843

ÖZET

Giriş: Dijital ikiz teknolojisi, fiziksel bir sistemin gerçek zamanlı verilerle sürekli güncellenen sanal temsili olarak tanımlanmakta ve sağlık alanında simülasyon, öngörü ve karar destek süreçlerinde giderek artan bir kullanım alanı bulmaktadır. Son yıllarda dijital ikizlerin yalnızca hasta düzeyinde değil, klinik iş akışları ve operasyonel süreçler düzeyinde de uygulanmaya başladığı görülmektedir. Hemşirelik bakımında risk tahmini, klinik izlem ve bakım planlamasında önemli bir potansiyel sunan bu teknoloji, hemşirelik eğitiminde özellikle cerrahi beceri öğretimi açısından yeni bir paradigma olarak değerlendirilmektedir.

Amaç: Bu çalışmanın amacı, dijital ikiz teknolojilerinin hemşirelik eğitimindeki yerini açıklamak, özellikle cerrahi beceri öğretimindeki kullanım alanlarını değerlendirmek ve mevcut literatür doğrultusunda bu teknolojilerin sağlık alanı özelinde hemşirelik eğitimi süreçlerine olası katkılarını ortaya koymaktır.

Materyal-Metot: Bu çalışma, 2020–2026 yılları arasında yayımlanan çalışmaları kapsayan kapsamlı bir literatür derlemesi olarak yürütülmüştür. PubMed, Scopus, Web of Science, ScienceDirect, Google Scholar ve IEEE Xplore veri tabanları kullanılmıştır. Tarama sürecinde İngilizce ve Türkçe anahtar kelimelerden yararlanılmıştır. Temel olarak; “digital twin”, “digital twin technology”, “nursing education”, “surgical nursing education”, “surgical skill training”, “simulation in nursing”, “virtual simulation”, “digital transformation in nursing education”, “artificial intelligence and nursing education”, “cerrahi hemşireliği eğitimi”, “dijital ikiz teknolojisi”, “hemşirelik eğitiminde dijital dönüşüm” anahtar kelimeleri kullanılmıştır. Elde edilen veriler doğrultusunda hemşirelik eğitiminde dijital ikiz teknolojilerinin mevcut kullanım alanları, cerrahi beceri öğretimine katkıları, avantajları, sınırlılıkları ve geleceğe yönelik potansiyelleri tematik olarak analiz edilerek raporlanmıştır.

Bulgular: Literatür, dijital ikizlerin cerrahi beceri öğretiminde üç temel katkı sunduğunu göstermektedir: (1) ameliyathane süreçlerinin yüksek gerçeklikli ve tekrarlanabilir biçimde modellenmesi, (2) öğrenci performansına dayalı kişiselleştirilmiş geri bildirim ve veri temelli değerlendirme imkânı sağlaması, (3) hasta güvenliği ve ekip koordinasyonu gibi sistem temelli yeterliklerin simülasyon ortamında bütüncül biçimde ele alınabilmesi. Bununla birlikte, veri güvenliği, model doğrulama, teknik altyapı gereksinimleri ve müfredat entegrasyonu önemli sınırlılıklar olarak öne çıkmaktadır.

Sonuç: Dijital ikiz teknolojileri, hemşirelik eğitiminde cerrahi beceri öğretimini veri odaklı, kişiselleştirilmiş ve sistem temelli bir yapıya dönüştürme potansiyeline sahiptir. Gelecekte yapılacak deneysel ve uygulamalı çalışmaların, dijital ikiz tabanlı eğitim modellerinin klinik yeterlik, hasta güvenliği ve öğrenme çıktıları üzerindeki etkisini nicel ve nitel yöntemlerle değerlendirmesi önerilmektedir.

Anahtar Kelimeler: Dijital ikiz, hemşirelik eğitimi, dijital dönüşüm, cerrahi beceri öğretimi, hemşirelik eğitiminde beceri öğretimi

DIGITAL TRANSFORMATION IN NURSING EDUCATION: THE IMPACT OF DIGITAL TWIN TECHNOLOGIES ON THE TEACHING OF SURGICAL SKILLS

ABSTRACT

Introduction: Digital twin technology refers to a dynamic virtual representation of a physical system that is continuously updated through real-time data integration. In healthcare, digital twins are increasingly utilized for simulation, predictive modeling, and clinical decision support. Beyond patient-level applications, recent developments demonstrate their growing use in modeling clinical workflows and operational processes. In nursing practice, digital twins hold promise for risk prediction, clinical monitoring, and care planning. Within nursing education, particularly in surgical skills training, this emerging technology represents a paradigm shift toward data-driven and system-oriented learning environments.

Aim: The purpose of this study is to explain the role of digital twin technologies in nursing education, evaluate their applications specifically in the teaching of surgical skills, and highlight their potential contributions to nursing education processes in the healthcare sector based on the existing literature.

Materials and Methods: This study was conducted as a comprehensive literature review covering studies published between 2020 and 2026. The databases PubMed, Scopus, Web of Science, ScienceDirect, Google Scholar, and IEEE Xplore were utilized. English and Turkish keywords were used during the search process. Primarily, the following keywords were used: “digital twin,” “digital twin technology,” “digital twin in “nursing education,” “surgical nursing education,” “surgical skill training,” “simulation in nursing,” “virtual simulation,” “digital transformation in nursing education,” “artificial intelligence and nursing education,” were used. Based on the data obtained, the current applications of digital twin technologies in nursing education, their contributions to surgical skill training, their advantages, limitations, and future potential were thematically analyzed and reported.

Results: The findings suggest that digital twin technologies offer three primary contributions to surgical skills training: (1) high-fidelity and repeatable modeling of operating room processes; (2) personalized feedback and data-driven performance evaluation based on learner analytics; and (3) comprehensive simulation of system-level competencies such as patient safety and team coordination. Nevertheless, challenges including data security, model validation, technological infrastructure requirements, and curriculum integration remain significant barriers to widespread implementation.

Conclusion: Digital twin technologies have the potential to transform surgical skills training in nursing education into a data-informed, personalized, and systems-based learning framework. Future experimental and practice-based research is needed to evaluate the impact of digital twin–supported educational models on clinical competence, patient safety outcomes, and measurable learning performance.

Keywords: Digital twin, nursing education, digital transformation, surgical skills training, teaching skill in nursing education

INTRODUCTION

Digital transformation in healthcare has fundamentally transformed not only clinical practices but also the educational processes of healthcare professionals in recent years. Artificial intelligence, augmented reality, virtual reality, big data, learning analytics, and simulation technologies are increasingly being used in nursing education; innovative approaches aimed at improving student success are being developed, particularly in skills-based education (1,2). Surgical nursing education, being one of the fields that requires a high level of technical skill, rapid decision-making, error management, and patient safety, has become one of the disciplines most affected by digital transformation (3).

For many years, traditional methods of teaching surgical skills have relied on the “master-apprentice model,” laboratory exercises, and mannequin-based simulations. However, the need for next-generation educational technologies has grown due to factors such as increasing student numbers, limited clinical

training spaces, patient safety concerns, complex surgical procedures, and insufficient opportunities for practice (4). In this context, digital twin technologies stand out as one of the innovative approaches gaining attention in healthcare education.

A digital twin is defined as a virtual replica of a physical object, system, or person that is continuously updated with real-time data (5). Although this technology was first developed in the industrial sector, it is now being used in healthcare, surgical planning, patient monitoring, and medical education (6). Digital twin systems operate using sensors, artificial intelligence algorithms, data analytics, simulation technologies, and real-time feedback mechanisms (5). They offer significant opportunities, particularly in surgical settings, for personalized training, a safe practice environment, and performance analysis (7).

Although the use of digital twin technologies in nursing education is still in its developmental phase, current studies indicate that these technologies increase student engagement, support learning motivation, and enhance skill acquisition (8). In surgical skill instruction, digital twins allow students to experience the dynamics of real surgical environments in a safe virtual setting, reanalyze their mistakes, and receive immediate feedback on their performance (9). Additionally, the ability to repeatedly simulate complex surgical scenarios contributes to standardization in educational processes (4).

With the increasing prevalence of technology-supported learning models in healthcare education in recent years, it is anticipated that digital twin technologies will be utilized more effectively in nursing education in the future (1). In particular, it is believed that digital twin platforms integrated with artificial intelligence-supported learning systems will play a significant role in enhancing students' clinical decision-making skills in surgical skill instruction (6).

The aim of this review is to explain the role of digital twin technologies in nursing education, evaluate their applications particularly in surgical skill instruction, and highlight the potential contributions these technologies can make to nursing education processes within the healthcare field based on the current literature.

MATERIALS AND METHODS

This study is a traditional review designed to evaluate the effects of digital twin technologies on the teaching of surgical skills in nursing education. The study examined recent national and international literature published over the past five years (5,8).

The literature review was conducted between January 2020 and May 2026 using the PubMed, Scopus, Web of Science, ScienceDirect, Google Scholar, and IEEE Xplore databases. English and Turkish keywords were used during the search process. Primarily, the following keywords were used: "digital twin," "digital twin technology," "nursing education," "surgical nursing education," "surgical skill training," "simulation in nursing," "virtual simulation," "digital transformation in nursing education," "artificial intelligence and nursing education," "surgical nursing education," "digital twin technology," "digital transformation in nursing education" were used. During the database searches, combinations were created using Boolean operators ("AND," "OR"). The inclusion criteria for the study were determined as follows:

- Published between 2020 and 2026,
- Full text available,
- Published in English or Turkish,
- Related to digital twin technologies, simulation systems, surgical education, or nursing education,
- Being a research article, review, or systematic review published in peer-reviewed journals,

The exclusion criteria were defined as:

- Letters to the editor,
- Abstracts,
- Studies for which the full text was unavailable,
- Publications not directly related to the topic (10,11)

The studies identified through the screening process were preliminarily evaluated based on their titles and abstracts, and the full texts of publications deemed relevant to the research were reviewed. The

reviewed studies were evaluated in terms of the use of digital twin technologies in nursing education, the application areas of digital twin technologies, their applications in surgical skill instruction, simulation-based learning processes, their effects on student performance, their contributions to patient safety, and the limitations encountered in education (3,6). Based on the data obtained, the current applications of digital twin technologies in nursing education, their contributions to surgical skill instruction, their advantages, limitations, and future potential were thematically analyzed and reported (2,12).

DEVELOPMENT/BACKGROUND

The Basic Structure of Digital Twin Technology

Digital twin technology is an integrated framework that enables the real-time modeling of a physical system in a digital environment. This framework typically consists of three core components: the physical system, the virtual model, and a real-time data connection (5). In the healthcare field, digital twins are used for modeling patients' physiological data, simulating clinical processes, planning surgical procedures, and in educational applications (6). In particular, thanks to real-time data transmission, the virtual model is continuously updated, creating a dynamic learning environment (5).

In the context of surgical training, digital twins can simulate the operating room environment, surgical instruments, patient anatomy, and clinical processes with high accuracy (7). Thus, students not only acquire theoretical knowledge but also develop clinical decision-making and technical application skills (4).

Digital Transformation in Nursing Education

Nursing education is currently evolving toward technology-supported learning models. The widespread adoption of distance learning practices in the post-pandemic era has accelerated the use of digital platforms; virtual simulations, augmented reality applications, and artificial intelligence-supported learning systems have been integrated into educational processes (1,2). In particular, the use of technology-supported systems in skills training enhances students' clinical confidence, reduces learning anxiety, provides opportunities for repetition, minimizes the risk of errors, and personalizes learning processes (8).

Recent studies have shown that digital educational technologies enhance nursing students' psychomotor skills and positively impact clinical performance (4). Digital twin systems, however, represent a more advanced stage of this transformation. This is because these systems do not merely provide simulations; they can analyze the student's performance and provide real-time feedback (9).

The Use of Digital Twins in Surgical Skills Training

Surgical skills training is a critical area of learning for nursing students. Skills such as sterile technique, surgical instrument management, operating room coordination, patient safety, and rapid decision-making require a high degree of attention and hands-on experience (3). Digital twin technologies can be used in surgical training in the following areas:

1. Realistic Surgical Simulations

Digital twin systems can model the operating room environment in real time (7,13). This allows students to experience the surgical process firsthand and practice on clinical scenarios (6). For example, in a virtual surgical environment, a student can:

- Establish a sterile field,
- Manage surgical equipment,
- Resolve emergency complication scenarios,

- Experience surgical team communication.

This provides a significant advantage, particularly in educational institutions where clinical training facilities are limited (4,13).

2. Real-Time Performance Analysis

One of the most important features of digital twin systems is their ability to perform real-time data analysis (5). The system analyzes the student's hand movements, procedure duration, error rate, and sequence of actions to generate feedback (9, 13). This allows students to track their own progress, enables instructors to provide objective evaluations, and allows skill deficiencies to be identified early on. The use of AI-supported systems in surgical skill assessment is particularly noteworthy in terms of objective performance evaluation (9,13).

3. Patient Safety and Error Management

Errors made in real clinical settings can pose serious risks to patient safety. Digital twin systems provide students with a risk-free learning environment, offering them the opportunity to make mistakes and learn from them (6,13). Students:

- Can experience surgical complication scenarios,
- Can manage critical situations,
- Can develop clinical decision-making skills.

This particularly enhances the quality of education in high-risk surgical procedures (3,13).

4. Personalized Learning Processes

Digital twin systems can provide personalized education tailored to students' learning pace and performance levels (8,13). The system identifies areas where the student is deficient and creates customized scenarios. These systems enhance learning motivation, support academic achievement, and strengthen the sense of self-efficacy (1,13).

Advantages of Digital Twin Technologies

The use of digital twins in nursing education offers significant advantages:

✓ Students can practice in a safe learning environment without the risk of harming a real patient (6,13).
✓ The same clinical scenario can be repeated an unlimited number of times (4,13).
✓ Because it ensures standardization, all students can have a similar educational experience (8,13).
✓ Data-driven performance measurement is possible (9). This is crucial for objective evaluation.
✓ Digital systems can be accessed remotely (1).
✓ Interactive learning environments increase students' motivation and engagement in the teaching-learning process (2).

Limitations of Digital Twin Technologies

Although digital twin technologies offer significant advantages, they also have certain limitations.

- Infrastructure, software, and hardware costs are quite high (12).
- Some educational institutions lack the necessary technological infrastructure (1).
- Educators' technology skills may not be sufficient (8).
- The use of real-time data raises ethical and legal issues (5,13).
- Educational processes based entirely on digital systems may weaken the human care dimension (6).

In the literature, data privacy, ethical management, and technological inequalities are highlighted as key areas of discussion (2,13).

Digital Twins in Future Nursing Education

In the future, digital twin technologies are expected to be used more widely in nursing education. In particular, digital twin systems integrated with artificial intelligence, learning analytics, augmented reality, and virtual reality technologies will enhance personalized educational processes (1,13). In the future:

- Smart simulation laboratories,
- AI-supported surgical training platforms,
- Real-time skill analysis systems,
- Personalized learning algorithms are projected to become more widespread in nursing education (6).

Additionally, digital systems developed through multidisciplinary collaborations are expected to support healthcare professionals' clinical decision-making processes (5,13).

CONCLUSION

Digital transformation is reshaping all aspects of healthcare education; in particular, it is contributing to the development of innovative learning models in surgical skills training. Digital twin technologies hold significant potential in nursing education due to their ability to provide real-time data analysis, high-fidelity simulation, personalized learning, and a safe practice environment. The use of digital twin systems in surgical skills training enhances students' technical skills, supports clinical decision-making processes, and increases awareness of patient safety. However, certain limitations -such as high costs, lack of technical infrastructure, data security issues, and instructor competencies- need to be addressed.

In the future, digital twin systems integrated with artificial intelligence, augmented reality, virtual reality, and learning analytics are expected to be used more widely in nursing education. Particularly when evaluated from the perspective of the nursing education field, it is anticipated that these technologies will become important educational tools that support not only the teaching of technical skills but also clinical decision-making, critical thinking, problem-solving, patient safety awareness, and personalized learning processes. In this regard, it is of great importance to restructure nursing education programs to align with digital transformation processes, integrate technology-based teaching approaches into curricula, and increase the number of elective courses focused on digital health and simulation-based learning. Additionally, it is necessary to enhance faculty members' awareness and competencies in digital pedagogy, AI-supported learning systems, and innovative educational technologies. Furthermore, there is a need for experimental, multi-center, and longitudinal studies evaluating the effects of digital twin technologies on student success, clinical competence, learning motivation, self-efficacy, and patient safety.

What Is Known About This Topic

- Digital transformation processes have increased the use of simulation, artificial intelligence, and virtual learning environments in health education.
- Digital twin technologies are among the innovative approaches gaining attention in surgical education by enabling real-time data analysis and high-fidelity simulation.
- The use of digital technologies in surgical skills training can positively impact student performance, clinical decision-making skills, and patient safety awareness.
- Studies on digital twin technologies in nursing education are still limited, and more evidence is needed regarding their educational effects, particularly on nursing students.

The Importance of This Study for Nursing Education and Practice

- This study examines the potential contributions of digital twin technologies to surgical skills training in nursing from an educational perspective.
- The study contributes to the development of technology-based learning processes and the strengthening of digital pedagogical approaches in nursing education.
- Digital twin systems are considered an important approach that can support standardization in clinical skills training by providing student-centered, safe, and repeatable learning environments.
- Based on the findings, it is recommended that nursing curricula be restructured to align with digital transformation processes, that faculty members' digital competencies be enhanced, and that technology-supported learning environments be widely adopted.

Author Contributions

Concept/Design: B.I.; **Data Collection and/or Processing:** B.I.; **Analysis and/or Interpretation:** B.I., Ç.A; **Literature Review:** B.I.; **Manuscript Writing:** B.I.;**Critical Review:** B.I., Ç.A.

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REFERENCES

1) Rajamäki, J. (2024). Digital twin technology training and research in health higher education: A review. Exploration of Digital Health Technologies, 2, 188–201. https://doi.org/10.37349/edht.2024.00021
2) Ning, G., Luo, H., Yin, W., & Zhang, Y. (2024). Exploration of the application and practice of digital twin technology in teaching driven by smart city construction. Sustainability, 16(23), 10312.
3) Häberle, F., & Nickel, F. (2023). Modern digital technologies in surgical training. Swiss Knife, 24, 8–2023.
4) Quek, F. F., Meldrum, S., & Hislop, J. (2025). A systematic scoping review of the current applications of digital technology in undergraduate surgical education. Cureus, 17(1), e77593.
5) Vallée, A. (2023). Digital twin for healthcare systems. Frontiers in Digital Health, 5, 1253050. https://doi.org/10.3389/fdgth.2023.1253050
6) David-Olawade, A. C., Abdi, A. M., Amusa, A. O., Daniel, R. I. A., Olasilola, O. R., & Olawuyi, O. F. (2026). Digital twin technology in surgery: A narrative review of applications, evidence, and implementation challenges. Laparoscopic, Endoscopic and Robotic Surgery.
7) Shu, H., Liang, R., Li, Z., Goodridge, A., Zhang, X., Ding, H., ... & Unberath, M. (2023). Twin-S: A digital twin for skull base surgery. International Journal of Computer Assisted Radiology and Surgery, 18(6), 1077–1084.
8) Yang, W. X., Shen, S. Y., Yang, D. C., Yu, S. Y., Yao, Z. W., & Cao, S. H. (2024). Digital twin applications in medical education: A scoping review. Education Science and Management, 2(4), 188–196.
9) Yanik, E., Intes, X., Kruger, U., Yan, P., Diller, D., Van Voorst, B., ... & De, S. (2022). Deep neural networks for the assessment of surgical skills: A systematic review. The Journal of Defense Modeling and Simulation, 19(2), 159–171.
10) Aslan, A. (2018). Sistematik derleme ve meta-analizi. Acta Medica Alanya, 2(2), 62–63. https://doi.org/10.30565/medalanya.439541
11) Pati, D., & Lorusso, L. N. (2018). How to write a systematic review of the literature. HERD: Health Environments Research & Design Journal, 11(1), 15–30. https://doi.org/10.1177/1937586717747384
12) Ünal, A. K., & Toraman, A. (2023). Evaluation of digital twin technology. SDÜ Sağlık Yönetimi Dergisi, 5(1), 1–25.
13) Khan, A. S., Fan, F., Kim, D. D., Alshareef, A., Chen, D., Kim, J., ... & Zeigler, B. (2025). A comprehensive survey on surgical digital twin (arXiv Preprint No. arXiv:2512.00019). arXiv. https://arxiv.org/abs/2512.00019

AMELİYATHANE HEMŞİRELİĞİ BECERİ EĞİTİMİNDE ARTTIRILMIŞ GERÇEKLİK VE SANAL GERÇEKLİK UYGULAMALARI

Çiğdem AKSU

Doç. Dr., Gaziantep İslam Bilim ve Teknoloji Üniversitesi, Sağlık Bilimleri Fakültesi, Hemşirelik Bölümü, Gaziantep, TÜRKİYE, ORCID: 0000-0002-7275-4843

Burçin IŞIK

Doç. Dr., Gaziantep İslam Bilim ve Teknoloji Üniversitesi, Sağlık Bilimleri Fakültesi, Hemşirelik Bölümü, Gaziantep, TÜRKİYE, | ORCID: 0000-0002-5469-017X

Özet

Ameliyathane hemşireliği, yüksek düzeyde teknik beceri, klinik karar verme ve güvenli hasta bakımını gerektiren kompleks bir meslektir. Geleneksel öğretim yöntemleri, yüksek riskli klinik ortamlarda uygulama fırsatlarının sınırlılığı nedeniyle hemşire adaylarının beceri kazanımını tam olarak sağlayamayabilmektedir. Bu bağlamda, artırılmış gerçeklik ve sanal gerçeklik teknolojileri eğitimde yenilikçi öğrenme ortamları sunarak hemşirelik öğrencilerinin beceri kazanımında potansiyel avantajlar sağlamaktadır. Literatürde sanal gerçeklik destekli ameliyathane ortamı turlarının, arttırılmış gerçeklik tabanlı vaka öğretimi ve interaktif simülasyon gibi uygulamaların hem bilgi hem de uygulama becerilerinin geliştirilmesi üzerine etkileri incelenmiştir. Bu çalışma, ameliyathane hemşireliği eğitiminde arttırılmış gerçeklik ve sanal gerçeklik uygulamalarının klinik beceriler, stres/anksiyete, özgüven ve öğrenme çıktıları üzerindeki etkilerini değerlendiren 2021–2025 tarihli bilimsel çalışmaları sentezlemeyi hedefleyen, kapsamlı bir literatür derlemesi olarak yürütülmüştür. Ayrıca konuya kuramsal çerçeve sağlamak amacıyla sık atıf alan önceki çalışmalar da incelenmiştir. PubMed, Scopus ve Web of Science veri tabanlarında hem Türkçe hem İngilizce anahtar sözcükler kullanılarak tarama yapılmıştır. Tarama sürecinde “operating room nursing skills training (ameliyathane hemşireliği beceri eğitimi)”, “augmented reality in nursing skills training (hemşirelik beceri eğitiminde arttırılmış gerçeklik)”, “virtual reality in nursing skills training (hemşirelik beceri eğitiminde sanal gerçeklik)”, “virtual and augmented reality in operating room nursing skills training (ameliyathane hemşireliği beceri eğitiminde sanal ve arttırılmış gerçeklik)” anahtar kelimeleri kullanılmıştır. Elde edilen çalışmalar içerik ve tematik analiz yaklaşımıyla değerlendirilmiş; bulgular “ameliyathane hemşireliği beceri eğitiminde sanal gerçeklik”, “ameliyathane hemşireliği beceri eğitiminde arttırılmış gerçeklik” ve “eğitim entegrasyonu” başlıkları altında sınıflandırılmıştır.

Literatürde sanal gerçeklik ve arttırılmış gerçeklik tabanlı uygulamalarının öğrencilerin ameliyathane ortamına özgü kaygı ve streslerini azaltırken özgüvenlerini artırdığı gösterilmiştir; bu da ön klinik uygulamalar öncesinde stres yükünü düşürmekte ve uygulama odaklı öğrenimi desteklemektedir. Ayrıca sanal gerçeklik ve arttırılmış gerçeklik tabanlı eğitim içerikleri, cerrahi hemşirelik pratiğine hazırlık sürecinde hem teknik hem de kavramsal becerileri geliştirme eğilimindedir. Arttırılmış gerçeklik tabanlı vaka öğretimi ve simülasyonlar, öğrencilerin teorik bilgi, klinik karar verme ve operasyon işleme becerilerini artırdığı, öğrenme ilgi ve memnuniyetini yükselttiği yönünde bulgular vermiştir. Deneysel çalışmalarda, arttırılmış gerçeklik/sanal gerçeklik destekli eğitim alan hemşire adaylarının geleneksel yöntemlere kıyasla klinik beceri kazanımında daha iyi performans gösterdiği ve öğrenme tatmininin daha yüksek olduğu bildirilmiştir. Bu teknolojiler, geleneksel öğretim yöntemlerini tamamlayıcı nitelikte olup özellikle riskli ve karmaşık klinik uygulamaların pratiğinde öğrenme fırsatlarını genişletmektedir. Gelecekte, daha fazla kontrol gruplu ve randomize çalışmaların Arttırılmış gerçeklik/sanal gerçekliğin uzun dönem etkinliklerini ve hasta bakım çıktıları üzerindeki etkilerini incelemesi önerilmektedir.

Anahtar Kelimeler: Ameliyathane hemşireliği, hemşirelik beceri eğitimi, arttırılmış gerçeklik, sanal gerçeklik

AUGMENTED REALITY AND VIRTUAL REALITY APPLICATIONS IN OPERATING ROOM NURSING SKILLS TRAINING

Abstract

Operating room nursing is a complex profession that requires a high level of technical skill, clinical decision-making, and safe patient care. Traditional teaching methods may not fully facilitate skill acquisition among nursing students due to limited opportunities for hands-on practice in high-risk clinical settings. In this context, augmented reality and virtual reality technologies offer innovative learning environments in education, providing potential advantages for nursing students' skill acquisition. The literature has examined the effects of virtual reality-supported operating room environment tours, augmented reality-based case-based teaching, and interactive simulations on the development of both knowledge and practical skills. This study was conducted as a comprehensive literature review aimed at synthesizing scientific studies from 2021 to 2025 that evaluate the effects of augmented reality and virtual reality applications in operating room nursing education on clinical skills, stress/anxiety, self-confidence, and learning outcomes. Additionally, frequently cited previous studies were reviewed to provide a theoretical framework for the topic. A search was conducted in the PubMed, Scopus, and Web of Science databases using both Turkish and English keywords. During the search process, the terms "operating room nursing skills training," "augmented reality in nursing skills training,"

The literature has shown that virtual reality and augmented reality-based applications reduce students' anxiety and stress specific to the operating room environment while boosting their self-confidence; this helps lower stress levels prior to pre-clinical practice and supports practice-oriented learning. Additionally, virtual reality and augmented reality-based educational content tends to develop both technical and conceptual skills during the preparation process for surgical nursing practice. Findings indicate that augmented reality-based case-based instruction and simulations enhance students' theoretical knowledge, clinical decision-making, and surgical procedure skills, while also increasing learning interest and satisfaction. Experimental studies have reported that nursing students who receive augmented reality/virtual reality-supported education demonstrate better performance in clinical skill acquisition and higher learning satisfaction compared to those using traditional methods. These technologies serve as complementary tools to traditional teaching methods, particularly expanding learning opportunities in the practice of high-risk and complex clinical procedures. In the future, it is recommended that more controlled and randomized studies examine the long-term effectiveness of augmented reality/virtual reality and its impact on patient care outcomes.

Keywords: Operating room nursing, nursing skills training, augmented reality, virtual reality

Introduction

Today, there is a need to develop and utilize new tools in the education of healthcare professionals in order to avoid harming patients, minimize errors, prevent ethical violations, adapt to evolving technology in the healthcare field, meet patients' rising expectations, and provide high quality care. Consequently, virtual reality and augmented reality systems which allow for the unlimited application of clinical scenarios in a risk free environment, thereby reducing student anxiety and boosting self confidence, enhancing clinical decision making skills, and facilitating effective learning through feedback provided after practice are emerging as a valuable asset in nursing education.[1] Nursing education is a discipline that requires the integration and alignment of clinical and theoretical instruction due to its practical nature.[2] For this reason, nursing educators must continuously update themselves to utilize innovative teaching and learning methods at every stage of the educational process to support students' cognitive, affective, and psychomotor development. Research indicates that technology based and innovative practical teaching models improve learning outcomes in this field.[3,4]

With the advancement of technology, augmented reality and virtual reality have become essential teaching methods in nursing education.[5] Virtual reality has proven benefits in enhancing knowledge acquisition in nursing education and improving the quality and safety of clinical practice by complementing other simulation strategies.[5] It is noted that the realism provided by virtual and

augmented reality strengthens the sense of presence by allowing nursing students to experience the entire surgical process in a virtual environment.[6,7] Virtual reality enables interaction with sensory stimuli such as sound and visuals in a computer generated three dimensional environment. Augmented reality, on the other hand, supports learning by overlaying computer generated additional information, three dimensional objects, or text onto the real world.[8] Just as in many specialized fields where nursing students receive training, education using virtual reality and augmented reality can be provided in the operating room to enhance the quality of education and prevent errors.[9]

The complexity of surgical techniques used in the operating room and the limitations of the operating room environment in training students have led to the use of new training methods, such as virtual reality and augmented reality, to improve performance and reduce errors.[10] Virtual reality and augmented reality applications enable students to develop their clinical skills in a safe environment during operating room nursing education.[11] Thanks to this method, students can learn critical skills such as team communication, time management, and responding to crisis scenarios without taking risks by experiencing real operating room conditions firsthand. Additionally, virtual reality reduces students' fear of making mistakes, thereby increasing their active participation in the learning process and strengthening their professional competence during the pre-clinical phase.[12] This study was conducted to determine the effects of augmented reality and virtual reality applications in operating room nursing skills training.

Background

This study was conducted as a comprehensive literature review covering studies published between 2021 and 2025. Additionally, frequently cited previous studies were examined to provide a theoretical framework for the topic. A search was conducted in the PubMed, Scopus, and Web of Science databases using both Turkish and English keywords. During the search process, the following terms were used: "operating room nursing skills training," "augmented reality in nursing skills training," "virtual reality in nursing skills training," and "virtual and augmented reality in operating room nursing skills training" were used. The identified studies were evaluated using a content and thematic analysis approach; the findings were classified under the headings "virtual reality in operating room nursing skills training," "augmented reality in operating room nursing skills training," and "training integration." Following the literature review, six studies related to the topic were identified.

Studies on augmented reality and virtual reality applications in operating room nursing skills training

The results of a study by Wunder et al.[13], an experimental study conducted with nurse anesthesia students using a mixed reality method in a simulated operating room fire scenario, revealed an increase in the students' learning levels regarding the subject.

In a study conducted by Sen and colleagues[11] to determine the impact of mobile virtual reality on operating room nursing education, it was concluded that participants performed better than the control group in most surgical aseptic skills following the VR-based application, and that control group participants reported anxiety during traditional education.

Similarly, in an experimental study by Kim[14] on the development and usability assessment of virtual reality and haptic technology-based educational content for pre and post operative nursing education, it was found that nursing students experienced a high sense of presence in the operating room, demonstrated greater success in practical applications, and reported higher satisfaction with the education compared to students who did not use virtual reality.

In a study by Zabaleta et al.[15] evaluating satisfaction and outcomes in nurse education using a virtual reality simulation of an operating room, it was concluded that training delivered via virtual reality improved students' ability to perform complex procedures, encouraged adaptability and critical thinking, and increased satisfaction.

In a study by Güngör and colleagues[16] on the design, implementation, and examination of student perceptions regarding a training program for nursing students on surgical hand washing, donning surgical caps and masks, putting on gowns, and wearing gloves, the researchers concluded that students felt as if they were actually in the operating room during the VR-based practice.

In a study by Parlak and colleagues[17] examining the effect of a virtual reality based operating room tour on nursing students' anxiety, stress, and self confidence levels in the operating room environment, it was found that the virtual reality based operating room tour, conducted prior to clinical practice, reduced students' stress and anxiety related to the environment and increased their self confidence levels.

Conclusion:

It was concluded that VR and AR based training in operating room nursing skills enhances students' learning levels, facilitates improvements in training related skills, creates a strong sense of being in an operating room among students, increases satisfaction with the training, encourages adaptability and critical thinking, and boosts self confidence by reducing anxiety and stress in students. Based on the literature review, it can be stated that VR and AR based educational content tends to develop both technical and conceptual skills during the preparation process for surgical nursing practice; AR based case based instruction and simulations enhance students' theoretical knowledge, clinical decision making, and surgical procedure skills, and increase learning interest and satisfaction.

Developing nursing students' skills in sterilization, equipment use, and patient safety through a realistic simulation of the operating room environment using AR/VR; emergency scenarios; assessing nurses' crisis management skills through simulations of critical situations such as cardiac arrest, bleeding control, or anaphylaxis in a VR environment; and improving team communication and coordination; Developing role distribution and communication skills within the surgical team using AR-supported applications; learning efficiency comparisons: comparing the effects of traditional education methods versus AR/VR supported education methods on knowledge retention, skill acquisition, and self-confidence; user experience and acceptance levels: Examining the challenges nursing students face when using AR/VR technologies, their motivation levels, and their adaptation processes to the technology, as well as exploring distance learning opportunities; conducting studies to determine how students in different cities can simultaneously participate in a shared operating room simulation using VR based platforms and assess the contribution of this to educational equity is expected to contribute to the literature and technological teaching methods. Such studies could demonstrate the effectiveness of technology integration in nursing education, thereby providing scientific contributions to curriculum development and clinical practice processes.

Author Contributions

Concept/Design: Ç.A.; **Data Collection and/or Processing:** Ç.A.; **Analysis and/or Interpretation:** Ç.A., B.I; **Literature Review:** Ç.A.; **Manuscript Writing:** Ç.A.;**Critical Review:** Ç.A., B.I.

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References

1.Gündoğdu H, Dikmen Y. Simulation in nursing education: virtual reality and haptic systems. *J hum rhythm* – December. 2017;3(4):172-176

2.Ozcelik R, Ayhan H. The effect of standardized patient use in teaching preoperative care practices on students' knowledge, skills and anxiety in clinical practice. *Clin. Simul. Nurs.* 2021;61:54–64. https://doi.org/10.1016/j.ecns.2021.08.020

3.Fiedler R, Giddens J, North S. Faculty experience of a technological innovation in nursing education. *Nursing Education Perspectives*. 2014;35(6):387–391. https://doi.org/10.5480/13-1188

4.Karkada S, Radhakrishnan J, Natarajan J, Matua G, Kaddoura M. Knowledge and competency of novice nursing students in nasogastric tube feeding: Is simulation better than case scenario?. *Oman Medical Journal.* 2019;34(6):528–533. https://doi.org/10.5001/omj.2019.96

5.Ergin Doğan S, Aslan H. Current Teaching Methods and Techniques Used in Nursing Education. *BÜSAD*. 2024;5(1):224-235. https://doi.org/10.58605/bingolsaglik.1448021

6.Lai YH, Chang MY, Weng MR, Chiu PL, Wu TY, Wang SC. Effectiveness of virtual reality in training operating room nurses for robotic arm surgery. *Clinical Simulation in Nursing*. 2025;103:1-10. https://doi.org/10.1016/j.ecns.2025.101728

7.Hwang GJ, Chang CC, Chien SY. A motivational modelbased virtual reality approach to prompting learners' sense of presence, learning achievements, and higher-order thinking in professional safety training. *British Journal of Educational Technology*. 2022;53(5):1343-1360. https://doi.org/10.1111/bjet.13196.

8.Scavarelli A, Arya A, Teather RJ. Virtual reality and augmented reality in social learning spaces: A literature review. Virtual Reality. 2020;25:257–277. https://doi.org/10.1007/s10055-020-00444-8

9.Erkan HN, Zeyrek Kurtoğlu Ş, Eyi S, Kersu Ö. The Use of Virtual Reality and Simulation in Surgical Nursing Education: A Traditional Review. *YIU Saglik Bil Derg.* 2026;6:1-1. https://izlik.org/JA82FE37GD

10.Sargolzaei F, Ghadami A, Omid A, Azarmehr T, Shahnazari F. The effect of training using the combination of virtual reality and augmented reality in coronary artery surgery on the learning rate of undergraduate students in the operating room. *Horizon of Medical Education Development.* 2023;14(4):43-52.

11.Sen S, Usta E, Bozdemir H. The effect of mobile virtual reality on operating room nursing education. Teaching and Learning in Nursing. 2022;17:199-202. https://doi.org/10.1016/j.teln.2022.01.008

12.Emekli, Emre. Virtual Reality Applications Used in Medical Undergraduate Education. figshare. Thesis. 2023. https://doi.org/10.6084/m9.figshare.23895924.v2

13.Wunder L, Gomez NA, Gonzalez JE, Mitzova-Vladinov G, Cacchione M, Mato J. Fire in the operating room: use of mixed reality simulation with nurse anesthesia students. *Informatics* 2020;7:40. https://doi.org/10.3390/informatics7040040

14.Kim YH. Development and usability assessment of virtual reality- and haptic technology-based educational content for perioperative nursing education. *Healthcare*. 2024;12; 1-14. https://doi.org/10.3390/healthcare12191947

15.Zabaleta J, Blasco A, Esnal T, Aguinagalde B, Lo´pez IJ, Fernandez-Monge A, Lizarbe JAL, Ba´ ez J, Aldazabal J. Clinical trial on nurse training through virtual reality simulation of an operating room: assessing satisfaction and outcomes. *Cırugı´A Espan˜ Ola.* 2024;102(9):469-476. http://dx.doi.org/10.1016/j.cireng.2024.04.012

16.Güngör S, Yava A and Koyuncu A. Designing and implementing a training program on surgical hand scrubbing, wearing surgical cap and surgical mask, gowning, and gloving using HMD-based virtual

reality technologies for nursing students: an exploration of student perceptions. *Front. Med.* 2024;11:1-10. https://doi.org/10.3389/fmed.2024.1364465

17.Parlak EA, Ayhan H, Erer İ, Iyigün E. The effect of virtual reality-based operating room tour on nursing students' anxiety, stress and self-confidence levels in an operating room setting: A randomized controlled trial. *Nurse Education in Practice.* 2025;85:2-8. https://doi.org/10.1016/j.nepr.2025.104380

BİR EĞİTİM VE ARAŞTIRMA HASTANESİNDE SAĞLIK HİZMETİ İLİŞKİLİ ENFEKSİYON SIKLIĞI: TEK MERKEZ DENEYİMİ

FREQUENCY OF HEALTHCARE-ASSOCIATED INFECTIONS IN A TRAINING AND RESEARCH HOSPITAL: A SINGLE-CENTER EXPERIENCE

Musa ŞENYÜZ

Siirt Eğitim ve Araştırma Hastanesi Eğitim Birimi, Siirt, Türkiye, ORCID: 0009-0002-4853-3060

Prof. Dr. Ali CEYLAN

Balıkesir Üniversitesi Tıp Fakültesi Halk Sağlığı Anabilim Dalı-Balıkesir-Türkiye, ORCID: 0000-0002-3446-7640

Amaç: Sağlık hizmeti ilişkili enfeksiyonlar (SHİE), hastane mortalite ve morbiditesini artıran, sağlık hizmetlerinin kalitesini ve güvenliğini olumsuz etkileyen önemli halk sağlığı sorunlarıdır. Bu çalışmada, bir eğitim ve araştırma hastanesinde 2016–2024 yılları arasında izlenen SHİE sıklığının ve dağılımının değerlendirilmesi amaçlanmıştır.

Materyal ve Yöntem: Çalışma izleme-değerlendirme tasarımında planlanmıştır. 01.01.2016–31.12.2024 tarihleri arasında yataklı servisler ve yoğun bakım ünitelerinde takip edilen hastalara ait SHİE verileri geriye dönük olarak incelenmiştir. Enfeksiyon tanıları, Centers for Disease Control and Prevention kriterleri ile Ulusal Sağlık Hizmeti İlişkili Enfeksiyonlar Sürveyans Ağı (USHİESA) tanımlarına göre yapılmıştır. Genel insidans hızı, insidans dansitesi (1000 hasta günü başına) ve invaziv araç ilişkili enfeksiyon hızları hesaplanmıştır.

Bulgular: Çalışma döneminde toplam 373 SHİE olgusu kaydedilmiştir. Genel SHİE insidans hızı 0,12; insidans dansitesi ise 0,34/1000 hasta günü olarak bulunmuştur. Araştırma dönemi içerisinde yoğun bakım ünitesinde toplam 199 sağlık hizmetiyle ilişkili enfeksiyon olgusu saptanmıştır. Bu süreçte ünitenin genel enfeksiyon oranı 1,88 olarak hesaplanmış, enfeksiyon dansitesi ise 3,15 olarak belirlenmiştir. En sık görülen enfeksiyon türü %39,2 ile kan dolaşım enfeksiyonu olup, bunu %31,2 ile cerrahi alan enfeksiyonu izlemiştir. İnvaziv araç ilişkili enfeksiyon oranı %32,4 olarak saptanmıştır. Araç ilişkili enfeksiyon hızları; santral kateter ilişkili kan dolaşım enfeksiyonu (SKİ-KDE) için 1,36; kateter ilişkili üriner sistem enfeksiyonu (Kİ-ÜSE) için 0,46 ve ventilatör ilişkili pnömoni (VİP) için 0,82 olarak hesaplanmıştır. SHİE gelişen hastalarda mortalite oranı %42,09 olarak belirlenmiştir.

Sonuç: Çalışma hastanesinde SHİE oranlarının ulusal sürveyans verileriyle benzer eğilim gösterdiği saptanmıştır. Özellikle invaziv araç ilişkili enfeksiyonların azaltılmasına yönelik demet (bundle) uygulamalarının güçlendirilmesi, aktif sürveyansın sürdürülmesi ve hedefe yönelik enfeksiyon kontrol stratejilerinin uygulanması gerekmektedir.

Anahtar Kelimeler: Sağlık hizmeti ilişkili enfeksiyon, insidans, yoğun bakım, invaziv araç, sürveyans

Objective: Healthcare-associated infections (HAIs) are significant public health problems that increase hospital morbidity and mortality and adversely affect the quality and safety of healthcare services. This study aimed to evaluate the frequency and distribution of HAIs observed between 2016 and 2024 in a tertiary education and research hospital.

Materials and Methods: This study was designed as a monitoring and evaluation study. HAI data of patients hospitalized in inpatient wards and intensive care units between January 1, 2016 and December 31, 2024 were retrospectively reviewed. Infections were defined according to the criteria of the Centers for Disease Control and Prevention and the Ulusal Sağlık Hizmeti İlişkili Enfeksiyonlar Sürveyans Ağı (National Healthcare-Associated Infections Surveillance Network). Overall incidence rate, incidence density (per 1,000 patient-days), and device-associated infection rates were calculated.

Results: A total of 373 HAIs were recorded during the study period. The overall HAI incidence rate was 0.12, and the incidence density was 0.34 per 1,000 patient-days. During the study period, a total of 199 healthcare-associated infection cases were identified in the intensive care unit. In this period, the overall

infection rate was calculated as 1.88, and the infection density was determined to be 3.15. The most common infection type was bloodstream infection (39.2%), followed by surgical site infection (31.2 %). The rate of device-associated infections was 32.4%. Device-associated infection rates were calculated as 1.36 for central line-associated bloodstream infection (CLABSI), 0.46 for catheter-associated urinary tract infection (CAUTI), and 0.82 for ventilator-associated pneumonia (VAP). The mortality rate among patients who developed HAI was 42.09%.

Conclusion: HAI rates in the study hospital showed a similar trend to national surveillance data. Strengthening bundle interventions for the prevention of device-associated infections, maintaining active surveillance, and implementing targeted infection control strategies are essential to reduce HAI rates.

Keywords: Healthcare-associated infection, incidence, intensive care unit, invasive device, surveillance

GİRİŞ

Hastane enfeksiyonları (HE), en yalın tanımıyla hastanede yatış sürecinde ortaya çıkan enfeksiyonlardır. Bu durum, kökeni Latince *nosos* (hastalık) ve *komeion/komion* (bakım, tedavi yeri) sözcüklerine dayanan ve "hastane kaynaklı enfeksiyon" anlamına gelen "nozokomiyal enfeksiyon" terimiyle de ifade edilmektedir.

Son yıllarda ise bu kavramın kapsamı genişletilmiş ve "sağlık hizmeti ilişkili enfeksiyon" (SHİE) tanımı kullanılmaya başlanmıştır. Bu yeni yaklaşım, enfeksiyonların yalnızca hastane ortamıyla sınırlı olmadığını; uzun süreli bakım kuruluşları, ağız ve diş sağlığı merkezleri, aile sağlığı merkezleri, ayaktan tanı ve tedavi birimleri, diyaliz merkezleri ve evde bakım hizmetleri gibi sağlık hizmeti sunulan tüm alanlarda gelişebileceğini vurgulamaktadır.(1, 2).

Sağlık hizmeti ilişkili enfeksiyonlar (SHİE), günümüz sağlık sistemlerinin karşı karşıya olduğu en önemli sorunlardan biri olarak değerlendirilmektedir. Bu enfeksiyonlar, hastaların mevcut klinik durumunu ağırlaştırabilmekte, tedavi ve iyileşme sürecini uzatabilmekte ve bazı durumlarda ölümle sonuçlanabilmektedir. Ortaya çıkan bu tablo yalnızca bireysel sağlık sonuçlarını değil, aynı zamanda sağlık hizmetlerinin niteliğini ve hastaların sisteme duyduğu güveni de olumsuz yönde etkilemektedir (3).

Sağlık hizmeti ilişkili enfeksiyonlar, yaşam kalitesini olumsuz etkilemesi, mortaliteyi artırması, antibiyotik direncinin gelişimine katkıda bulunması ve sağlık sistemine ek mali yük getirmesi gibi çok boyutlu etkileri nedeniyle önemli bir halk sağlığı sorunu oluşturmaktadır. Ayrıca, hukuki boyutları ve toplumun sağlık kurumlarına olan güveni zedeleyebilme potansiyeli, sorunun kapsamını daha da genişletmektedir.

Amerika Birleşik Devletleri'nde yayımlanan *Transforming Health Care Quality* başlıklı raporda da sağlık hizmeti ilişkili enfeksiyonların önlenmesi, ulusal düzeyde öncelik verilmesi gereken temel kalite hedeflerinden biri olarak belirtilmiştir. Tüm bu nedenlerle hastane enfeksiyonları, 21. yüzyılın başından itibaren tıp dünyasının öncelikli çözüm alanlarından biri olmayı sürdürmektedir. (4-5)

Dünya Sağlık Örgütü verilerine göre, hastane enfeksiyonlarının görülme oranı ülkeler arasında farklılık göstermektedir. Örneğin Amerika Birleşik Devletleri'nde bu oran %3,2 olarak tahmin edilirken, Akdeniz Bölgesi'nde %12,5 ve Afrika Bölgesi'nde %27 seviyelerinde bildirilmektedir. Avrupa'da ise Centers for Disease Control and Prevention Europe verileri, hastane enfeksiyon hızının %7,1 civarında olduğunu ve her yıl yaklaşık 4 milyon kişinin bu enfeksiyonlardan etkilendiğini göstermektedir. Ayrıca Avrupa'da herhangi bir gün gözlemlendiğinde yaklaşık 93.000 hastada en az bir hastane enfeksiyonu saptandığı bildirilmektedir. Yatan her 100 hastadan gelişmiş ülkelerde 7'si, gelişmekte olan ülkelerde ise 10'u hastane enfeksiyonu geliştirmektedir. Türkiye'de ise Sayıştay raporuna göre hastane enfeksiyonu ile ilgili verilere ulaşmak zor olmakla birlikte, oranların %5 ile %15 arasında değiştiği bildirilmektedir. Hastane enfeksiyonlarının görülme sıklığı, ülkelere, hastanelere, birimlere ve hastaların demografik ve klinik özelliklerine göre farklılık göstermektedir (3-6).

Bu çalışma, Türkiye'de bir eğitim ve araştırma hastanesinde sağlık hizmeti ilişkili enfeksiyonların sıklığını belirlemeyi amaçlamaktadır.

Sağlık Hizmeti İlişkili Enfeksiyon Türleri

Sağlık hizmeti sunulan ortamlarda en sık rastlanan enfeksiyonlar arasında cerrahi alana bağlı enfeksiyonlar, kan dolaşımı kaynaklı enfeksiyonlar, üriner sistem enfeksiyonları ve ventilatör ilişkili pnömoniler yer almaktadır. Bu enfeksiyonların türleri, hizmet verilen hastaların klinik özellikleri ve uygulanan tıbbi müdahalelere bağlı olarak değişkenlik göstermektedir.

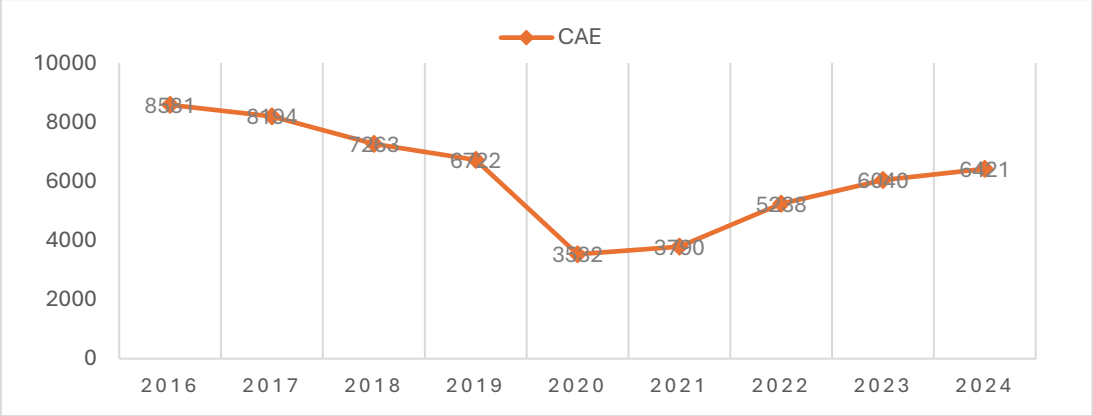
Cerrahi Alan Enfeksiyonları

Cerrahi alan enfeksiyonu (CAE), bir ameliyatı takiben ilk 30 gün içinde insizyon bölgesinde veya cerrahi işlem sırasında müdahale edilen organ ve dokularda ortaya çıkan enfeksiyonlar olarak tanımlanır. Ayrıca, hastaya kalıcı olarak yerleştirilen implant veya protezler sonrasında, ameliyattan sonraki 90 gün içinde gelişen enfeksiyonlar da CAE kapsamına alınmaktadır. Bu enfeksiyonlar, hasta ameliyat edilmemiş olsaydı ortaya çıkmayacak olması nedeniyle doğrudan sağlık hizmeti ve yapılan cerrahi işlemle ilişkilidir (7).

Cerrahi alan enfeksiyonlarının belirtileri ve şiddeti enfeksiyonun türüne bağlı olarak değişiklik gösterebilir. Kızarıklık, şişlik, ağrı, hassasiyet ve kesi yerinden akıntı veya irin çıkışı en sık gözlenen klinik bulgular arasında yer alır.

Hastane enfeksiyonları içinde önemli bir paya sahip olan CAE'ler, sağlık sistemleri açısından ciddi bir sorun teşkil etmektedir. Bu enfeksiyonlar, hastanın yaşam kalitesini düşürmekte, tedavi maliyetlerini artırmakta ve hastanede yatış süresini uzatarak bireyin sosyal ve psikolojik açıdan olumsuz etkilenmesine yol açmaktadır. Düşük ve orta gelirli ülkelerde cerrahi işlem geçiren hastaların yaklaşık üçte birinde cerrahi alan enfeksiyonu (CAE) geliştiği bildirilmektedir. Amerika Birleşik Devletleri'nde 2006–2008 yılları arasında genel CAE oranı %1,9 olarak kaydedilmiştir; bu da her 100 ameliyattan yaklaşık ikisinde enfeksiyon görüldüğü anlamına gelmektedir (4).

Sağlık Bakanlığı yıllık istatistik raporlarına göre CAE şekilde gösterilmiştir (20-22).



Şekil 1. Sağlık Bakanlığı yıllık istatistik raporlarına göre CAE sıklığı

Ulusal Sağlık Hizmeti İlişkili Enfeksiyonlar Sürveyans Ağı Özet Raporu verilerine göre, 2024 yılında bildirilen 60.370 SHİE'nin 6.421'i CAE olarak raporlanmıştır; SHİE'ler arasında CAE'ler dördüncü sırada yer almaktadır. Bu durum, ABD verileri ile karşılaştırıldığında, sürveyans kapsamındaki ameliyat türlerinin dağılımı ile taburculuk öncesi ve sonrası sürveyans duyarlılığındaki farklılıklar göz önünde bulundurularak değerlendirilmelidir. Buna rağmen, ülkemizde CAE'lerin de önemli bir sağlık yükü oluşturduğu açıktır.

Cerrahi alan enfeksiyonlarının (CAE) ortaya çıkmasına yönelik risk faktörleri, ameliyat öncesi, ameliyat sırasında ve ameliyat sonrasında farklı dönemlerde etkili olabilmektedir. Hastaya bağlı riskler arasında obezite, bağışıklık sistemi baskılanması, diyabet, sigara kullanımı, ileri yaş ve beslenme durumu yer alır. Bu faktörler sağlık hizmeti kapsamında yönetilebilir olduğundan, enfeksiyon gelişimi açısından sağlık hizmeti ile ilişkili olarak değerlendirilir. Ancak CAE oluşumunda en temel ve kaçınılmaz risk faktörü, cerrahi işlemin kendisidir; başka bir deyişle, ameliyat yapılmadığı sürece CAE gelişmez (7).

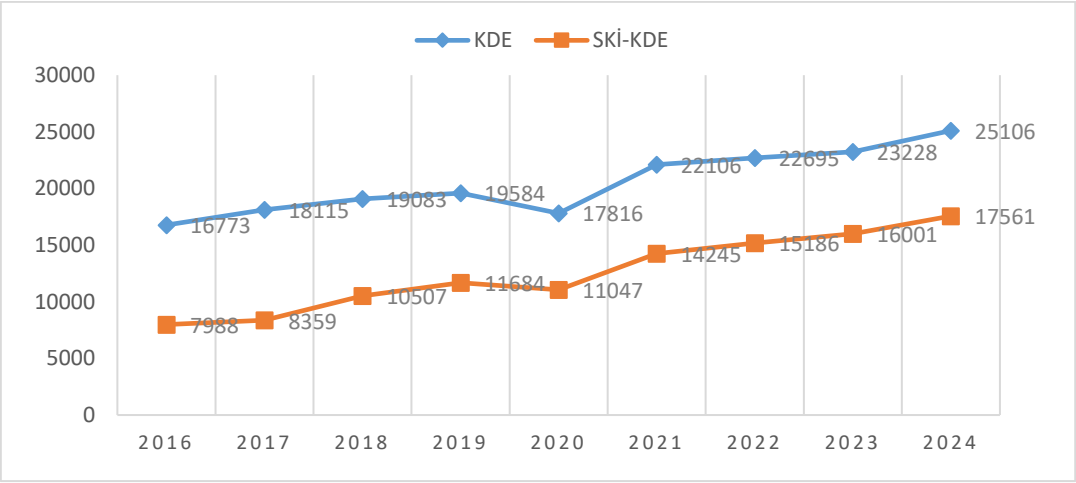
Cerrahi alan enfeksiyonlarının (CAE) önlenmesinde enfeksiyon kontrol önlemlerinin etkin bir şekilde uygulanması kritik öneme sahiptir. Bu önlemler, ameliyat öncesi (preoperatif), ameliyat sırasında (intraoperatif) ve ameliyat sonrası (postoperatif) dönemleri kapsayan çeşitli adımları içerir. Preoperatif dönemde, cerrahi alanın antiseptik solüsyonlarla temizlenmesi, cilt hazırlığı, bölgedeki kıl ve saçların uygun şekilde uzaklaştırılması ve hastanın genel sağlık durumunun optimize edilmesi gereklidir. Ayrıca, profilaktik antibiyotik uygulamaları da sık kullanılan stratejiler arasında yer almakta ve cerrahi alanın kontaminasyon riskini azaltarak enfeksiyon oluşumunu önlemeye yardımcı olmaktadır. İntraoperatif dönemde**,** cerrahi tekniklerin doğru uygulanması, cerrahi el hijyeni, steril cerrahi giysiler ve malzemelerin kullanımı, asepsi ve antisepsi uygulamaları, ameliyathane ortamının temizliği ve dezenfeksiyonu, havalandırma ve nem kontrolü ile ameliyathane trafiğinin düzenlenmesi, CAE'lerin önlenmesinde önemli rol oynamaktadır. Postoperatif dönemde**,** cerrahi alanın düzenli bakımı ve yara iyileşmesinin izlenmesi büyük önem taşır. Yara bakımında bölgenin temiz ve kuru tutulması, enfeksiyon bulgularının erken tespit edilmesi ve gerekirse antibiyotik tedavisinin uygulanması gerekmektedir. Bunun yanı sıra, sağlık personeli ile hasta ve yakınlarının eğitimi, sürveyans çalışmaları ve cerrahi alanın düzenli kontrolü, enfeksiyon riskinin azaltılmasında etkili olmaktadır. CAE'ların izlenmesi ve raporlanması ise, bu enfeksiyonların yaygınlığını azaltmaya yönelik stratejilerin geliştirilmesine katkı sağlar (8-10

Kan Dolaşım Enfeksiyonları

Dünya genelinde her gün milyonlarca hastaya tanı ve tedavi amacıyla damar içi kateterler (DİK) uygulanmaktadır. Bu kateterler, hastanenin neredeyse tüm birimlerinde yaygın şekilde kullanılmakta olup, yatan hastalarda en sık gerçekleştirilen klinik girişimlerden biri olarak öne çıkmaktadır. Ancak, DİK'lerin uzun süreli kullanımı kan dolaşımı enfeksiyonlarının ortaya çıkmasına yol açabilmektedir. Bu enfeksiyonlar, sağlık hizmeti ilişkili enfeksiyonlar arasında en sık rastlanan türlerden biridir (11).

Damar içi kateterler (DİK), sıvı ve elektrolit dengesinin sağlanması, ilaç uygulamaları, parenteral beslenme, hemodiyaliz, kan ve kan ürünlerinin transfüzyonu, hemodinamik izlemler ile kan örneklerinin alınması gibi birçok farklı amaçla kullanılmaktadır. Bu geniş kullanım alanı, DİK'lerin doğru ve özenli şekilde uygulandığında yaşam kurtarıcı olmasını sağlarken, hatalı uygulamalar veya yetersiz bakım durumunda çeşitli komplikasyonlara yol açabilmektedir. Kateter kullanımına bağlı olumsuz etkiler arasında lokal sorunlar (selülit, apse, deri enfeksiyonları, tromboflebit) ve sistemik sorunlar (bakteriyemi, sepsis, endokardit) görülebilmektedir. Kan dolaşımı enfeksiyonlarının klinik belirtileri genellikle ateş, titreme ve hipotansiyon gibi semptomlarla kendini göstermektedir (11-12).

Sağlık Bakanlığı verileri, bu enfeksiyonların yıllık dağılımını Şekil 3'te sunmaktadır (13).



Şekil 3. Sağlık Bakanlığı yıllık istatistik raporlarına göre KDE sıklığı

Kan dolaşımı enfeksiyonlarının büyük çoğunluğu, yaklaşık %85'i, santral venöz kateter kullanımına bağlı olarak gelişmektedir. Bu enfeksiyonlar, mortaliteyi %12–%35 oranında artırabilmekte, hastanede kalış süresini ortalama 7 gün uzatabilmekte ve her bir enfeksiyonun maliyetinin 3.700 ila 29.000 dolar

arasında olduğu tahmin edilmektedir (24). Centers for Disease Control and Prevention tarafından yayımlanan 2015–2017 dönemi sürveyans raporuna göre, santral kateter ilişkili kan dolaşımı enfeksiyonları (SKİ-KDE) sıklık açısından üçüncü sırada yer almaktadır. Türkiye'de ise Türkiye Ulusal Sağlık Hizmeti İlişkili Enfeksiyonlar Sürveyans Ağı verileri, SKİ-KDE'lerin 17.561 vaka ile en sık görülen sağlık hizmeti ilişkili enfeksiyon türü olduğunu ortaya koymaktadır (13-14).

Santral kateter uygulaması invazif bir işlem olup, hem kısa hem de uzun dönemde ciddi komplikasyonlara yol açabilir. SKİ-KDE, damar içine yerleştirilen kateterler nedeniyle gelişen ve kan dolaşımını etkileyen enfeksiyonları tanımlar. Enfeksiyona neden olan mikroorganizmalar, kateterin dış yüzeyinde veya lümen boyunca ilerleyerek ve vücudun başka bir odak noktasından kana karıştıktan sonra katetere yerleşir. Bu mikroorganizmaların kaynağı; hem sağlık personelinin hem de hastanın cilt florası, infüzyon sıvıları veya hastanın vücudunda mevcut başka enfeksiyon odakları olabilir.

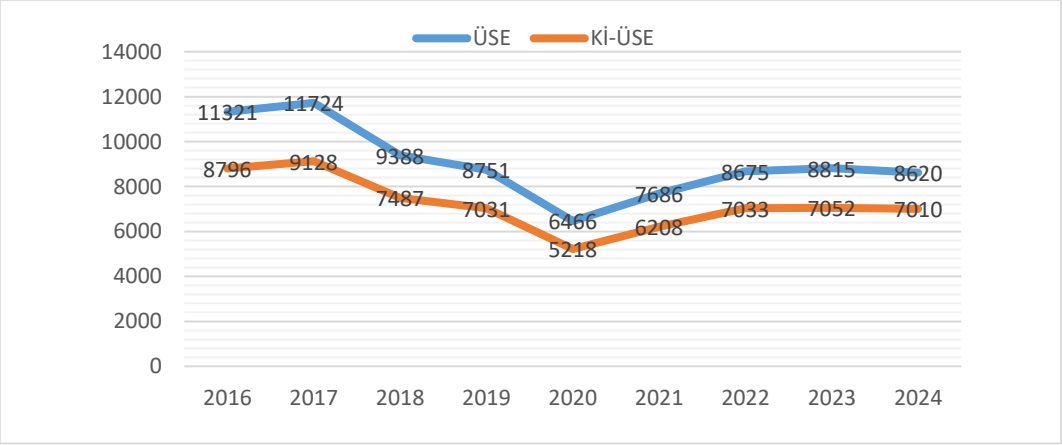
Santral kateter ilişkili kan dolaşımı enfeksiyonlarının (SKİ-KDE) ortaya çıkmasında bir dizi risk faktörü etkili olmaktadır. Bu faktörler, hastaya ait özellikler, kateterle ilgili etkenler ve çevresel koşullar olmak üzere üç ana grupta incelenebilir. Hastaya ait riskler arasında yaş, bağışıklık sisteminin durumu, diyabet, obezite ve diğer kronik hastalıklar öne çıkar. Kateterle ilgili riskler ise kateterin türü, uygulama süresi ve bakım uygulamalarının doğruluğu ile ilişkilidir. Çevresel riskler ise hastane ortamındaki sterilizasyon uygulamaları, enfeksiyon kontrol önlemleri ve sağlık personelinin el hijyeni uygulamalarını kapsamaktadır.

Santral kateter ilişkili kan dolaşımı enfeksiyonlarının (SKİ-KDE) önlenmesinde enfeksiyon kontrol önlemlerinin uygulanması büyük önem taşır. Bu kapsamda, invaziv cihazlara bağlı enfeksiyonların önlenmesi için "önlem paketi" (bundle) yaklaşımı etkili bir strateji olarak öne çıkmaktadır. Önlem paketleri, etkinliği kanıtlanmış 3–6 uygulamanın eş zamanlı olarak hayata geçirilmesini içerir. Bu yaklaşım, tek başına uygulanan önlemlerin etkisi ile karşılaştırıldığında, bir arada uygulandığında toplam etkisinin daha yüksek olduğunu göstermektedir. Bu yöntem, enfeksiyon kontrol çalışmalarına yeni bir perspektif kazandırmış ve "demet uygulamaları" kavramının benimsenmesini sağlamıştır. Demet yaklaşımı, belirli hedeflere ulaşmak amacıyla hastane enfeksiyonlarını kontrol etmek ve önlemek için birden fazla uygulamanın birlikte yürütülmesini öngörür (15).

Üriner Sistem Enfeksiyonları

Üriner sistem enfeksiyonları (ÜSE), mesane, üretra, üreterler ve böbrekleri kapsayan üriner sistem organlarında patojen mikroorganizmaların çoğalması sonucu ortaya çıkar. Mikroorganizmalar genellikle periüretral bölgede kolonize olur ve kateter yerleştirilmesi sırasında kateter lümeni veya kateter ile mukozal yüzey arasından üriner sisteme geçerek enfeksiyona yol açar.

ÜSE, sağlık hizmeti ilişkili enfeksiyonlar (SHİE) arasında en sık görülen türlerden biridir. Bu enfeksiyonlar, hastanın konforunu bozmakta, hastanede kalış süresini uzatmakta ve gereksiz antibiyotik kullanımına sebep olarak sağlık bakım maliyetlerini artırmaktadır. Türkiye'deki yıllık ÜSE görülme sıklığı, Sağlık Bakanlığı verileri ile Şekil 5'te gösterilmiştir (16-17).



Şekil 5. Sağlık Bakanlığı yıllık istatistik raporlarına göre ÜSE sıklığı

2024 yılında yayımlanan Ulusal Sağlık Hizmeti İlişkili Enfeksiyonlar Sürveyans Ağı (USHİESA) verilerine göre, ülke genelinde 60.370 sağlık hizmeti ilişkili enfeksiyon bildirilmiş ve bunlardan 8.620'si üriner sistem enfeksiyonu (ÜSE) olarak kaydedilmiştir. ÜSE, sağlık hizmeti ilişkili enfeksiyonlar arasında sıklık açısından üçüncü sırada yer almaktadır. Türkiye genelindeki yoğun bakım ünitelerinde kateter ilişkili ÜSE insidansı, 1.000 kateter günü başına ortalama 0,89 olarak belirlenmiş olup, birimler arasında 0,1 ile 1,8 arasında değişiklik göstermiştir.Üriner sistem enfeksiyonlarında (ÜSE) sık görülen klinik belirtiler arasında idrar yapma sıklığında artış, ani idrar yapma ihtiyacı, idrar yaparken yanma hissi ve pelvik ağrı yer almaktadır (13).

ÜSE gelişiminde rol oynayan risk faktörleri ise çok yönlüdür. Bunlar arasında uzun süreli kateterizasyon, kateter tıkanıklıkları, gereksiz kateter kullanımı, uzun süreli antibiyotik tedavisi, üriner sistemin yapısal bozuklukları ve hastalıkları, meatus bölgesindeki kolonizasyon, vücutta başka bir aktif enfeksiyonun varlığı, kadın cinsiyet, ileri yaş, bağışıklık sisteminin baskılanması, diyabet, malnütrisyon, drenaj sistemindeki hasarlar, kateterin deneyimsiz kişilerce yerleştirilmesi ve asepsi kurallarına uyulmaması gibi bakım eksiklikleri sayılabilir (18)

Üriner sistem enfeksiyonlarının (ÜSE) yaklaşık %60–80'i üriner kateter kullanımına bağlı olarak gelişmektedir. Üriner kateterler, idrar çıkışını sürekli sağlamak amacıyla kullanılan önemli tıbbi araçlardır. Hastanede yatan hastaların yaklaşık %15–25'ine, yatış süreleri boyunca en az bir kez kateter uygulanmaktadır. Yoğun bakım ünitelerinde ise kateter kullanım oranı %90'ın üzerinde bildirilmiştir. Üriner kateter vücut için yabancı bir cisim iken, normal üriner sistem steril bir ortamdır. Kateterizasyon başladıktan sonra günlük bakteriüri riski %1–10 arasında değişir. Bakteriüri veya kandidüri riski, kateterin 7. günden sonra artmakta ve her ek gün için enfeksiyon riski yaklaşık %5 oranında yükselmektedir (17).

Üriner sistem enfeksiyonlarının yaklaşık %60–80'inin önlenebilir olduğu bilinmektedir. Bu nedenle kateter ilişkili üriner enfeksiyonların (Kİ-İYE) önlenmesinde en önemli adım, gereksiz kateter kullanımından kaçınmaktır. Sağlık profesyonellerinin, kanıta dayalı uygulamalar ve multidisipliner bir yaklaşım benimseyerek bu konuya odaklanmaları gerekmektedir. Kİ-İYE önleme paketleri kapsamında, üriner kateterin yerleştirilmesi ve bakımına ilişkin çeşitli kanıt düzeylerine sahip öneriler bulunmaktadır (15).

Ventilatör İlişkili Pnömoni

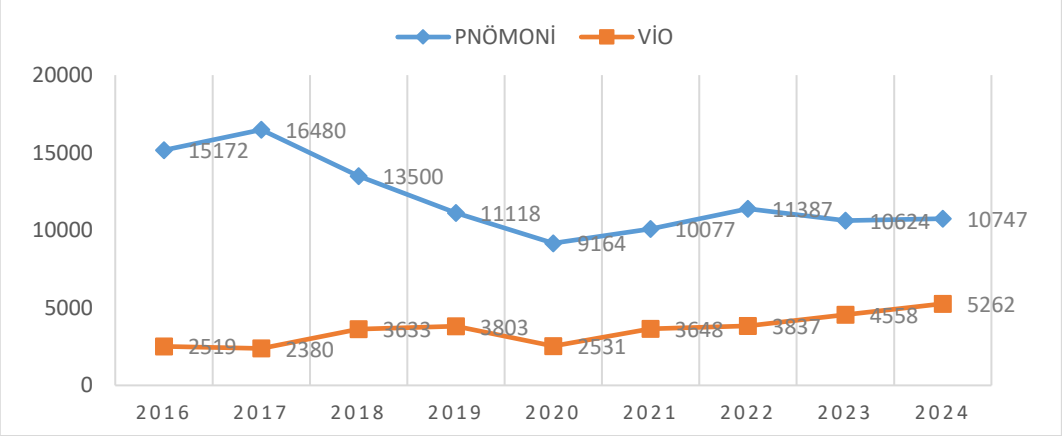
Mekanik ventilasyon, solunum yetmezliği yaşayan hastalar için hayati öneme sahip bir tedavi yöntemidir. Ancak bu tedavi sırasında bazı komplikasyonlar gelişebilir; bunlar arasında ventilatör ilişkili pnömoni (VİP), akut solunum sıkıntısı sendromu (ARDS), pulmoner emboli ve akciğer ödemi sayılabilir. VİP, özellikle yoğun bakım ünitelerinde en sık rastlanan sağlık hizmeti ilişkili enfeksiyonlardan biri olarak öne çıkmaktadır.

Ventilatör destekli hastalarda, entübasyon öncesinde pnömoni öyküsü olmayan kişilerde VİP genellikle mekanik ventilasyonun başlamasından 48–72 saat sonra ortaya çıkar. Mikroorganizmalar hızlı bir şekilde çoğalabilir, midede kolonize olabilir ve hava yolları, bronşlar ile akciğerlerde enfeksiyona yol açabilir. Pnömoni, hastada farklı nedenlerden dolayı da gelişebilir; ancak VİP, sağlık hizmeti sunumuna bağlı, önlenebilir bir enfeksiyon türüdür. Bu enfeksiyon, sağlık hizmeti ilişkili enfeksiyonlar arasında sık görülmesinin yanı sıra, morbidite ve mortaliteyi artırarak ciddi bir sağlık sorunu oluşturur (19).

2013 yılında Hastalık Kontrol ve Önleme Merkezi (CDC), ventilatöre bağlı bazı komplikasyonların tanım kapsamı dışında kalması ve mevcut tanımların sınırlılıkları nedeniyle "ventilatör ilişkili olay" (VİO) kavramını gündeme getirmiştir. Türkiye'de ise 2020 yılında Sağlık Bakanlığı, sağlık hizmeti ilişkili enfeksiyonlar (SHİE) sürveyansı kapsamında VİO'ya ilişkin bir kılavuz yayımlamıştır (20).

Ventilatör ilişkili pnömoni (VİP) görülme sıklığı, ülkeler, hastaneler ve birimler arasında değişiklik göstermekle birlikte, gelişmiş sağlık sistemlerine sahip olunsa da yaygın olarak karşılaşılan bir sorun olmaya devam etmektedir. Son 20 yılda bilimsel ve teknolojik ilerlemeler sayesinde VİP oranlarında azalma görülse de istenilen düzeylere henüz ulaşılamamıştır. Türkiye'de 2024 yılında toplam 10.747 pnömoni olgusu ve 5.262 ventilatör ilişkili olay (VİO) rapor edilmiştir. Ülke genelindeki yoğun bakım ünitelerinde VİO hızı, 1.000 ventilatör günü başına ortalama 3,66 olarak ölçülmüş ve birimler arasında

1,8 ile 9,4 arasında değişiklik göstermiştir. Sağlık Bakanlığı tarafından yayımlanan yıllık istatistik raporlarında pnömoni ve VİO görülme sıklığı Şekil 7'da sunulmuştur (13).



Şekil 7. Sağlık Bakanlığı yıllık istatistik raporlarına göre Pnömoni sıklığı

Hastanelerde gelişen pnömoni vakaları farklı nedenlere bağlı olarak ortaya çıkabilmektedir; ancak en önemli faktör yoğun bakım ünitelerinde kullanılan mekanik ventilatörlerdir. Araştırmalar, mekanik ventilasyonun pnömoni riskini yaklaşık yedi kat artırdığını göstermektedir. Yoğun bakımda hastaların uzun süre ventilatör desteği alması, sık invaziv girişim uygulanması ve geniş spektrumlu antibiyotik kullanımı, ventilatör ilişkili pnömoni (VİP) oranlarının artmasına katkıda bulunmaktadır. VİP, mekanik ventilasyon desteği alan hastalarda gelişebilecek en ciddi komplikasyonlardan biri olarak kabul edilmektedir (21).

Ventilatör ilişkili pnömoni (VİP) oluşumunda en önemli mekanizma, orofarenks sekresyonlarının aspirasyonudur. VİP'in önlenmesinde temel hedefler şunlardır (22):

1. Kontamine cihaz ve malzeme kullanımını engellemek,
2. Solunum ve sindirim yollarının mikroorganizma ile kolonize olmasını önlemek,
3. Sekresyonların aspirasyonunu engelleyerek hava yollarını temiz tutmak.

Ventilatör ilişkili pnömoni (VİP) gelişiminde birçok risk faktörü rol oynar. Enfeksiyon genellikle hastanın kendi mikroflorasından kaynaklansa da, dış kaynaklı bulaşma da söz konusu olabilir. Hastaya bağlı riskler arasında yaş, kronik obstrüktif akciğer hastalığı, diğer pulmoner rahatsızlıklar, diyabet, böbrek yetmezliği ve bağışıklık sisteminin baskılanması gibi mevcut hastalıklar bulunur.

Buna ek olarak, enfeksiyon kontrolü ile ilgili bakım uygulamalarında önlemlere uyulmaması VİP riskini artırır. Örneğin yetersiz el hijyeni, izolasyon protokollerine uyulmaması, kişisel koruyucu ekipman kullanımının eksikliği, kontamine cihazların kullanımı, hastaya uygunsuz veya gereksiz geniş spektrumlu antibiyotik uygulanması ve hasta bakımına gereken özenin gösterilmemesi (ağız bakımı, göz bakımı gibi) önemli risk faktörleri arasında yer almaktadır.

VİP'in önlenmesinde, endotrakeal entübasyon ve mekanik ventilasyon gereksiniminin her gün gözden geçirilmesi ve uygun olduğunda mümkün olan en kısa sürede ekstübasyonun planlanması büyük önem taşır. Ayrıca, invaziv olmayan ventilasyon yöntemleri, yüksek akım oksijen tedavisi veya spontan solunum denemeleri tercih edilmelidir. Hasta izlemi sırasında sedasyondan kaçınmak mümkünse en uygunudur; sedasyon gerekli olduğunda ise aralıklı intravenöz dozlar tercih edilmelidir. Eğer aralıklı dozlar yeterli gelmez ve infüzyon uygulanması gerekiyorsa, sedasyon skorlamaları kullanılarak hafif sedasyon hedeflenmeli, sedatif ilaç kullanımı her gün gözden geçirilmeli (sedasyon tatili) ve sedasyon mümkün olan en kısa sürede kesilmelidir (18,23)

Ventilatör ilişkili pnömoniyi (VİP) önlemek için uygulanacak klinik stratejilerin, güncel araştırmalar ve kanıta dayalı yöntemler ışığında planlanması büyük önem taşır. Ventilatör desteği alan hastalarda bakım

süreci, hastanın mekanik ventilasyona başlandığı andan ventilasyondan ayrılana kadar kesintisiz olarak sürdürülmelidir.

Diğer Enfeksiyon Türleri

2024 yılında bildirilen sağlık hizmeti ilişkili enfeksiyonların (SHİE) yaklaşık %6,9'u bu kategoriye aittir. Her ne kadar bu enfeksiyonlar sık görülmese de, ciddi sağlık sorunlarına yol açabilirler. En yaygın olarak yumuşak doku enfeksiyonları, gastrointestinal enfeksiyonlar, pnömoni ve alt solunum yolu enfeksiyonları görülür. Ayrıca bu grupta kemik ve eklem enfeksiyonları, merkezi sinir sistemi enfeksiyonları, kardiyovasküler enfeksiyonlar, göz, kulak, burun, boğaz ve ağız enfeksiyonları ile genital sistem enfeksiyonları da yer almaktadır (13).

MATERYAL VE YÖNTEM

Araştırmanın yürütüldüğü yer ve zaman: Çalışma, Siirt Eğitim ve Araştırma Hastanesi'nde 2024 yılında gerçekleştirilmiştir. Hastane enfeksiyon verilerine geriye dönük olarak erişilmiştir. Araştırmanın evrenini, hastanede yataklı servisler ve yoğun bakım ünitelerinde tedavi gören hastalar oluşturmaktadır. Sağlık hizmeti ilişkili enfeksiyonların (SHİE) tanısı, CDC ve Sağlık Bakanlığı Ulusal Hastane Enfeksiyonları Sürveyans Ağı kriterlerine göre konmuştur. Bir enfeksiyonun SHİE olup olmadığı, klinik gözlem ve muayene, laboratuvar ve radyolojik bulgular, hasta kayıtlarının incelenmesi ve diğer destekleyici veriler dikkate alınarak belirlenmiştir. Aynı hastada birden fazla enfeksiyon gelişmesi durumunda her enfeksiyon ayrı vaka olarak değerlendirilmiştir. SHİE ile ilgili bilgiler veri toplama formu aracılığıyla kaydedilmiştir.

Verilerin analizi Statistical Package for the Social Sciences (SPSS) 21.0 programı kullanılarak yapılmıştır. Frekans analizleri ile gruplara ait sayı (n) ve yüzde (%) değerleri belirlenmiştir. Grupların ortalama (Ort), standart sapma (SS), minimum (min) ve maksimum (maks) değerleri hesaplanmıştır. Gruplar arasındaki farklılıklar, değişkenlerin normal dağıldığı varsayımı ile bağımsız örneklem t-testi kullanılarak incelenmiş; kategorik değişkenler arasındaki ilişkiler için ki-kare testi uygulanmıştır. İstatistiksel anlamlılık için $p<0,05$ değeri esas alınmıştır.

Elde edilen veriler, Sağlık Bakanlığı Halk Sağlığı Genel Müdürlüğü Ulusal Sağlık Hizmetleri Sürveyans Ağı (USHİESA) özet raporundaki verilerle karşılaştırılmıştır. Analiz ve değerlendirmelerde ilgili hesaplamalar için gerekli formüller uygulanmıştır.



Araştırmanın izni

Dicle Üniversitesi tıp fakültesi girişimsel olmayan klinik araştırmalar Etik Kurulu'ndan 28.05.2025 tarih ve 300 no'lu izin alındı Ayrıca çalışamaya başlamak için Siirt il Sağlık Müdürlüğü'nden kurumsal izin alındı

BULGULAR

Tablo 1. Demografik özelliklere ilişkin frekans dağılım tablosu

Değişken	Kategori	n	%
Yatış yapılan servis	Yoğun Bakım	199	53,35
	Servis	174	46,65
Yaş	Çocuk[1]	30	8,04
	Erişkin[2]	202	54,16
	Yaşlı[3]	141	37,80
Cinsiyet	Kadın	230	61,66
	Erkek	143	38,34
Sonuç	Ölüm	157	42,09
	Taburcu	190	50,94
	Sevk	26	6,97
Değişken		Ort. ± SS	Min.-Maks.
Yaş		50,78 ± 25,38	0-100
Hastane Yatış Süresi (Gün)		60,87 ± 146,09	2-1546
Hastane Enfeksiyonu Sonrası Hastanede Kalma Süresi (Gün)		26,86 ± 59,29	0-800

Çocuk 0-18[1], Erişkin 19-65[2], Yaşlı 65 yaş üstü[3]

Araştırma kapsamında değerlendirilen toplam 373 hastanın %53,35'i yoğun bakım servisinde (n=199), %46,65'i ise diğer servislerde (n=174) SHİE tanısı konulmuştur. Hastaların yaş grubu dağılımı incelendiğinde, %8,04'ü çocuk (0–18 yaş; n=30), %54,16'sı erişkin (19–65 yaş; n=202) ve %37,80'i yaşlı (65+ yaş; n=141) olarak belirlenmiştir. Cinsiyet dağılımı açısından, hastaların %61,66'sı kadın (n=230) ve %38,34'ü erkek (n=143) olarak tespit edilmiştir. Hastaneden ayrılma sonuçları incelendiğinde, hastaların %42,09'unun ölüm (n=157), %50,94'ünün taburcu edildiği (n=190) ve %6,97'sinin başka bir merkeze sevk edildiği (n=26) görülmektedir. Tanımlayıcı istatistiklere göre hastaların yaş ortalaması 50,78 ± 25,38 yıl olup yaşlar 0 ile 100 arasında değişmektedir. Hastanede yatış süresi ortalama 60,87 ± 146,09 gün olarak bulunmuş ve bu süre 2 ile 1546 gün arasında değişmiştir. Hastane enfeksiyonu sonrası hastanede kalma süresi ise ortalama 26,86 ± 59,29 gün olup minimum 0, maksimum 800 gün olarak kaydedilmiştir.

Tablo 2. Hastane enfeksiyon tanı ve etkenlerine ilişkin frekans dağılım tablosu

Değişken	Kategori	n	%
Sağlık hizmeti ilişkili enfeksiyon	Cerrahi Alan Enfeksiyonu (CAE)	116	31,2
	Kan Dolaşım Enfeksiyonu (KDE)	146	39,2
	Üriner Sistem Enfeksiyonu (ÜSE)	41	11

	Ventilatör İle İlişkili Olaylar (VIO)	35	9,3
	Pnömoni	21	5,6
	Yumuşak doku enfeksiyonu(YDE)	14	3,7
Sağlık hizmeti ilişkili enfeksiyon etkeni	Acinetobacter Baumanni	47	12,6
	Escherichia Coli	38	10,1
	Klebsiella Spp	50	13,4
	Pseudomonas Spp	32	8,5
	Staphylococcus Aureus	43	11,5

Araştırmaya dahil edilen 373 hastada gözlenen hastane enfeksiyonu tanılarına bakıldığında, en sık karşılaşılan enfeksiyon türü %39,2 oranıyla kan dolaşım enfeksiyonlarıdır (n=146). Bunu %31,2 ile cerrahi alan enfeksiyonları (CAE; n=116) takip etmektedir. Üriner sistem enfeksiyonu (ÜSE) %11 (n=41), ventilatör ile ilişkili olaylar (VİO), pnömoniler %5,6 (n=21), yumuşak doku enfeksiyonu %3,7 (n=14) olarak yer almaktadır.

Hastane enfeksiyonlarında izole edilen etken mikroorganizmalar arasında en sık rastlanan patojenler sırasıyla Klebsiella spp. (%13,4; n=50), Acinetobacter baumannii (%12,6; n=47) ve Staphylococcus aureus (%11,5; n=43) olmuştur. Diğer yaygın mikroorganizmalar arasında Escherichia coli (%10,1; n=38), Pseudomonas Spp (%8,5; n=32) yer almaktadır.

Tablo 3. Yıllık sağlık hizmeti ilişkili enfeksiyon sıklığı

Yıllar	Hasta günü	Hasta sayısı	SHİE sayısı	SHİE hızı	Enfeksiyon dansitesi
2016	84838	31547	30	0.09	0,35
2017	128978	32826	30	0,09	0,23
2018	126611	35831	31	0,08	0,24
2019	122759	37313	44	0,11	0,35
2020	95134	27799	22	0,07	0,23
2021	129774	35241	20	0,05	0,14
2022	158179	38145	68	0,17	0,43
2023	124638	36863	65	0,17	0,52
2024	117229	35234	64	0,18	0,55
Toplam	3107991	1088140	373	0,12	0,34

Bu çalışmada toplam 1.088.140 hastada 3.107.099 hasta günü üzerinden 373 SHİE olgusu saptanmış olup, genel SHİE hızı %0,12 ve enfeksiyon dansitesi 0,34 olarak hesaplanmış, 2021 yılında belirgin düşüş (hız: %0,05) izlenirken 2022–2024 döneminde artış eğilimi gözlenmiştir. Araştırma kapsamında 373 sağlık hizmeti ilişkili enfeksiyon kaydedilmiş SHİE insidansı 0,12 ve 1000 hasta gününe karşılık

gelen SHİE dansitesi ise 0,34 bulundu. Bu çalışmanın yapıldığı sağlık yatan hasta sayısı ve hasta günü tablo 3'te verilmiştir.

Tablo 4. Cerrahi alan enfeksiyon sıklığı

Yıl	Ameliyat sayısı	CAE sayısı	CAE hızı
2016	1312	6	0,45
2017	1377	5	0,36
2018	1692	12	0,70
2019	2124	15	0,70
2020	2007	6	0,29
2021	2373	10	0,42
2022	2487	25	1
2023	1966	15	0,76
2024	1779	17	0,95
Toplam	17 117	116	0,67

Araştırma dönemi içerisinde 17.117 ameliyat gerçekleştirilmiş, 116 CAE olgusu saptanmış olup genel CAE hızı %0,67 olarak hesaplanmış; hızın 2020 yılında en düşük düzeyde (%0,29) olduğu, 2022 yılında belirgin artış göstererek en yüksek değere (%1,00) ulaştığı ve izleyen yıllarda görece yüksek seyrini sürdürdüğü belirlenmiştir.

Tablo 5. Erişkin yoğun bakımda enfeksiyon sıklığı

Dönem	(n)	Hasta sayısı	Hasta günü	Enfeksiyon hızı	Enfeksiyon dansitesi
Genel	199	10537	63158	1,88	3,15

Yoğun bakım ünitesinde 199 sağlık hizmeti ilişkili enfeksiyon kaydedildi. Yoğun bakımda genel enfeksiyon hızı 1,88 enfeksiyon dansitesi 3,15 bulundu.

Tablo 6. Yıllara göre erişkin yoğun bakımda invaziv araç kullanımı

Yıl	Hasta sayısı	Hasta günü	Üriner kateter günü	Santral kateter günü	Ventilatör günü
2016	1107	4607	3755	654	1754
2017	913	5889	4550	1775	2965
2018	835	5879	5173	1646	3085
2019	978	6008	5632	2433	2968
2020	871	5092	4761	1178	2209
2021	1114	6846	6633	1906	2630
2022	1285	9417	9040	3538	4283
2023	1674	9655	9188	3378	3631
2024	1760	9765	9390	3942	3289
Toplam	10537	63158	58122	20000	26814

Erişkin yoğun bakım ünitesinde toplam 10.537 hasta ve 63.158 hasta günü izlenmiş olup, 58.122 üriner kateter günü, 20.000 santral kateter günü ve 26.814 ventilatör günü kaydedilmiş; üriner kateter için 0,92 santral kateter için 0,31 ventilatör kullanım oranı 0,42 bulundu. invaziv araç kullanımının özellikle 2021 yılı sonrasında belirgin artış eğilimi gösterdiği saptanmıştır.

Tablo 7. Erişkin yoğun bakımda invaziv araç hızı

Dönem	Üriner kateter günü	Kİ-İYE sayısı	Kİ-İYE hızı	Santral kateter günü	SKİ-KDE sayısı	SKİ-KDE hızı	Vent günü	Ventilatör ilişkili olay sayısı	VİO hızı
Genel	58122	27	0,46	20000	28	1,36	26814	22	0,82

Yoğun bakım ünitesinde 77 invaziv araç ilişkili enfeksiyon bildirimi yapılmıştır. Tablo 7'de invaziv araç ilişkili enfeksiyon hızları belirtilmiştir. İnvaziv araç ilişkili enfeksiyon hızı 0,7 ve 1000 kateter günü başına düşen enfeksiyon sayısı 1,12 bulundu. Kateter ilişkili üriner sistem enfeksiyon hızı 0,46 santral kateter ilişkili kan dolaşım enfeksiyon hızı 1,36 ventilatör ilişkili olay hızı ise 0,82 olarak belirlendi.

TARTIŞMA

Nosokomiyal enfeksiyonlar, yani hastanede kazanılan enfeksiyonlar, sağlık sistemlerinin karşılaştığı ciddi sorunlardan biridir. Günümüzde enfeksiyon kontrolü ve önleme çalışmalarıyla bazı ilerlemeler sağlanmış olsa da bu enfeksiyonlar hâlâ önemli bir problem olarak görülmektedir. Yeni patojenlerin ortaya çıkması ve tedavi seçeneklerinin karmaşıklaşması, hasta sonuçlarını olumsuz yönde etkilemektedir (24).

Bu enfeksiyonlar, dünya genelinde çok sayıda hastayı etkileyerek mortaliteyi artırmakta ve sağlık sistemleri üzerinde ek yük yaratmaktadır. Küresel SHİE sıklığının tahmin edilmesi ise raporlama eksiklikleri, veri kalitesindeki sorunlar ve standart yöntemlerin bulunmaması nedeniyle güçlük arz etmektedir. Bu durum özellikle düşük ve orta gelirli ülkelerde güvenilir veri elde edilmesini zorlaştırmaktadır. Ayrıca, kültürel farklılıklar ve raporlama ile ilgili yaptırımlar, verilerin doğruluğunu ve raporlama davranışlarını etkileyebilir. Yetersiz veri ve enfeksiyon gelişiminin düzenli ve etkili biçimde izlenememesi, enfeksiyon kontrolü ve önleme çalışmalarının başarısını olumsuz yönde etkilemektedir (25).

SHİE'nin görülme sıklığı, hastaneler ve ülkeler arasında farklılık gösterebilmektedir. Bu farklılıklar, hasta demografisi, hastalığın epidemiyolojik özellikleri ve hastane organizasyon yapısı gibi çeşitli faktörlerden kaynaklanabilir. Hastaneler arasında enfeksiyon oranlarını karşılaştırırken yalnızca hesaplama yöntemlerinin aynı olması yeterli değildir; aynı zamanda hastanenin hizmet düzeyi, yatak sayısı, personel sayısı ve yoğun bakım gibi özel birimlerin fiziki koşulları da dikkate alınmalıdır.

Hastane enfeksiyon hızı genellikle hasta yatış süresi ve invaziv cihaz kullanımına göre hesaplansa da, enfeksiyon gelişimini etkileyen diğer faktörler de önemlidir. Bunlar arasında hastaların sağlık durumları, hasta odalarının fiziksel yapısı, birim başına düşen sağlık personeli sayısı, sağlık çalışanlarının enfeksiyon kontrolü eğitim düzeyi ve enfeksiyon önleme uygulamalarına uyum oranı gibi unsurlar yer almaktadır (25-26).

Avrupa'da her yıl tahminen 3,5 milyondan fazla sağlık hizmeti ilişkili enfeksiyon vakası görülmekte ve bunlardan 90 binden fazlası ölüme yol açmaktadır. Bu enfeksiyonların yaklaşık yarısının önlenebilir olduğu düşünülmektedir. Önleme çabalarının ilk adımı, SHİE vakalarının düzenli olarak izlenmesi ve toplanan verilerin analiz edilmesidir. Enfeksiyonların tanınması ve ortaya çıkışına neden olan faktörlerin bilinmesi, enfeksiyon oranlarının takip edilmesi ve farklı sağlık merkezleriyle karşılaştırılması açısından önem taşır. (27,28).

Alanlı ve ark. tarafından yapılan bir çalışmada 14599 hasta yatışı ve 77 777 yatış günü gerçekleşmiştir. Bu süreçte 171 hastada(%1,2) toplam 178 hastane kaynaklı enfeksiyon atağı saptandı. Enfeksiyon gelişenlerin %49,7'si (n=85) kadın ve %50,3'ü (n=86) erkekti. Hastalar 26 ile 95 yaş aralığında idi. Hastaların ortalama yaşı 72,6 ± 14,2 (erkeklerin 69,1 ± 14,4; kadınların 76,3± 13,2) olarak saptandı. Bu

çalışma kapsamında değerlendirilen toplam 373 hastanın %53,35'i yoğun bakım servisinde (n=199), sağlık hizmeti alırken SHİE tanısı konulmuştur. Hastaların yaş grubu dağılımı incelendiğinde, %8,04'ü çocuk (0–18 yaş; n=30), %54,16'sı erişkin (19–65 yaş; n=202) ve %37,80'i yaşlı (65+ yaş; n=141) olarak belirlenmiştir. Cinsiyet dağılımı açısından, hastaların %61,66'sı kadın (n=230) olarak tespit edilmiştir. Tanımlayıcı istatistiklere göre hastaların yaş ortalaması 50,78 ± 25,38 yıl olup yaşlar 0 ile 100 arasında değişmektedir. Hastanede yatış süresi ortalama 60,87 ± 146,09 gün olarak bulunmuş ve bu süre 2 ile 1546 gün arasında değişmiştir. Hastane enfeksiyonu sonrası hastanede kalma süresi ise ortalama 26,86 ± 59,29 gün olup minimum 0, maksimum 800 gün olarak kaydedilmiştir Tanımlayıcı demografik özellikler hasta popülasyonuna göre değişmektedir. (29).

Sağlık kuruluşlarının hasta profili, hastane florası ve antimikrobiyal direnci birbirinden farklıdır. En sık görülen SHİE'ler üniteden üniteye göre değişiklik göstermektedir. Bu çalışmada kan dolaşım enfeksiyonu %39,2 ile (n=146) en sık görülen sağlık hizmeti ilişkili enfeksiyon olarak belirlenmiştir. Tüfek ve ark. tarafından 10 yıllık sürede gelişen hastane enfeksiyonlarının değerlendirildiği bir çalışmada kan dolaşım enfeksiyonu (%35,5) en sık enfeksiyon olarak belirlenmiştir. Karagun ve ark. (2020) 1 yıllık hastane enfeksiyonları sürveyans çalışmasına göre kan dolaşım enfeksiyonu %29,4 olarak kaydedilmiştir. Benzer şekilde Sağlık Bakanlığı verilerine göre kan dolaşım enfeksiyonu en sık SHİE olarak belirlenmiştir. Bu paralellik kan dolaşımı enfeksiyonlarının hastanelerde kritik bir sorun olmaya devam ettiğini göstermiştir (30,31).

Sebahat Şen Taş ve arkadaşları tarafından palyatif bakım merkezinde gerçekleştirilen çalışmada, hastane enfeksiyonu oranları 2014 yılı için %2,59, 2015 yılı için %2,39 ve 2016 yılı için %1,74 olarak rapor edilmiştir. Üç yıllık dönemin tamamı değerlendirildiğinde, en sık görülen enfeksiyon türünün üriner sistem enfeksiyonları olduğu belirlenmiştir.

Avrupa'da bir uzun dönem bakım merkezinde yürütülen nokta prevalans araştırmasında da, en yaygın bildirilen sağlık hizmeti ilişkili enfeksiyonun (SHİE) üriner sistem enfeksiyonları olduğu ortaya konmuştur. Aynı çalışmada, hastaların %69,9'unun idrar ve/veya gaita inkontinansı yaşadığı, %45,5'inin ise hareket kısıtlılığı bulunduğu (tekerlekli sandalye kullanımı ya da yatağa bağımlılık) bildirilmiştir. Bu bulgular, özellikle uzun dönem bakım ve palyatif bakım merkezlerinde üriner sistem enfeksiyonlarının yüksek sıklıkta görülmesinin; hastaların fonksiyonel bağımlılık düzeyi ve inkontinans gibi risk faktörleriyle yakından ilişkili olabileceğini düşündürmektedir (32).

Üriner sistem enfeksiyonları (ÜSE), sağlık hizmeti sunulan ortamlarda sık karşılaşılan enfeksiyon türleri arasında yer almaktadır. ÜSE'ye bağlı komplikasyonlar; hastada konfor kaybına, hastanede kalış süresinin uzamasına, tedavi maliyetlerinin artmasına ve mortalite oranlarında yükselmeye yol açabilmektedir. Karagun ve arkadaşlarının çalışmasında ÜSE oranı %19,6 olarak rapor edilmiştir. T.C. Sağlık Bakanlığı verilerine göre ise üriner sistem enfeksiyonları, tüm sağlık hizmeti ilişkili enfeksiyonlar (SHİE) arasında %14'lük pay ile üçüncü sırada bulunmaktadır. Bu çalışmada ÜSE oranı %11 (n=41) olarak saptanmıştır. Elde edilen bulgu, hem ulusal verilerle hem de mevcut literatürde bildirilen oranlarla genel olarak uyum göstermekte olup beklenen sınırlar içerisinde değerlendirilebilir. (13,31,33)

Yoğun bakım ünitelerinde (YBÜ) izlenen hastalara tanı ve tedavi amacıyla çok sayıda invaziv işlem uygulanmaktadır. Bu girişimlerin türü ve süresi ile hastanede kalış süresi, hastane enfeksiyonlarının gelişiminde belirleyici rol oynamaktadır. YBÜ'de invaziv araç kullanımı ile enfeksiyon ilişkisini değerlendiren bir araştırmada, en yüksek kullanım oranının üriner kateterlere ait olduğu bildirilmiştir. Üriner sistem enfeksiyonlarının büyük çoğunluğu, idrar yoluna yerleştirilen kateterlerle ilişkilidir. Yoğun bakıma kabul edilen hastaların önemli bir bölümüne üriner kateter uygulanmakta ve kateterin takılı kaldığı her gün enfeksiyon riski yaklaşık %3–7 oranında artmaktadır. İlgili çalışmada, YBÜ'de takip edilen hastaların %92'sine üriner kateter takıldığı belirtilmiştir. Kateterizasyon süresi, enfeksiyon gelişimi açısından temel risk faktörlerinden biridir. Bu nedenle kateter endikasyonu günlük olarak gözden geçirilmeli ve klinik gereklilik ortadan kalktığında mümkün olan en kısa sürede çıkarılması sağlanmalıdır. Bu yaklaşım, kateter ilişkili üriner sistem enfeksiyonlarının azaltılmasında etkili bir strateji olarak değerlendirilmektedir. (17,32,33).

Ameliyathane ortamında havalandırma sistemlerinin iyileştirilmesi, sterilizasyon uygulamalarının geliştirilmesi, cerrahi tekniklerdeki ilerlemeler ve uygun profilaktik antibiyotik kullanımı gibi

enfeksiyon kontrolüne yönelik önemli adımlar atılmış olmasına rağmen, cerrahi alan enfeksiyonları (CAE) halen ciddi morbidite, uzamış hastane yatışı ve artmış mortalite ile ilişkili olmaya devam etmektedir. Bu araştırmada 373 hasta üzerinde gerçekleştirilen değerlendirmede, CAE oranı tüm sağlık hizmeti ilişkili enfeksiyonlar (SHİE) içinde %31,2 (n=116) ile ikinci en sık görülen enfeksiyon türü olarak saptanmıştır. Karagun ve arkadaşlarının çalışmasında bu oran %21,5 olarak bildirilirken, Erdem ve arkadaşları tarafından Ege Üniversitesi Hastanesi'nde 23 Aralık 2013 tarihinde gerçekleştirilen nokta prevalans çalışmasında CAE oranı %8,5 olarak rapor edilmiştir. Mevcut çalışmada elde edilen oranın literatürde bildirilen bazı sonuçlara kıyasla daha yüksek olması; hastaneye özgü uygulama farklılıkları, hasta ve cerrahi vaka çeşitliliği, enfeksiyon kontrol önlemlerinin etkinliği ve sürveyans yöntemlerindeki değişkenlik gibi etmenlerle ilişkili olabilir. (8,31,34).

European Centre for Disease Prevention and Control (ECDC) tarafından yürütülen ve 2018–2020 yıllarını kapsayan yıllık epidemiyolojik değerlendirmede, Avrupa'daki hastanelerde CAE oranı %1,56 olarak bildirilmiştir. Bu çalışmada cerrahi alan sürveyansı kapsamında izlenen 17.117 cerrahi girişim sonrasında 116 CAE olgusu belirlenmiş ve bu örneklemde enfeksiyon oranı %0,67 olarak hesaplanmıştır. INICC tarafından yürütülen ve 25 ülkeyi kapsayan 10 yıllık çok merkezli bir araştırmada cerrahi alan enfeksiyonları değerlendirilmiştir. Çalışma kapsamında gerçekleştirilen 56.617 cerrahi girişim sırasında toplam 1.251 cerrahi alan enfeksiyonu olgusu kaydedilmiştir. Cerrahi alan enfeksiyonu (CAE) oranı %2,20 olarak saptanmıştır. Bulgular, düşük gelir düzeyine sahip ülkelerde CAE görülme sıklığının daha yüksek olduğunu göstermekte; bu durum, enfeksiyon oranlarını azaltmaya yönelik etkili ve sürdürülebilir müdahale stratejilerinin gerekliliğine işaret etmektedir.

Cerrahi alan enfeksiyonları; hastanede kalış süresinin uzaması, ek cerrahi müdahalelere gereksinim duyulması ve hastanın yoğun bakım ünitesine yatış olasılığının artması ile ilişkilidir. Bu durum, morbidite ve mortalite oranlarında artışa yol açabilmektedir. Bu nedenle CAE, enfeksiyon kontrol programları ve sürveyans çalışmaları açısından öncelikli izlem alanlarından biri olarak değerlendirilmektedir. (35-37).

Cerrahi alan enfeksiyonlarının (CAE) önemli bir kısmı, hastaların hastaneden taburcu edildikten sonra ortaya çıkmaktadır. Bu enfeksiyonların saptanabilmesi için hastaların taburculuk sonrası takip edilmesi gerekmektedir; aksi takdirde birçok CAE vakası fark edilmeyebilir. CAE'nin gelişimi ve tespiti açısından altı temel durum söz konusudur:

- CAE, hastane yatışı sırasında tespit edilebilir.
- Taburculuk sonrası CAE gelişen hasta, ameliyatın yapıldığı hastaneye yeniden yatabilir.
- Taburculuk sonrası CAE gelişen hasta, aynı hastanenin polikliniğinde tedavi olabilir.
- Taburculuk sonrası CAE gelişen hasta, farklı bir hastaneye yatabilir.
- Taburculuk sonrası CAE gelişen hasta, başka bir hastanenin polikliniği veya bir aile sağlığı merkezinde tedavi görebilir.
- Taburculuk sonrası CAE gelişen hasta, hiçbir sağlık kurumuna başvurmayabilir.

Bu nedenle, taburculuk sonrası telefon görüşmeleri veya benzeri takip yöntemleri ile hastaların durumu izlenebilir (4).

Mekanik ventilasyon, kritik durumda bulunan ve solunum yetmezliği gelişen hastalarda yaşamsal destek sağlayan temel tedavi yöntemlerinden biridir. Bununla birlikte, invaziv ventilasyon uygulaması bazı ciddi komplikasyonlarla ilişkilidir. Ventilatörle ilişkili olaylar (VİO); sepsis, akut solunum sıkıntısı sendromu (ARDS), pulmoner emboli ve pulmoner ödem gibi klinik tabloları içerebilir ve mekanik ventilasyon desteği alan hastalarda gelişebilmektedir. Bu komplikasyonların ortaya çıkması, ventilasyon süresinin uzamasına, yoğun bakım ünitesinde ve hastanede kalış süresinin artmasına ve buna bağlı olarak sağlık bakım maliyetlerinin yükselmesine yol açabilmektedir. Ayrıca, söz konusu durumlar hastalarda kalıcı fonksiyon kaybı ve mortalite riskinde artış ile ilişkilendirilmektedir.

2015 yılında gerçekleştirilen bir nokta prevalans çalışmasında, hastane enfeksiyonları arasında en sık görülen tablo pnömoni olup oranı %23,6 olarak bildirilmiştir. Aynı araştırmada ventilatör ilişkili pnömoni (VİP) oranı ise %10,4 olarak saptanmıştır. Bu çalışmada ise pnömoni oranı %5,6 (n=21) olarak

belirlenirken, ventilatör ilişkili olay (VİO) oranı %9,3 (n=35) olarak bulunmuştur. Centers for Disease Control and Prevention (CDC), 2013 yılında ventilatör ilişkili pnömoni tanımının mekanik ventilasyona bağlı gelişen bazı önemli komplikasyonları kapsam dışında bırakması ve tanısal sınırlılıkları nedeniyle, daha geniş bir çerçeve sunan ventilatör ilişkili olay (VİO) kavramını sürveyans sistemine dahil etmiştir. Mevcut çalışmada pnömoni oranının görece düşük, buna karşılık VİO oranının daha yüksek bulunması, 2015 yılı itibarıyla uygulanmaya başlanan VİO sürveyans yaklaşımıyla ilişkili olabilir. Bunun yanı sıra araştırmanın retrospektif tasarımı nedeniyle, pnömoni ve VİO olgularında enfeksiyonun kaynağı ve patogenezine ilişkin ayrıntılı ve güçlü çıkarımlar yapmak sınırlı kalmıştır. (22,34).

Tüfek ve ark. 2012 yılında Türkiye'de Dicle Üniversitesi Tıp Fakültesi Anestezi ve Reanimasyon Ünitesi'nde yaptığı çalışmada, on yıllık bir süreçte yoğun bakım hastalarında hastane enfeksiyonu gelişimi incelenmiş ve toplam 1208 hasta arasında 222 hastada 327 hastane enfeksiyonu atağı saptanmıştır. Çalışmada hastane enfeksiyonu hızı %27,6 enfeksiyon dansitesi ise 15,2 olarak bildirilmiştir. Tüfek ve arkadaşlarının çalışmasında hastane enfeksiyonu gelişiminde uzamış yatış süresinin önemli bir risk faktörü olduğu vurgulanmıştır. Bizim çalışmamızda 2016-2024 yılları arasında toplam 373 hasta incelenmiş ve 1000 hasta günü olarak ifade edilen hastane enfeksiyonu dansitesi 3,3 olarak belirlenmiştir. Son yıllarda enfeksiyon insidansında düşmeler olsa da yoğun bakımlarda önemini korumaktadır (30).

Dünya çapında sağlık hizmeti ilişkili enfeksiyonlara atfedilen kesin ölüm oranı bilinmemektedir ancak yapılan çalışmalar mortalitenin incelenen popülasyonlara bağlı olarak %12 ile %80 arasında değişebileceği belirtilmektedir. Uluslararası bir çalışmada yoğun bakım ünitesinde sağlık hizmeti ilişkili enfeksiyonlara maruz kalan hastalarda mortalite oranının maruz kalmayanlara kıyasla sırasıyla %25 ve %11 olduğunu göstermiştir. Aynı çalışma hastane genelinde mortalite oranının sağlık hizmeti ilişkili enfeksiyonu olan hastalarda olmayanlara kıyasla sırasıyla %30 ve %15 olarak iki katına çıktığını göstermiştir. 2002'de ABD hastanelerinde sağlık hizmeti ilişkili tahmini ölümler 99 000 civarında idi. Tüfek ve arkadaşlarının bildirdiği mortalite oranı %19 iken, bizim çalışmamızda %42,09 olarak bulunmuştur. Bir çalışmada 12 hastaneden toplam 6178 hasta araştırmaya alındı. Hastaların ortalama yatış süresi 10,7 gün, mortalite oranı %21,3 olarak belirlendi. Bu sonuçlar; enfeksiyon gelişiminin mortalite üzerindeki etkisini vurgulamakta ve enfeksiyon kontrol önlemlerinin gerekliliğini göstermektedir (38-41).

Bir hastanenin sürveyans sonuçlarına göre hastane enfeksiyonları ile hastanede kalış süresi arasında ilişki analizi yapıldı. SHİE türüne göre hastanede kalış süresi değişmekle birlikte tüm sağlık hizmeti ilişkili enfeksiyonlar için ilave hastanede kalış süresi 12 gün idi. Üriner sistem enfeksiyonları için 3,3 gün, cerrahi alan enfeksiyonları ve kan dolaşımı enfeksiyonları sırasıyla 12,9 ve 12,5 gün olarak bulundu. Aynı hastada birden fazla SHİE bulunması hastanede kalış süresini 25,6 gün uzatmaktadır. Sağlık hizmeti ilişkili enfeksiyonu olan hastanın hastanede kalış süresi 26,30 iken sağlık hizmeti ilişkili enfeksiyonu olmayan hastanın hastanede kalış süresi 5,69 gün olarak bulundu. Gelişmiş ülkelerde hastanede kalış süresi 5-23 gün arasında bildirilmektedir. Bu çalışmada SHİE sonrası hastanede kalış süresi 26,86 ± 59,29 gün olarak bulunmuştur. Bu sonuçlar enfeksiyon gelişimi ile hastanede kalış süresi arasındaki pozitif yönlü ilişkiyi desteklemektedir (42)

CDC'ye göre, ABD'de sağlık hizmeti ilişkili enfeksiyonların (SHİE) sağlık sistemine yıllık maliyeti 28 ila 45 milyar dolar arasında değişmektedir. Avrupa'da ise SHİE kaynaklı yıllık maliyet yaklaşık 7 milyar avro olarak tahmin edilmektedir. Bu çalışmada doğrudan maliyet analizi yapılmamış olsa da, SHİE'ler hastaların hastanede kalış süresini uzattığı ve ek tedavi ile bakım gereksinimi doğurduğu için dolaylı olarak maliyeti artırmaktadır. Özellikle, hastanede geçen her ek gün, sağlık harcamalarını yükselten başlıca faktörlerden biri olarak öne çıkmaktadır. Bu nedenle, SHİE'lerin önlenmesi yalnızca hasta sağlığı açısından değil, sağlık sisteminin ekonomik sürdürülebilirliği açısından da önem taşımaktadır(43-44)

Hastane enfeksiyonuna sebep olan patojenlerin varlığı ve sıklığı ülkeler hastaneler ve hatta aynı hastane içinde birimler arasında bile önemli farklılıklar göstermektedir. Son dönemlerde yapılan çalışmalarda fungal enfeksiyonların sıklığı giderek artmaktadır. Erdem ve ark. çalışmasında en sık izole edilen mikroorganizmalar E. coli %21,5, klebsiella pneumoniae %16,5 ve acinetobacter baumannii %13,9 olmuştur. Karagun ve ark çalışmasında hastane enfeksiyonu gelişen hastalarda en sık izole edilen

mikroorganizmalar Klebsiella spp. %29,5, E. coli %22,7, maya mantarları %20,5 ve S. aureus %9 olarak rapor edilmiştir. Bizim çalışmamızda da klebsiella spp., acinetobacter baumanni, pseudomonas spp. E. coli, ve staphylococus aureus en sık izole edilen patojenler arasında yer almıştır. Bu paralellik, gram negatif bakterilerin nosokomiyal enfeksiyonların başlıca etkenleri olduğunu göstermiştir (31,34).

Sağlık hizmetlerindeki ilerlemelere/gelişmelere rağmen enfeksiyon oranları tüm dünyada görülmeye devam etmektedir. Hastaneye yatışı yapılan hastaların sadece %5-10'u yoğun bakım ünitesinde takip edilmesine karşın tüm sağlık hizmeti ilişkili %20-25'i yoğun bakım ünitelerinde görülmektedir. Bir nokta prevalans yaygınlık araştırmasına göre tüm SHİE'lerin %30'u yoğun bakım ünitelerinde görülmektedir. Bu ünitelerde takip edilen hastalar ise ileri derecede metabolik bozukluğu bilinç değişiklikleri ve komorbid hastalakları olan komplike hastalardır. Bu hastaların immün dirençlerinin düşük olması, çoklu organ disfonksiyonlarına sahip olması, enfeksiyonların bulaşmasını ve kolonizasyonunu kolaylaştırmaktadır. Ayrıca bu hastalarda uzun süre santral kateter, endotrakeal tüp ve üriner kateter kullanılması enfeksiyonlara yatkınlığı arttırmaktadır. Yoğun bakımda görülen SHİE'lerin çoğu kullanılan invaziv araçlarla ilişkilidir ve önemli bir kısmının önlenebilir olduğu düşünülmektedir. Son yıllarda kanıta dayalı uygulamaların yer aldığı demet yaklaşımı *(bundle approach)* ön plana çıkmıştır. Önlem paketi olarak ifade edilen demet uygulamaları invaziv araç ilişkili enfeksiyonların önlemede kilit rol oynar (18,72).

Uluslararası Hastane Enfeksiyon Kontrol Konsorsiyumu (INICC) 2015-2020 sağlık hizmeti ilişkili enfeksiyon verilerin yer aldığı raporda 6 yıl süren prospektif çalışmaya 45 ülkeden 630 yoğun bakım ünitesinden veriler toplanarak analizler yapıldı. Buna göre 204 770 hasta sayısına karşılık 1 milyon 480 bin 620 hasta günü belirlendi. Sağlık hizmeti ilişkili enfeksiyon hızı %7,8 olup 1000 hasta günü başına düşen invaziv araç ilişkili enfeksiyon sayısı 10,07 bulundu. 4270 santral kateter ilişkili kan dolaşım enfeksiyonu (1000 Santral kateter günü başına düşen enfeksiyon sayısı 4,55), 7635 ventilatör ilişkili pnömoni (1000 ventilatör başına düşen enfeksiyon sayısı 1,96) ve 3005 kateter ilişkili üriner sistem enfeksiyonu (1000 üriner kateter başına düşen enfeksiyon sayısı 2,91) saptandı. INICC tarafından yapılan çalışmada invaziv araç hızları daha yüksek bulundu. INICC sistemine daha çok sürveyans sistemleri gelişmemiş düşük ve orta gelire sahip ülkeler veri akışı sağlamaktadır. SHİE sıklığı; literatüre göre düşük ve orta gelire sahip ülkelerde daha yüksektir. Bu farklılık elbette beklenen bir durum olarak karşılanabilir (45).

Hastane enfeksiyonlarının hastane içinde ve diğer hastaneler ile karşılaştırmada invaziv araç ilişkili enfeksiyon hızlarının karşılaştırılması değerli bir yöntemdir. İnvaziv araç ilişkili enfeksiyonlar yoğun bakım ünitelerinde yaygın olarak görülmektedir. Mert ve ark tarafından invaziv araç ilişkili nosocomiyal enfeksiyonların değerlendirildiği bir çalışmada 6 yıllık süreçte toplam 425 invazif araç ilişkili enfeksiyon tanısı kaydedildi. Santral kateter ilişkili kan dolaşım enfeksiyonu %42,1 (n=179), ventilatör ilişkili pnömoni % 41,4 (n=176), kateter ilişkili idrar yolu enfeksiyonu %16,5 (n=70) olarak belirlendi. Erişkin yoğun bakımda yapılan bir çalışmada 31138 ventilatör gününde 141 (1000 ventilatör günü başına düşen enfeksiyon hızı 4,5) yoğun bakıma yatan her hastaya idrar sondası takıldığı için 77777 idrar sondası gününde 24 (1000 idrar sondası günü başına düşen enfeksiyon hızı 0,3) üriner sistem enfeksiyonu saptanmıştır. Hastalarda 30956 santral katater gününde beş (1000 santral katater günü başına düşen enfeksiyon hızı 0,2) adet kan dolaşımı enfeksiyonu saptanmıştır. Bu çalışmada 26814 ventilatör gününde 22 (VİO hızı 0,82) 58122 idrar sondası gününde 27 (Kİ-İYE hızı 0,46) 20000 santral katater gününde 28 (SKİ-KDE enfeksiyon hızı 1,36) olarak saptanmıştır. Bu çalışmalardaki farklı sonuçlar kullanılan metodolojinin ve çalışmaya dahil edilen yoğun bakım ünitelerinin farklılığından kaynaklanabilir (29,46).

Bir çalışmada VINCat sürveyans programına dahil olan yoğun bakım ünitelerinde 13 yıl boyunca (2010-2022) elde edilen veriler incelendi. İnvaziv araç kulllanma oranı üriner kateter için 0,66 iken ventilatör ve santral kateter için kullanma oranı sırasıyla 0,39-0,60 idi. Kİ-ÜSE hızı 3,4 VİP hızı 6,4 ve SKİ-KDE hızı 1,9 bulundu. Bu çalışmada kateter ilişkili üriner sistem enfeksiyon hızı 0,46 santral kateter ilişkili kan dolaşım enfeksiyon hızı 1,36 ventilatör ilişkili olay hızı ise 0,82 olarak belirlendi. Kateter ilişkili üriner sistem enfeksiyonları ve ventilatör ilişkili olay yüksek, santral kateter ilişkili kan dolaşım enfesiyon hızı benzer bulundu. Çalışmaya dahil edilen yoğun bakım türü, hastane yatak sayısı ve invaziv araç kullanma oranı gibi değişkenler enfeksiyon sıklığını etkileyebilir. Bizim çalışmada üriner kateter

kullanım oranı 0,92 idi. Bu farklılıklar; neredeyse yatan her hastaya üriner kateter (%92) yerleştirilmiş olmasının paydayı arttırarak enfeksiyon oranının düşük bulunmasına neden olabilir (47).

SONUÇ VE ÖNERİLER

Sağlık hizmeti ilişkili enfeksiyonlar (SHİE), günümüzde önemli sağlık sorunlarından biri olarak kabul edilmektedir. Son on yılda birçok ülkede bu enfeksiyonların önlenmesine yönelik ilerlemeler kaydedilmiş, sağlık hizmetlerinin iyileştirilmesi ve teknolojik gelişmeler sayesinde özellikle yoğun bakım ünitelerinde invaziv araç kaynaklı enfeksiyonlar azalma göstermiştir. Ancak sağlık hizmetine olan talebin artması, nüfusun yaşlanması, yoğun bakımda yatan ciddi hastalıkları olan bireylerin sayısının yükselmesi, kronik hastalık yükünün artması, doğumda beklenen yaşam süresinin uzaması ve hem hastane hem toplum ortamında çoklu ilaç dirençli mikroorganizmaların yayılması nedeniyle SHİE'nin önümüzdeki yıllarda da önemli bir sağlık sorunu olmaya devam etmesi beklenmektedir.

- Araştırmada 373 hastada gözlenen hastane enfeksiyonu tanılarına bakıldığında; kan dolaşım enfesiyonları en sık görülen enfeksiyon türü olmuştur. Cerrahi alan enfeksiyonu 2. üriner sistem enfeksiyonu 3. sırada yer almaktadır.
- Araştırmada en sık saptanan üç SHİE etkeni sırasıyla Klebsiella spp., Acinetobacter baumannii ve Staphylococcus aureus olarak tespit edilmiştir.
- Çalışma süresince 373 hastaya SHİE tanısı konulmuş, enfeksiyon insidansı 0,12 ve 1000 hasta-günü başına enfeksiyon yoğunluğu 0,35 olarak hesaplanmıştır.
- SHİE tanısı alan hastalarda mortalite oranı %42,09 olarak belirlenmiştir.
- Hastaların SHİE sonrası hastanede kalış süresi ortalama 26,86 ± 22,31 gün olarak kaydedilmiştir.
- Araştırma dönemi içerisinde yoğun bakım ünitesinde toplam 199 sağlık hizmetiyle ilişkili enfeksiyon olgusu saptanmıştır. Bu süreçte ünitenin genel enfeksiyon oranı 1,88 olarak hesaplanmış, enfeksiyon dansitesi ise 3,15 olarak belirlenmiştir.
- Erişkin yoğun bakımda izlenen hastalarda invaziv araç kullanım oranları; üriner kateter %92**,** santral venöz kateter %31 ve ventilatör %42 olarak belirlenmiştir.
- Tespit edilen tüm SHİE'ler arasında, 52 santral kateter ilişkili kan dolaşım enfeksiyonu (SKİ-KDE)**,** 34 kateter ilişkili idrar yolu enfeksiyonu (Kİ-ÜSE) ve 35 ventilatör ilişkili olay (VİO) olmak üzere toplam 121 (%32,4) invaziv araç ilişkili enfeksiyon kaydedilmiştir.
- İnvaziv araç ilişkili enfeksiyonları önlemede en etkili yöntemler arasında el hijyeni ve bakım paketlerinin (bundle) uygulanması gibi enfeksiyon kontrol önlemleri yer almaktadır.
- Hastane enfeksiyonlarıyla mücadelede günümüzde en yaygın kabul gören yaklaşım, aktif, prospektif ve hasta bazlı sürveyans çalışmalarının düzenli yürütülmesi ve elde edilen verilere göre kontrol önlemlerinin alınmasıdır. Etkin bir sürveyans sistemi, hastaneler arası enfeksiyon oranlarının bilinmesini sağlayarak doğru enfeksiyon kontrol stratejilerinin geliştirilmesine imkân verir. Ayrıca, sağlık hizmeti ortamında görülen enfeksiyon etkenlerinin belirlenmesi, bu enfeksiyonların önlenmesi ve tedavisinde kritik öneme sahiptir.
- SHİE'ler, hastanede kalış süresi uzadıkça daha kolay gelişebilir. Bu nedenle, koruyucu sağlık hizmetlerinin yaygınlaştırılması ve günübirlik sağlık hizmetlerinin teşvik edilmesi**,** enfeksiyon oranlarını düşürmede uygulanabilecek etkili stratejiler arasında sayılabilir.

KAYNAKLAR

1. Karatay G., Gürarslan Baş, N. Sağlık hizmeti ilişkili enfeksiyonlar. Bulaşıcı Hastalıklar Epidemiyolojisi Yönetimi ve Bakımı. 2020; 223-237.
2. Yataklı Tedavi Kurumları Enfeksiyon Kontrol Yönetmeliği. Resmi Gazete Sayısı: 25903. Resmi Gazete Tarihi: 11.08.2005. Erişim tarihi: 20 Nisan 2025. https://www.resmigazete.gov.tr/eskiler/2005/08/20050811-6.htm
3. 3World Health Organization. Report on the burden of endemic health care-associated infection worldwide. 2011

4. Hekimoğlu, C. H. Sağlık hizmeti ilişkili enfeksiyon salgınlarının incelenmesi. BUHASDER Kongresi, 2019; 8, 77-86.

5. Corrigan, J. M., Adams, K. Priority areas for national action: transforming health care quality. 2003

6. T.C. Sayıştay Başkanlığı Performans Denetimi Raporu. Hastane enfeksiyonları ile mücadele. 2007; s:31

7. T.C. Sağlık Bakanlığı Halk Sağlığı Genel Müdürlüğü Bulaşıcı Hastalıklar Dairesi Başkanlığı. Cerrahi alan enfeksiyonu sürveyansı. 2018

8. National Healthcare Safety Network (NHSN). Surgical site infections. 2025;9(1): 1-2

9. Anderson D. J., Podgorny K., Berríos-Torres S. I., Bratzler D. W., Dellinger, E. P., Greene L., Kaye K. S. Strategies to prevent surgical site infections in acute care hospitals: 2014 update. Infection Control & Hospital Epidemiology, 2014; 35(S2), S66-S88.

10.Berríos-Torres S. I., Umscheid C. A., Bratzler D. W., Leas, B., Stone, E. C., Kelz, R. R., Healthcare Infection Control Practices Advisory Committee. Centers for disease control and prevention guideline for the prevention of surgical site infection. JAMA surgery, 2017; 152(8), 784-791

11.Çetinkaya Şardan Y., Güner R., Çakar N., Ağalar F., Bolaman Z., Yavaşoğlu, İ. Yılmaz, G. R. Damar içi kateter infeksiyonlarının önlenmesi kılavuzu. Hastane İnfeksiyonları Dergisi, 2013; 17(2), 233-79

12.Türk Hastane İnfeksiyonları Ve Kontrolü Derneği. Ulusal damar erişim rehberi. Hastane Infeksiyonları Dergisi. 2019 ;15-35

13.13T.C. Sağlık Bakanlığı Halk Sağlığı Genel Müdürlüğü Bulaşıcı Hastalıklar Dairesi Başkanlığı. Ulusal sağlık hizmeti ilişkili enfeksiyonlar sürveyans ağı özet raporu (USHIESA). 2024

14.14 National Healthcare Safety Network (NHSN). Bloodstream infection events (Central line-associated bloodstream infection and non-central line-associated infections). 2025; 9(1): 1-2

15.Türe Yüce Z, Alp E. Infection control bundles for the prevention of hospital infections. Mediterranean Journal of Infection Microbes and Antimicrobials. 2016; 5(8): 5
16.T.C. Sağlık Bakanlığı Halk Sağlığı Genel Müdürlüğü Bulaşıcı Hastalıklar Dairesi Başkanlığı. Ulusal Sağlık Hizmeti Ilişkili Enfeksiyonlar Sürveyans Ağı (USHIESA)Etken Dağılım Ve Direnç Raporu-2024

17.National Healthcare Safety Network (NHSN). Urinary tract ınfection (Catheter-Associated Urinary Tract Infection and Non-Catheter-Associated Urinary Tract Infection). 2025; 9(1): 3-4

18.T.C. Sağlık Bakanlığı Halk Sağlığı Genel Müdürlüğü Ulusal Enfeksiyon Önleme Ve Kontrol Danışma Kurulu Çalışması. sağlık hizmeti ilişkili enfeksiyonlar ulusal önlem paketi uygulamaları. 2021

19.Çalışkaner D. Ventilatör ilişkili pnömoninin önlenmesinde risk faktörlerine yönelik koruyu önlemler ve klinik uygulamalar. Yoğun Bakım Hemşireliği Dergisi, 2020; 24(3), 237-244.

20.T.C. Sağlık Bakanlığı Halk Sağlığı Genel Müdürlüğü Bulaşıcı Hastalıklar Dairesi Başkanlığı, Sağlık Hizmeti Ilişkili Enfeksiyonları Önleme Ve Kontrol Birimi. Ventilator ilişkili olay klavuzu. 2020

21.Tağrıkulu H., Memiş D., İnal M. T., Turan N. Yoğun bakım hastalarında ventilatör ilişkili pnömoni insidansının araştırılması. Journal of the Turkish Society of Intensive Care/Türk Yogun Bakım Dernegi Dergisi. 2016; 14(1).

22.National Healthcare Safety Network (NHSN). Ventilator-associated event. 2025; 9(1): 2-3
23.Martinez-Reviejo R., Tejada S., Jansson, M., Ruiz-Spinelli A., Ramirez-Estrada S., Ege D., Rello J. Prevention of ventilator-associated pneumonia through care bundles: A systematic review and meta-analysis. Journal of Intensive Medicine, 2023; 3(04), 352-364.

24.Blot, S., Ruppé, E., Harbarth, S., Asehnoune, K., Poulakou, G., Luyt, C. E., ... & Zahar, J. R. (2022). Healthcare-associated infections in adult intensive care unit patients: Changes in epidemiology, diagnosis, prevention and contributions of new technologies. *Intensive and Critical Care Nursing*, *70*, 103227.

25.Sikora, A., & Zahra, F. (2020). Nosocomial infections.
26.26. Revelas, A. (2012). Healthcare-associated infections: A public health problem. *Nigerian medical journal*, *53*(2).
27.27. https://www.ecdc.europa.eu/en/healthcare-associated-infections. Erişim tarihi: 11 Haziran 2025
28.28. Sönmez, A., Öztürk, Ş. B., & Abacıgil, F. (2021). Sağlık hizmeti ilişkili enfeksiyon epidemiyolojisi ve sürveyansı. *Hemşirelik Bilimi Dergisi*, *4*(1), 41-45.
29.Alanlı, R., & Beşirbellioğlu, B. A. (2023). Erişkin Yoğun Bakım Ünitesindeki Hastane Enfeksiyonu Etkenlerinin Değerlendirilmesi: Retrospektif Çalişma. *Akdeniz Tıp Dergisi*, *9*(1), 37-43.
30.30. Tüfek, A., Tekin, R., Dal, T., Tokgöz, O., Doğan, E., Kavak, G. Ö., & Hoşoğlu, S. (2012). Reanimasyon ünitesinde on yıllık sürede gelişen hastane enfeksiyonlarının değerlendirilmesi ve literatürün gözden geçirilmesi. *Dicle Medical Journal*, *39*(4), 492-498.
31.31. Karagun, B. Ş., Akyıldız, Ö., Onaç, H., Kaya, F., Erdemler, F., Çetin, T. Ö., ... & Alhan, E. (2020). Adana Acıbadem Hastanesinde hastane enfeksiyonları surveyansı: bir yıllık analiz sonuçları. *Acıbadem Üniversitesi Sağlık Bilimleri Dergisi*, (3), 478-482.
32. ECDC. Annual epidemiological report for 2021. Healthcare associated infections acquired in intensive care units. 2021
33.Çoksak, A., Çelik, Y., Danacı, C., & Sökel, S. Yoğun bakım ünitelerinde invaziv uygulamalar ve enfeksiyon ilişkisi
34.Erdem, H. A., Sipahi, O. R., Kepeli, N., Dikiş, D., Küçükler, N. D., Ulusoy, B., ... & ULUSOY, S. (2015). Ege Üniversitesi Hastanesi'nde hastane infeksiyonları nokta prevalansı. *Mediterranean Journal of Infection Microbes Antimicrobials*, *4*, 12-24.
35.35. https://www.inicc.org/site/about-health-care-associated-infections/. Erişim tarihi : 10 Haziran 2025
36.36. Rosenthal, V. D., Yin, R., Jin, Z., Alkhawaja, S. A., Zuñiga-Chavarria, M. A., Salgado, E., ... & Memish, Z. A. (2024). International Nosocomial Infection Control Consortium (INICC) report of health care-associated infections, data summary of 25 countries for 2014 to 2023, Surgical Site Infections Module. *American Journal of Infection Control*, *52*(10), 1144-1151.
37.37. ECDC. Annual epidemiological report. Healthcare associated infections: surgical site infections 2018-2020. 13 February 2023
38.38. Gaid, E., Assiri, A., McNabb, S., & Banjar, W. (2017). Device-associated nosocomial infection in general hospitals, Kingdom of Saudi Arabia, 2013–2016. *Journal of epidemiology and global health*, *7*(Suppl 1), S35-S40.
39.39. Koch, A. M., Nilsen, R. M., Eriksen, H. M., Cox, R. J., & Harthug, S. (2015). Mortality related to hospital-associated infections in a tertiary hospital; repeated cross-sectional studies between 2004-2011. *Antimicrobial resistance and infection control*, *4*, 1-8.
40.40. Vincent, J. L., Rello, J., Marshall, J., Silva, E., Anzueto, A., Martin, C. D., ... & EPIC II Group of Investigators, X. (2009). International study of the prevalence and outcomes of infection in intensive care units. *Jama*, *302*(21), 2323-2329.
41.41. Klevens, R. M., Edwards, J. R., Richards Jr, C. L., Horan, T. C., Gaynes, R. P., Pollock, D. A., & Cardo, D. M. (2007). Estimating health care-associated infections and deaths in US hospitals, 2002. *Public health reports*, *122*(2), 160-166.
42.Arefian, H., Hagel, S., Fischer, D., Scherag, A., Brunkhorst, F. M., Maschmann, J., & Hartmann, M. (2019). Estimating extra length of stay due to healthcare-associated infections before and after implementation of a hospital-wide infection control program. *PLoS One*, *14*(5), e0217159.
43.43 Shepard, J., Frederick, J., Wong, F., Madison, S., Tompkins, L., & Hadhazy, E. (2020). Could the prevention of health care–associated infections increase hospital cost? The financial impact of health

care–associated infections from a hospital management perspective. *American journal of infection control*, *48*(3), 255-260.
44.44. Esatoğlu, A. E., Agirbas, I., Onder, O. R., & Celik, Y. (2006). Additional cost of hospital-acquired infection to the patient: a case study in Turkey. *Health Services Management Research*, *19*(3), 137-143
45.. Rosenthal, V. D., Yin, R., Nercelles, P., Rivera-Molina, S. E., Jyoti, S., Dongol, R., ... & Jin, Z. (2024). International Nosocomial Infection Control Consortium (INICC) report of health care associated infections, data summary of 45 countries for 2015 to 2020, adult and pediatric units, device-associated module. *American Journal of Infection Control*, *52*(9), 1002-1011.
46.Mert, D., Demirkıran, B. Ç., İskender, G., Avşar, Z., Timuroğlu, A., Binay, S., ... & Ertek, M. (2024). Six-year evaluation of device-associated nosocomial infections in intensive care units. *The Journal of Infection in Developing Countries*, *18*(06), 937-942.
47.Nuvials, X., Fernández, I., Almendral, A., Limón, E., Pujol, M., & Diaz, E. (2025). Surveillance of device-associated infection rates at adult intensive care units in the VINCat program (2010–2022). *Enfermedades Infecciosas y Microbiología Clínica*.

CLINICOPATHOLOGICAL PREDICTORS OF RECURRENCE AND MORTALITY IN UTERINE LEIOMYOSARCOMA: THE POTENTIAL ROLE OF PREOPERATIVE INFLAMMATORY MARKERS

Orhan Ay

Department of Obstetrics and Gynecology, Necmettin Erbakan University Faculty of Medicine, Konya, Turkey, ORCID ID:0000-0002-9685-5374

Pelin Bahçeci

Department of Obstetrics and Gynecology, Necmettin Erbakan University Faculty of Medicine, Konya, Turkey, ORCID ID: 0009-0008-2615-3052

Ali Acar

Department of Obstetrics and Gynecology, Necmettin Erbakan University Faculty of Medicine, Konya, Turkey, ORCID ID :0009-0006-1474-3958

Objective: Uterine leiomyosarcoma is a rare uterine malignancy notable for its aggressive clinical course, high recurrence rate, and substantial mortality risk. This study aimed to evaluate the clinicopathological characteristics associated with recurrence and mortality, as well as preoperative hematological and inflammatory markers, in patients diagnosed with uterine leiomyosarcoma.

Materials and Methods: This retrospective study was conducted at Necmettin Erbakan University, Faculty of Medicine. A total of 19 patients diagnosed with uterine leiomyosarcoma between January 2018 and December 2025 were included. Demographic characteristics, tumor features, stage, grade, myometrial invasion, adjuvant treatments, and preoperative hematological parameters were analyzed. In addition to neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), and platelet-to-lymphocyte ratio (PLR), systemic immune-inflammation index (SII), systemic inflammation response index (SIRI), hemoglobin-albumin-lymphocyte-platelet (HALP) score, pan-immune-inflammation value (PIV), and neutrophil percentage-to-albumin ratio (NPAR) were calculated. Welch's t-test or Mann–Whitney U test were used for continuous variables, and categorical variables were analyzed using Fisher's exact test or chi-square test, as appropriate. A p-value of <0.05 was considered statistically significant.

Results: Recurrence occurred in 14 patients (73.7%), while mortality was observed in 6 patients (31.6%). Patients with recurrence had significantly higher NLR [3.56 (3.06–4.47) vs 2.67 (1.92–2.71), p=0.019], MLR (0.42±0.19 vs 0.21±0.11, p=0.010), and SIRI (2.93±1.59 vs 1.35±1.07, p=0.032). SII was also higher in the recurrence group and showed borderline significance (p=0.051). In terms of mortality, maximum tumor diameter (p=0.043), depth of invasion (p=0.007), advanced-stage disease (p=0.041), high grade (p=0.010), and ≥50% myometrial invasion (p=0.001) were significantly associated with death.

Conclusion: In uterine leiomyosarcoma, recurrence appears to be associated with markers of systemic inflammatory response, whereas mortality seems to be more closely related to clinicopathological features reflecting aggressive tumor biology. Easily obtainable preoperative indices, particularly NLR, MLR, and SIRI, may be useful in predicting recurrence.

Keywords: Uterine leiomyosarcoma; recurrence; mortality; inflammatory markers; neutrophil-to-lymphocyte ratio

Introduction

Uterine leiomyosarcoma (uLMS) is a rare but highly aggressive malignant mesenchymal tumor arising from the smooth muscle layer of the uterus. Although uterine sarcomas account for only a small proportion of all uterine malignancies, uLMS represents one of the most clinically relevant histological subtypes within this group, owing to its propensity for early metastasis, high risk of recurrence, and

limited response to available adjuvant treatment strategies (1). Unlike endometrial carcinoma, uLMS often lacks specific early clinical manifestations. Symptoms such as abnormal uterine bleeding, pelvic pain, or an enlarging uterine mass substantially overlap with those of benign leiomyomas. Therefore, preoperative diagnosis remains challenging, and in many cases the definitive diagnosis is established only after postoperative histopathological examination (2).

The clinical course of uLMS is often unpredictable. Even when the disease appears confined to the uterus and complete surgical resection is achieved, recurrence may occur early; moreover, distant metastases are relatively common because of the tumor's tendency for hematogenous dissemination (2,3). Recurrence rates reported in retrospective series remain high, and survival outcomes are markedly influenced by disease stage, tumor burden, resection status, time to recurrence, and recurrence pattern (3,4). In patients with recurrent uLMS, a shorter interval to first recurrence has been associated with poorer survival (5). This suggests that the timing of recurrence may reflect not only treatment response but also the intrinsic biological aggressiveness of the tumor. Accordingly, practical prognostic markers are needed to help identify patients at increased risk of recurrence or mortality during follow-up.

Prognostic assessment in uLMS has traditionally relied on clinicopathological factors. Advanced FIGO stage, larger tumor diameter, deep myometrial invasion, high tumor grade, lymphovascular space invasion, extrauterine spread, tumor-positive surgical margins, and residual disease are among the main variables that may be associated with recurrence and survival outcomes (3,4). Current international guidelines emphasize the importance of histology-specific management, expert pathological review, multidisciplinary decision-making, and structured follow-up strategies in patients with uterine sarcomas (1). Nevertheless, because uLMS is rare, prospective studies are difficult to conduct, and much of the available evidence is derived from retrospective cohorts. Therefore, real-world data remain valuable for improving our understanding of the prognostic features of this disease and for refining risk stratification.

In recent years, the relationship between cancer progression and systemic inflammation has attracted increasing attention. Tumor-associated inflammation may contribute to angiogenesis, immune escape, invasion, and metastatic dissemination. Peripheral blood parameters may serve as indirect but readily measurable indicators of this biological interaction. Indices such as the neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, monocyte-to-lymphocyte ratio, systemic immune-inflammation index, systemic inflammation response index, prognostic nutritional index, hemoglobin-albumin-lymphocyte-platelet score, and pan-immune-inflammation value combine inflammatory, immune, hematological, and nutritional components into practical markers. Their main advantage is that they can be calculated from routine preoperative laboratory tests without additional cost or advanced technical requirements.

Meta-analyses conducted in gynecologic malignancies and other solid tumors have shown that elevated inflammatory markers, particularly the systemic immune-inflammation index and systemic inflammation response index, may be associated with poorer oncologic outcomes (6,7). However, evidence specific to uLMS remains limited. This is mainly attributable to the rarity of the disease and the small sample sizes of most available studies. Although a recent study on uLMS reported that inflammation-based markers such as NLR and PLR may have prognostic value, the current literature is still insufficient to define reliable cut-off values or to support the use of these indices as independent clinical decision-making tools (8). Therefore, single-center series that evaluate both conventional clinicopathological variables and a broad panel of preoperative inflammatory markers may provide meaningful contributions to the literature.

In this context, the present study aimed to evaluate the clinicopathological characteristics associated with recurrence and mortality in patients diagnosed with uterine leiomyosarcoma and to investigate the potential prognostic role of preoperative hematologic and systemic inflammatory markers. By examining conventional tumor-related prognostic factors together with blood-based indices that can be easily derived from routine laboratory tests, this study sought to determine whether recurrence and mortality in uLMS are associated with distinct biological and clinical profiles.

Materials and Methods

Study design and patient population

This study was designed as a retrospective, single-center cohort study conducted at the Department of Obstetrics and Gynecology, Necmettin Erbakan University Faculty of Medicine. The medical records of patients diagnosed with uterine leiomyosarcoma at our institution between January 2018 and December 2025 were retrospectively reviewed. A total of 19 patients with a postoperative histopathological diagnosis of uterine leiomyosarcoma were included in the study.

Patient data were obtained from the electronic medical record system, operative notes, pathology reports, oncology follow-up records, and laboratory results. Patients with histological subtypes other than uterine leiomyosarcoma, those with primary extrauterine sarcoma, and those with unavailable essential clinicopathological or preoperative laboratory data were excluded from the study.

Evaluated variables

Age at diagnosis, parity, tumor location, maximum tumor diameter, depth of myometrial invasion, lymphovascular space invasion, peritoneal cytology findings, surgical margin status, lymph node metastasis, FIGO stage, tumor grade, and receipt of adjuvant chemotherapy and/or radiotherapy were recorded. Preoperative hematologic parameters were obtained from complete blood count and biochemical test results measured before surgery. These parameters included white blood cell count, neutrophil count, lymphocyte count, monocyte count, eosinophil count, basophil count, hemoglobin, hematocrit, platelet count, red cell distribution width, plateletcrit, platelet distribution width, and serum albumin level.

Calculation of inflammatory and nutritional indices

Hematologic, inflammatory, and nutritional indices were calculated using routine preoperative laboratory parameters. The neutrophil-to-lymphocyte ratio (NLR) was calculated by dividing the neutrophil count by the lymphocyte count; the monocyte-to-lymphocyte ratio (MLR) was calculated by dividing the monocyte count by the lymphocyte count; and the platelet-to-lymphocyte ratio (PLR) was calculated by dividing the platelet count by the lymphocyte count.

The systemic immune-inflammation index (SII) was calculated using the formula platelet count × neutrophil count / lymphocyte count, and the systemic inflammation response index (SIRI) was calculated using the formula neutrophil count × monocyte count / lymphocyte count. The derived neutrophil-to-lymphocyte ratio (dNLR) was calculated as neutrophil count / (white blood cell count − neutrophil count). The pan-immune-inflammation value (PIV) was calculated as neutrophil count × platelet count × monocyte count / lymphocyte count.

The prognostic nutritional index (PNI) was calculated using the formula 10 × serum albumin level (g/dL) + 0.005 × total lymphocyte count (/mm³). The hemoglobin-albumin-lymphocyte-platelet (HALP) score was calculated as hemoglobin × albumin × lymphocyte count / platelet count. The neutrophil percentage-to-albumin ratio (NPAR) was obtained by dividing the neutrophil percentage by the serum albumin level.

Outcome variables

The primary outcome variables of the study were recurrence and mortality. Recurrence was defined as the reappearance of disease after primary surgery and/or adjuvant treatment, documented clinically, radiologically, or histopathologically. The interval between diagnosis and recurrence was recorded in months. Mortality status was determined according to survival status at the last follow-up, and patients were categorized as alive or deceased.

For the analyses, patients were first compared according to recurrence status as those with and without recurrence. In the second step, patients who were alive and those who had died were compared in terms of clinicopathological variables and preoperative inflammatory indices.

Statistical analysis

The distribution of continuous variables was assessed using the Shapiro–Wilk test. Continuous variables with normal distribution were presented as mean ± standard deviation, whereas non-normally distributed variables were presented as median and interquartile range. For comparisons between two groups, Welch's t-test was used for normally distributed continuous variables, and the Mann–Whitney U test was used for non-normally distributed variables.

Categorical variables were compared using Fisher's exact test or Pearson's chi-square test, as appropriate. Exact methods were preferred when expected cell counts were small. A two-sided p value of <0.05 was considered statistically significant in all analyses.

Ethical approval

Ethical approval for this retrospective study was obtained from the Necmettin Erbakan University Non-Drug and Non-Medical Device Research Ethics Committee (Decision No: 2026/6441, March 27, 2026). Owing to the retrospective design of the study, the requirement for informed consent was waived by the ethics committee. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Results

A total of 19 patients with histopathologically confirmed uterine leiomyosarcoma were included in the study. The median age at diagnosis was 54.0 years (IQR: 50.0–63.5), and the median maximum tumor diameter was 8.0 cm (IQR: 2.5–12.5). During follow-up, recurrence occurred in 14 patients (73.7%), while death was observed in 6 patients (31.6%). Among patients who developed recurrence, the median interval from diagnosis to recurrence was 16.5 months (IQR: 4.8–23.0).

Regarding clinicopathological characteristics, 8 patients (42.1%) had advanced-stage disease, 7 patients (36.8%) had Grade 3 tumors, and 8 patients (42.1%) had ≥50% myometrial invasion. LVSI and positive/malignant peritoneal cytology were each detected in 4 patients (21.1%). Tumor-positive surgical margins were observed in 2 patients (10.5%), and lymph node positivity was identified in 1 patient (5.3%). Fourteen patients (73.7%) received chemotherapy, and 3 patients (15.8%) received radiotherapy. The general clinicopathological characteristics of the patients are shown in Table 1.

Table 1. General clinicopathological characteristics of the patients

Variable	Value
Number of patients	19
Age at diagnosis, years, median (IQR)	54.0 (50.0–63.5)
Maximum tumor diameter, cm, median (IQR)	8.0 (2.5–12.5)
Recurrence, n (%)	14 (73.7)
Death, n (%)	6 (31.6)
Time from diagnosis to recurrence, months, median (IQR)*	16.5 (4.8–23.0)
Advanced stage (FIGO stage III–IV), n (%)	8 (42.1)
Grade 3 tumor, n (%)	7 (36.8)
Deep myometrial invasion (≥50%), n (%)	8 (42.1)
LVSI, n (%)	4 (21.1)
Positive/malignant peritoneal cytology, n (%)	4 (21.1)

Tumor-positive surgical margin, n (%)	2 (10.5)
Positive lymph node, n (%)	1 (5.3)
Received chemotherapy, n (%)	14 (73.7)
Received radiotherapy, n (%)	3 (15.8)

*Calculated only among patients who developed recurrence.

IQR: interquartile range; FIGO: International Federation of Gynecology and Obstetrics; LVSI: lymphovascular space invasion.

In the comparison according to recurrence status, maximum tumor diameter and depth of invasion appeared to be higher among patients who developed recurrence; however, these differences did not reach statistical significance. Similarly, advanced-stage disease, Grade 3 tumors, and ≥50% myometrial invasion were more frequent in the recurrence group, but no statistically significant differences were observed in the binary comparisons. However, when grade distribution was evaluated, a statistically significant difference was observed between the groups (p=0.042). The rate of chemotherapy use was higher among patients who developed recurrence (p=0.006); however, this finding should be interpreted with caution, as chemotherapy may have been administered more frequently to patients with higher-risk clinicopathological features. Comparisons according to recurrence status are presented in Table 2.

Regarding preoperative inflammatory markers, NLR was significantly higher in patients who developed recurrence than in those without recurrence [3.56 (3.06–4.47) vs 2.67 (1.92–2.71), p=0.019]. Similarly, MLR was higher in the recurrence group (0.42±0.19 vs 0.21±0.11, p=0.010). SIRI was also significantly increased among patients with recurrence (2.93±1.59 vs 1.35±1.07, p=0.032). SII was higher in the recurrence group and showed borderline statistical significance (1339.42±771.69 vs 798.23±338.21, p=0.051). Although PLR, dNLR, PIV, and NPAR were numerically higher in patients who developed recurrence, these differences did not reach statistical significance.

Table 2. Comparison of selected clinicopathological and inflammatory variables according to recurrence status

Variable	No recurrence (n=5)	Recurrence (n=14)	p value
Age at diagnosis, years	58.00 ± 14.97	54.86 ± 9.02	0.677
Maximum tumor diameter, cm	2.50 (2.00–3.00)	10.50 (2.88–12.75)	0.163
Depth of invasion, mm	3.40 ± 2.30	5.71 ± 4.08	0.147
≥50% myometrial invasion, n (%)	1 (20.0)	7 (50.0)	0.338
Advanced stage (FIGO stage III–IV), n (%)	1 (20.0)	7 (50.0)	0.338
Grade 3 tumor, n (%)	1 (20.0)	6 (42.9)	0.603
Grade distribution (Grade 1/2/3), n	2/2/1	0/8/6	**0.042**
Received chemotherapy, n (%)	1 (20.0)	13 (92.9)	**0.006**
NLR	2.67 (1.92–2.71)	3.56 (3.06–4.47)	**0.019**

MLR	0.21 ± 0.11	0.42 ± 0.19	**0.010**
PLR	139.83 ± 42.52	188.48 ± 92.10	0.138
SII	798.23 ± 338.21	1339.42 ± 771.69	0.051
SIRI	1.35 ± 1.07	2.93 ± 1.59	**0.032**
dNLR	1.94 (1.55–2.24)	2.40 (1.96–2.99)	0.087
PIV	374.40 (192.12–755.87)	791.63 (503.75–1277.26)	0.156
NPAR	1.52 (1.52–1.53)	1.69 (1.61–1.95)	0.107

Values are presented as mean ± standard deviation or median (IQR), according to distribution. Categorical variables are presented as n (%).

NLR: neutrophil-to-lymphocyte ratio; MLR: monocyte-to-lymphocyte ratio; PLR: platelet-to-lymphocyte ratio; SII: systemic immune-inflammation index; SIRI: systemic inflammation response index; dNLR: derived neutrophil-to-lymphocyte ratio; PIV: pan-immune-inflammation value; NPAR: neutrophil percentage-to-albumin ratio.

In the analysis according to mortality status, the median maximum tumor diameter was significantly higher in deceased patients than in those who were alive [12.50 cm (IQR: 9.00–18.25) vs 2.50 cm (IQR: 2.00–11.00), p=0.043]. Similarly, the depth of invasion was significantly greater in patients who died [9.00 mm (IQR: 7.50–9.00) vs 3.00 mm (IQR: 1.00–4.00), p=0.007]. Myometrial invasion of ≥50% was observed in all deceased patients, compared with 15.4% of patients who were alive (p=0.001). Advanced-stage disease was more frequent among deceased patients than among surviving patients (83.3% vs 23.1%, p=0.041). The proportion of Grade 3 tumors was also markedly higher among deceased patients (83.3% vs 15.4%, p=0.010). Grade distribution also differed significantly between the groups (p=0.016). Comparisons according to mortality status are presented in Table 3.

When the relationship between mortality and preoperative inflammatory markers was evaluated, NLR, SII, SIRI, and NPAR were numerically higher in deceased patients, whereas PNI was lower. However, these differences did not reach statistical significance. Therefore, in the present series, mortality-related findings appeared to be associated primarily with clinicopathological features reflecting aggressive tumor biology, such as maximum tumor diameter, depth of invasion, advanced stage, high grade, and deep myometrial invasion, rather than with inflammatory markers.

Table 3. Comparison of selected clinicopathological and inflammatory variables according to mortality status

Variable	**Alive (n=13)**	**Deceased (n=6)**	**p value**
Age at diagnosis, years	53.69 ± 10.89	60.00 ± 8.99	0.210
Maximum tumor diameter, cm	2.50 (2.00–11.00)	12.50 (9.00–18.25)	**0.043**
Depth of invasion, mm	3.00 (1.00–4.00)	9.00 (7.50–9.00)	**0.007**
≥50% myometrial invasion, n (%)	2 (15.4)	6 (100.0)	**0.001**
Advanced stage (FIGO stage III–IV), n (%)	3 (23.1)	5 (83.3)	**0.041**

Grade 3 tumor, n (%)	2 (15.4)	5 (83.3)	**0.010**
Grade distribution (Grade 1/2/3), n	2/9/2	0/1/5	**0.016**
LVSI, n (%)	0 (0.0)	1 (16.7)	0.316
Tumor-positive surgical margin, n (%)	0 (0.0)	1 (16.7)	0.316
NLR	3.11 (2.67–3.39)	4.01 (3.21–4.47)	0.323
MLR	0.34 ± 0.13	0.40 ± 0.31	0.674
SII	1117.50 ± 554.43	1369.25 ± 1032.40	0.594
SIRI	2.22 ± 1.06	3.14 ± 2.45	0.415
PNI	53.15 ± 5.89	44.37 ± 12.21	0.144
NPAR	1.61 ± 0.24	2.27 ± 0.92	0.144

Values are presented as mean ± standard deviation or median (IQR), according to distribution. Categorical variables are presented as n (%).

IQR: interquartile range; LVSI: lymphovascular space invasion; NLR: neutrophil-to-lymphocyte ratio; MLR: monocyte-to-lymphocyte ratio; SII: systemic immune-inflammation index; SIRI: systemic inflammation response index; PNI: prognostic nutritional index; NPAR: neutrophil percentage-to-albumin ratio.

Discussion

In this study, two distinct prognostic patterns were observed among patients with uterine leiomyosarcoma. First, patients who developed recurrence had significantly higher preoperative inflammatory markers, including NLR, MLR, and SIRI, while SII showed borderline statistical significance. Second, among patients who died, conventional clinicopathological variables reflecting aggressive tumor biology such as maximum tumor diameter, depth of invasion, advanced-stage disease, Grade 3 tumor, and ≥50% myometrial invasion were more prominent than systemic inflammatory markers. This distinction suggests that the risk of recurrence in uLMS may be related not only to anatomical spread or tumor size but also to the host–tumor inflammatory response, whereas mortality appears to be driven mainly by the macroscopic and histopathological aggressiveness of the disease.

Despite its rarity, uterine leiomyosarcoma is considered one of the most aggressive subtypes of uterine sarcoma because of its tendency for early hematogenous dissemination, high recurrence rate, and limited treatment response. Current ESGO/EURACAN/GCIG and GEIS guidelines particularly emphasize histology-specific management, expert pathological review, multidisciplinary decision-making, and long-term follow-up in patients with uterine sarcomas (1,9). This emphasis is consistent with the findings of the present study, as the high recurrence rate observed in our series and the relatively short interval from diagnosis to recurrence among recurrent cases support the clinically aggressive nature of uLMS. Nevertheless, recurrence rates in single-center series with limited sample sizes should be interpreted with caution, as they may be influenced by institutional case mix, referral patterns, follow-up duration, and patient selection.

In the current literature, the most consistent factors associated with survival and recurrence in uLMS include disease stage, tumor size, tumor grade, LVSI, resection status, and extent of disease. In a multicenter Turkish series including 302 patients with uLMS, the 5-year disease-free survival and overall survival rates were reported as 42% and 54%, respectively, and variables such as LVSI, advanced stage, and age were associated with adverse outcomes (10). In an older but large population-based series,

disease-specific survival was also markedly lower in patients with lymph node positivity (11). In our series, the significantly higher frequency of advanced-stage disease, Grade 3 tumors, larger maximum tumor diameter, and deep myometrial invasion among deceased patients is consistent with this established prognostic framework. Therefore, our mortality-related findings appear to be explained primarily by the anatomical extent and histopathological aggressiveness of the tumor rather than by inflammatory indices.

Regarding recurrence, the most notable finding of our study was that preoperative NLR, MLR, and SIRI values were significantly higher in patients who developed recurrence. NLR is a simple marker reflecting the balance between neutrophil-mediated inflammatory activity and lymphocyte-mediated antitumor immune response. In a multicenter study of uterine sarcomas, elevated preoperative NLR was associated with poorer disease-free and overall survival, and it was identified as an independent prognostic factor together with advanced stage and high mitotic index (12). A more recent uLMS-specific study also suggested that inflammation-based markers may have prognostic relevance (8). In this context, the association between NLR and recurrence observed in our series is biologically plausible and consistent with the existing literature; however, larger cohorts are needed before concluding that this relationship has independent prognostic value.

The findings regarding MLR and SIRI are also noteworthy. Monocytes and neutrophils may participate in tumor microenvironment-related processes such as angiogenesis, stromal remodeling, immune suppression, and metastatic potential. Because SIRI incorporates neutrophil, monocyte, and lymphocyte components, it may reflect a broader inflammatory-immune response profile than NLR alone. Recent systematic reviews and meta-analyses in gynecologic cancers have shown that composite inflammatory indices such as SII and SIRI may have prognostic value for survival and recurrence outcomes (13-15). In our study, the significant association between SIRI and recurrence, together with the borderline significance observed for SII, is consistent with this broader literature; nevertheless, these findings should be viewed as hypothesis-generating and require further validation specifically in uLMS.

In contrast, it is important to note that inflammatory markers did not reach statistical significance in the mortality analysis. Although NLR, SII, SIRI, and NPAR values were numerically higher among deceased patients, these differences were not statistically significant. Several explanations may account for this finding. First, the small number of patients who died may have limited the statistical power of the analysis. Second, in uLMS, the main determinants of mortality are often stronger clinicopathological factors, such as disease stage, depth of invasion, tumor grade, and tumor burden. Third, even if preoperative inflammatory indices reflect the tendency for recurrence, the processes leading to death may be influenced by more complex factors, including treatment response, metastatic pattern, completeness of resection, therapeutic options after recurrence, and the patient's general condition. Therefore, the present findings should not be interpreted as evidence that inflammatory markers are strong direct predictors of mortality. Rather, they may serve as low-cost adjunctive markers that provide additional biological information, particularly regarding recurrence risk.

The higher rate of chemotherapy use among patients who developed recurrence in our study should also be interpreted with caution. This finding does not imply that chemotherapy increased the risk of recurrence. A more plausible explanation is that adjuvant treatment was administered more frequently to patients with high-risk features, such as larger tumors, advanced-stage disease, or more aggressive pathological characteristics. In retrospective studies, this issue is commonly referred to as confounding by indication and limits the direct interpretation of treatment effects. Current guidelines also recommend that adjuvant and systemic treatment decisions in uLMS should be individualized according to histological subtype, disease stage, resection status, patient performance status, and multidisciplinary evaluation (1,9). Therefore, the observed association between chemotherapy and recurrence in our study should be considered as a reflection of patient risk profile rather than as an indicator of treatment efficacy.

One of the strengths of this study is the combined evaluation of conventional clinicopathological factors and a broad panel of preoperative inflammatory and nutritional markers in uterine leiomyosarcoma, a rare malignancy. Because complete blood count parameters and serum albumin are readily available in routine clinical practice, these indices are particularly attractive from a practical and resource-conscious

perspective. Nevertheless, the current evidence is insufficient to support the use of inflammatory markers as stand-alone clinical decision-making tools. Therefore, markers such as NLR, MLR, and SIRI should be considered complementary indices that may support clinicopathological risk assessment, rather than independent tests capable of changing treatment decisions on their own.

This study has several limitations. Its retrospective and single-center design may limit the generalizability of the findings. The limited sample size reduced statistical power, particularly in the mortality analysis, and precluded meaningful multivariable modeling. In addition, preoperative inflammatory markers may be affected by infections, chronic inflammatory diseases, medication use, smoking, obesity, and other systemic comorbidities. Therefore, our findings should be viewed as preliminary and hypothesis-generating rather than confirmatory.

In conclusion, recurrence in uterine leiomyosarcoma appeared to be more closely associated with elevated preoperative systemic inflammatory markers, particularly NLR, MLR, and SIRI, whereas mortality was more strongly related to aggressive clinicopathological factors, including larger maximum tumor diameter, greater depth of invasion, advanced stage, high grade, and deep myometrial invasion. These findings suggest that recurrence and mortality in uLMS may not arise from the same prognostic background but may instead reflect partially distinct biological and clinical profiles. Larger, multicenter studies with longer follow-up are needed to clarify the true contribution of these easily accessible inflammatory indices to risk stratification in uLMS.

References

1. Ray-Coquard I, Casali PG, Croce S, et al. ESGO/EURACAN/GCIG guidelines for the management of patients with uterine sarcomas. *International Journal of Gynecological Cancer*. 2024;34(10):1499-1521.

2. Yang Q, Madueke-Laveaux OS, Cun H, et al. Comprehensive review of uterine leiomyosarcoma: pathogenesis, diagnosis, prognosis, and targeted therapy. *Cells*. 2024;13(13):1106.

3. Zapardiel I, Segovia MG, Macuks R, et al. Prognostic factors in patients with uterine sarcoma: the SARCUT study. *International Journal of Gynecological Cancer*. 2023;33(6):897-904.

4. Kontomanolis EN, Sapantzoglou I, Nikolettos K, et al. Clinicopathological Predictors of Recurrence in Uterine Sarcomas—A Narrative Review. *Journal of Clinical Medicine*. 2025;14(14):4883.

5. Yuan H, Wang Y, Li N, Wu L, Yao H. Clinical characteristics and treatment outcomes of women with recurrent uterine leiomyosarcoma. *Orphanet Journal of Rare Diseases*. 2024;19(1):395.

6. Ji Y, Wang H. Prognostic prediction of systemic immune-inflammation index for patients with gynecological and breast cancers: a meta-analysis. *World journal of surgical oncology*. 2020;18(1):197.

7. Guo F, Peng H, Hu H, Liu J. Prognostic Value of Systemic Immune-Inflammation Index in Patients With Gynecological Tumors: A Systematic Review and Meta-Analysis. *American Journal of Reproductive Immunology*. 2025;94(4):e70170.

8. Sekmek S, Köş FT, Uçar G, Bayram D, Civelek B. Comparison of the Clinical Features and Prognostic Value of Inflammation-Based Markers in Uterine Leiomyosarcoma. *Dicle Medical Journal*. 2024;51(3):325-332.

9. Pérez-Fidalgo JA, Ortega E, Ponce J, et al. Uterine sarcomas: clinical practice guidelines for diagnosis, treatment, and follow-up, by Spanish group for research on sarcomas (GEIS). *Therapeutic Advances in Medical Oncology*. 2023;15:17588359231157645.

10. Ayhan A, Gungorduk K, Khatib G, et al. Prognostic factors and survival outcomes of women with uterine leiomyosarcoma: A Turkish Uterine Sarcoma Group Study-003. *Current problems in cancer*. 2021;45(5):100712.

11. Kapp DS, Shin JY, Chan JK. Prognostic factors and survival in 1396 patients with uterine leiomyosarcomas: emphasis on impact of lymphadenectomy and oophorectomy. *Cancer*. 2008;112(4):820-830.

12. Jeong MJ, Park JH, Hur SY, Kim CJ, Nam HS, Lee YS. Preoperative neutrophil-to-lymphocyte ratio as a prognostic factor in uterine sarcoma. *Journal of Clinical Medicine*. 2020;9(9):2898.

13. Chu B, Chen Y, Pan J. Prognostic significance of systemic immune inflammation index for ovarian cancer: An updated systematic review and meta-analysis. *Journal of Ovarian Research*. 2025;18(1):41.

14. Choi M, Lee S-W, Park W, et al. Can posttreatment blood inflammatory markers predict poor survival in gynecologic cancer?: a systematic review and meta-analysis. *Frontiers in Immunology*. 2025;16:1676838.

15. Jiang F, Zhou P. Prognostic significance of systemic immune inflammation index and systemic inflammation response index for cervical cancer: A systematic review and meta-analysis. *Pakistan Journal of Medical Sciences*. 2025;41(11):3306.

HİDROSEL KESESİNDE İYİ DİFERANSİYE PAPİLLER MEZOTELYAL TÜMÖR: PARATESTİKÜLER LEZYONLARIN AYIRICI TANISINDA NADİR BİR ANTİTE

Şeyma Öztürk,

Kırıkkale Üniversitesi Tıp Fakültesi Tıbbi Patoloji Anabilim Dalı/ Doktor Öğretim Üyesi, ORCID:0000-0002-2167-4253

Şeyma Yılmaz Güneş

Tıbbi Patoloji Anabilim Dalı, Kırıkkale Üniversitesi, Tıp Fakültesi, Kırıkkale, Türkiye

Giriş

Paratestiküler mezotelyal tümörler; adenomatoid tümör, iyi diferansiye mezotelyal papiller tümör (WDPMT), mezotelyoma olmak üzere üçe ayrılır(1). WDPMT tek katlı küboidal hücrelerle çevrili papiller yapılardan oluşan noninvaziv bir neoplazmdır. Tunika vajinalis yerleşimi periton ve plevraya göre oldukça nadirdir. Olguların azlığı nedeniyle etiyopatogenezi tam aydınlatılamamıştır. Genellikle 18-70 yaş aralığında görülür(1). Yavaş seyirlidir ve çoğunlukla asemptomatiktir ancak bazen skrotal kitle, şişlik şeklinde prezente olur. Nadiren multifokal olup boyutları 3-30 mm arasında değişkenlik gösterir(1). Önceden bu lezyonlar iyi diferansiye mezotelyoma olarak adlandırılırken DSÖ (Dünya Sağlık Örgütü) bu terimin klinikte maligniteyi çağrıştırarak gereksiz agresif tedavilere yol açabilmesi nedeniyle WDPMT adlandırmasının kullanılmasını önermektedir(2). Bu çalışmada hidrosel kesesinde nadir görülen WDPMT olgusu sunulmuştur.

Olgu Sunumu

87 yaşında erkek hasta sağ testiste şişlik şikayeti ile Üroloji Polikliniğine başvurdu. Fizik muayenesinde skrotal şişliğin hidrosel kesesi nedeniyle oluştuğu düşünüldü. Laboratuvar bulgularında anormallik saptanmadı. Hastaya hidroselektomi yapıldı. Makroskopik incelemede 14x9x8 cm ölçülerinde ince bir kapsülle çevrili kistik yapı (Resim 1a) içerisinde bir alanda 1,7x1,8x1,5 cm ölçülerinde papiller yapı(Resim 1b) dikkati çekti. Bu yapıya 1,2 cm uzaklıkta 5x4x2,5 cm ölçülerinde testis dokusuna ait kahverenkli nodüler kısım görüldü. Mikroskopik incelemede tek katlı mezotel ile döşeli kistik yapı izlendi. Kist içerisinde tek sıralı kübik epitel ile döşeli fibrohyalinize stromaya sahip papiller yapı görüldü(Resim 2a). Epitelde aşikar atipi ve mitoz izlenmedi(Resim 2b,2c). İmmünhistokimyasal çalışmada papiller yapıyı döşeyen epitelde Kalretinin(Resim 3a), WT-1, PAX-8 ve CK7(Resim 3b) pozitif boyandı. D2-40 fokal pozitif(Resim 3c), Östrojen ve Progesteron Reseptörü negatifti(Resim 3d). Bu bulgularla olgu hidrosel kesesi ilişkili WDPMT olarak raporlandı.

Tartışma

WDPMT olgularında hastalar genellikle belirgin ve özgül klinik ya da radyolojik bulgularla başvurmaz. Çoğu vaka asemptomatik seyretmekte olup, az sayıda hasta skrotal şişlik, skrotal ağrı gibi şikayetlerle prezente olur. Lezyonlar genellikle hidrosel, skrotal şişlik/kitle veya inguinal herni ön tanılarıyla gerçekleştirilen cerrahi girişimler sırasında tesadüfen saptanmaktadır(3).Makroskopik incelemelerde tümör kabarık kesit yüzeyine sahip tek papiller nodüler oluşum gösterir ve genellikle hidrosel kesesi içerisinde yer alır(1). Mikroskopide tek katlı küboidal hücrelerle çevrili papiller yapılardan oluşan nükleer atipi göstermeyen bir lezyon görülür. Stromal invazyon genellikle görülmez(1). WDPMT genel olarak benign karakterli bir lezyon olarak kabul edilmekle birlikte, tanımlanan bazı kompleks morfolojik varyantların bu tanı kapsamında değerlendirilip değerlendirilemeyeceği konusunda görüş birliği bulunmamaktadır(1). İmmünohistokimyasal olarak Kalretinin, WT1, D2-40 gibi mezotelyal belirteçlerle pozitif boyanma gösterir. Pansitokeratin pozitifliği beklenir. Aynı zamanda BAP1 ekspresyonu korunmuştur ve CDKN2A homozigot delesyonu yoktur(1). WDPMT için en kritik ayırıcı

tanılar malign mezotelyoma ve adenomatoid tümördür. Adenomatoid tümör, paratestiküler bölgenin en sık görülen benign mezotelyal tümörüdür ve mezotelyal belirteçlerle pozitif boyanabilse de papiller proliferasyon göstermemesi ve belirgin vakuollü tübüler yapılardan oluşması ayırıcı tanıda yardımcıdır(3). Malign mezotelyomada WDPMT'nin aksine invazyon, belirgin nükleer atipi ve yüksek proliferatif aktivite izlenir. Aynı zamanda WDPMT'de genellikle metastaz görülmezken malign mezotelyomada öncelikle retroperitoneal lenf nodları, akciğer ve inguinal lenf nodları olmak üzere metastaz sık görülür. Tedavi açısından da WDPMT ve malign mezotelyoma birbirinden ayrılır. Malign mezotelyomanın standart tedavisi radikal orşiektomi olmakla birlikte kemoterapi ve radyoterapinin yeri sınırlıdır(3,4). WDPMT'de BAP1'in korunmuş ekspresyon göstermesi ve CDKN2A homozigot delesyonunun bulunmaması, mezotelyomadan ayırt edilmesinde destekleyici moleküler özelliklerdendir(1). Ayırıcı tanıda nadir görülen over tipi seröz tümörler de göz önünde bulundurulmalıdır. Bu lezyonlar WDPMT'ye benzer papiller mimari gösterebilmekle birlikte, genellikle kolumnar hücreler, daha belirgin sitolojik atipi ve karsinom belirteçleri (MOC-31, Claudin-4, BerEP4) ile pozitif boyanma sergiler. Buna karşılık WDPMT'de mezotelyal belirteç pozitifliği ön plandadır(2). Reaktif mezotelyal hiperplazide papiller yapılar görülebilmekle birlikte, WDPMT'den farklı olarak genellikle belirgin fibrovasküler korlara sahip organize papiller mimari bulunmaz. Ayrıca WDPMT'de izlenen tek katlı uniform mezotelyal hücre dizilimi ve neoplastik papiller yapılanma, reaktif proliferasyonlardan ayrımda yardımcıdır. Ayırıcı tanıda morfolojik bulguların klinik ve immünohistokimyasal verilerle birlikte değerlendirilmesi gereklidir(2). Lokalize olgularda cerrahi eksizyon genellikle yeterli tedavi sağlarken, daha geniş lezyonlarda orşiektomi tercih edilebilmektedir. Uzun dönem izlem uygun bir yaklaşım olarak değerlendirilmektedir(1). Progresyon izlenen WDPMT olgularında immünohistokimyasal olarak BAP1 ekspresyon kaybı ve multifokalite sık bildirilen bulgulardır.(5). Mevcut veriler, parsiyel ya da radikal orşiektominin tek başına yeterli olduğunu ve cerrahi sonrası hastalık nüksünün gözlenmediğini göstermektedir.(4).

Sonuç

WDPMT, tunika vajinaliste oldukça nadir görülen bir mezotelyal neoplazm olup, paratestiküler lezyonların ayırıcı tanısında akılda tutulmalıdır. Histomorfolojik ve immünohistokimyasal özelliklerinin bilinmesi, özellikle malign mezotelyoma ile karışmasının önüne geçerek gereksiz agresif tedavilerin engellenmesine katkı sağlayabilir. Bununla birlikte, sınırlı sayıda olgu ve yetersiz uzun dönem takip verileri nedeniyle biyolojik davranışı ve prognozu tam olarak aydınlatılamamıştır. Bu nedenle tanı alan hastalarda dikkatli klinik takip önerilmeli, gelecekte bildirilecek yeni olgularla WDPMT'nin klinikopatolojik özellikleri ve doğal seyri daha iyi ortaya konulmalıdır.

Referanslar

1. Raspollini MR, Tickoo SK, İdrees MT, Galateau-Salle F, Comperat EM, "Who Classification of Tumours Urinary and Male Genital Tumours (5th ed.)" in.

2. A. Churg, F. Galateau-Salle, Well differentiated papillary mesothelial tumor: a new name and new problems. *Modern Pathology* **35**, 1327–1333 (2022).

3. Y. Fang, *et al.*, Well-differentiated papillary mesothelial tumour of the tunica vaginalis: A case report. *Journal of Peking University (Health Sciences)* **56**, 741 (2024).

4. J. Kläger, F. Oberndorfer, C. Brunel, J. Veser, E. Compérat, Well-differentiated Papillary Mesothelial Tumour of the Tunica Vaginalis Testis - A Rare Lesion, but one Pathologists Should Know About Two Patient Reports and a Review of the Literature. *Int. J. Surg. Pathol.* **31**, 1126–1131 (2023).

5. S. Prabhakaran, *et al.*, Factors predictive of progression in lesions categorised as well-differentiated papillary mesothelial tumour of the pleura, tunica vaginalis and peritoneum: a scoping review. *Cancer Treat. Res. Commun.* **47**, 101137 (2026).

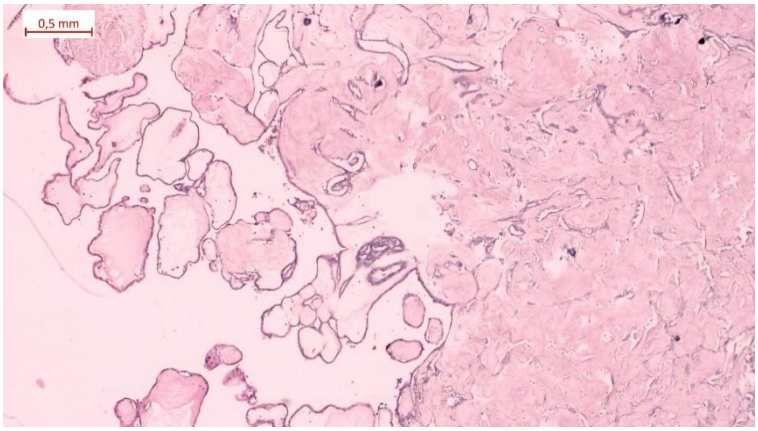
Resimler



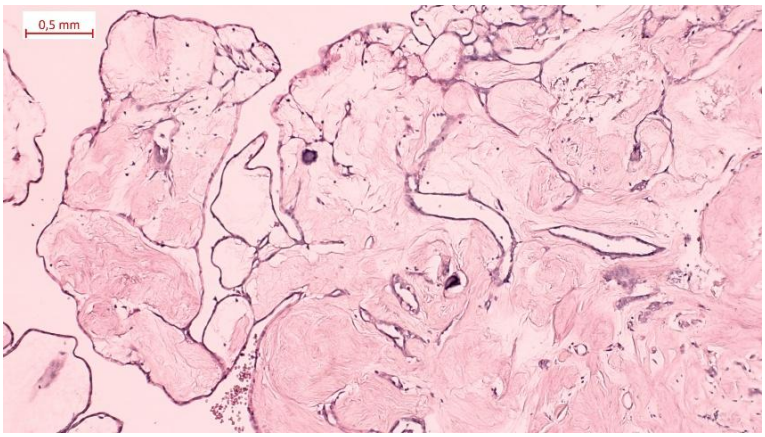
Resim 1a: İnce bir kapsülle çevrili açılmış halde kistik yapı izlendi.



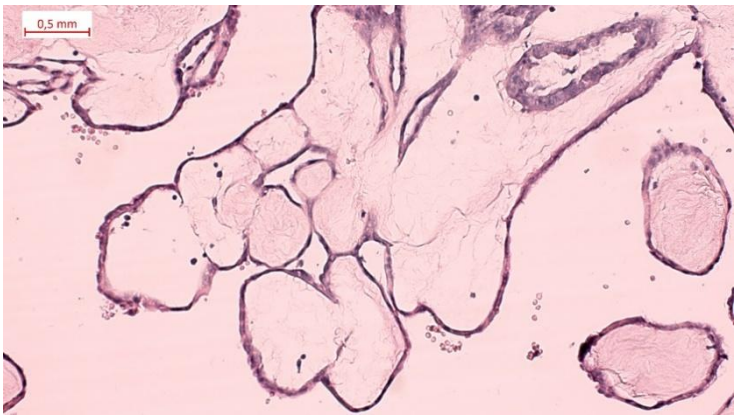
Resim 1b: Bir alanda (ok) yüzeye doğru büyüme gösteren papiller yapı görüldü.



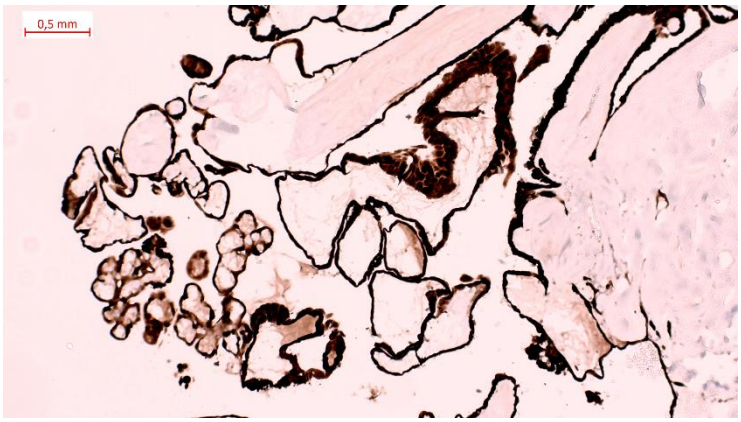
Resim 2a: Tek sıra kübik epitel ile döşeli fibrovasküler koru belirgin lezyon dikkati çekti(H&E x50)



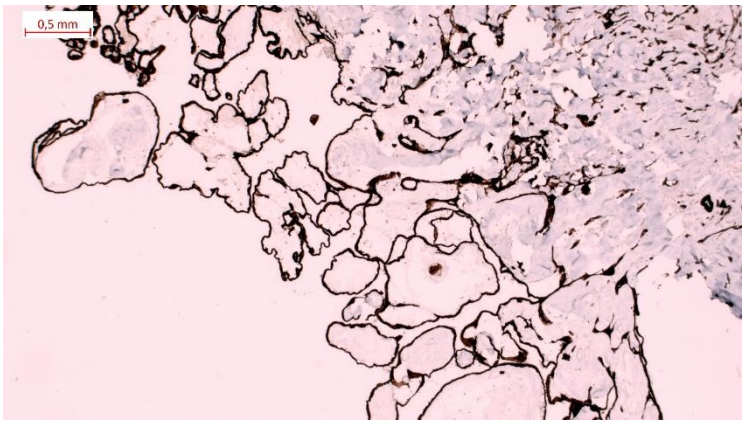
Resim 2b: Tek sıra kübik epitel ile döşeli fibrovasküler koru belirgin lezyon dikkati çekti(H&E x100)



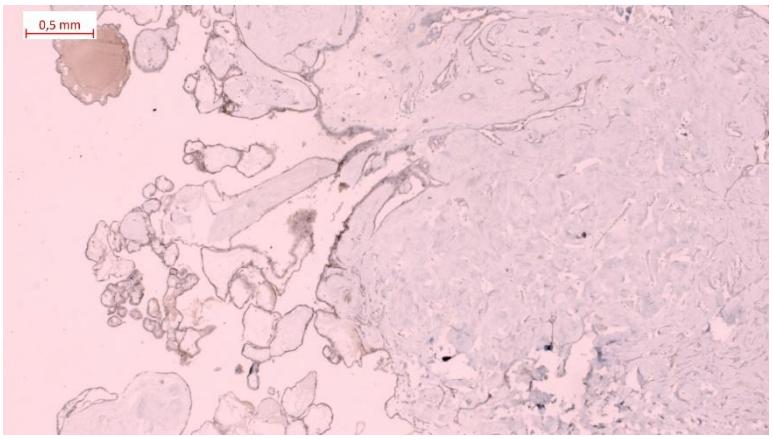
Resim 2c: Tek sıra kübik epitel ile döşeli fibrovasküler koru belirgin lezyon dikkati çekti(H&E x200)



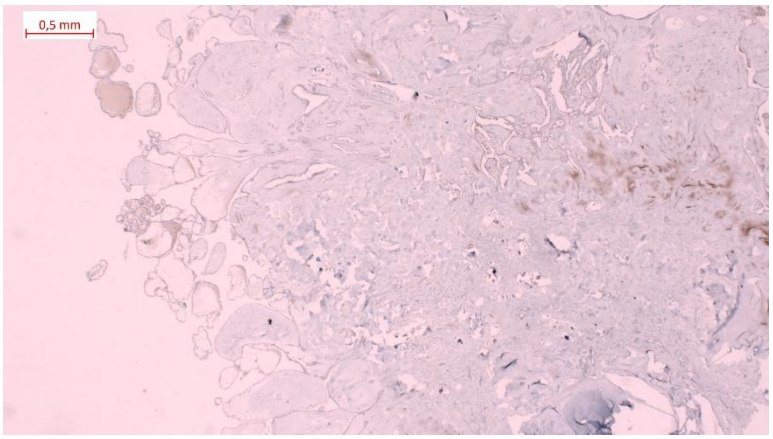
Resim 3a: Epitelde kalretinin ile sitoplazmik pozitiflik izlendi (İmmünperoksidaz x 100)



Resim 3b: Epitelde CK-7 ile sitoplazmik pozitiflik izlendi. (İmmünperoksidaz x 50)



Resim 3c: Epitelde D2-40 ile fokal sitoplazmik pozitif boyanma izlendi. (İmmünperoksidaz x 50)



Resim 3d: Epitelde Östrojen reseptörü ile negatif boyanma izlendi (İmmünperoksidaz x 25)

COMPARING THE PERFORMANCE OF GEMINI ADVANCED AND MEDICAL STUDENTS IN HISTOLOGY QUESTION ANSWERING

Tülay MORTAŞ

Kırıkkale University, Kırıkkale Üniversitesi Tıp Fakültesi, Histoloji ve Embriyoloji Anabilim Dalı, ORCID ID: https://orcid.org/0000-0003-3635-9923

ABSTRACT

Aim: Although large language models have rapidly become popular and are widely used in medical education, uncertainties regarding their integration into educational processes persist. This study compared the performance of the Gemini Advanced model with that of medical students by administering multiple-choice histology questions to both groups.

Materials and Methods: This study was conducted using 85 multiple-choice histology questions administered to 236 second-year medical students enrolled at Kırıkkale University Faculty of Medicine during the 2023–2024 academic year. The questions, categorized according to their difficulty levels, were also presented to the Gemini Advanced model.

Results: Gemini Advanced correctly answered 70 out of 85 questions, yielding an accuracy rate of 82.35%. Students correctly answered 39.9% of the questions that the model answered incorrectly, and 59.8% of those answered correctly by the model; this difference was statistically significant ($p < 0.05$). A significant difference was also observed between the item difficulty indices of the questions the model answered correctly and incorrectly. The mean item difficulty index was 0.4 for incorrectly answered questions and 0.6 for correctly answered ones ($p < 0.05$).

Conclusion: Although artificial intelligence model demonstrated strong overall performance, it showed limitations in items requiring detailed reasoning. Shared areas of difficulty between students and the model highlight the continued importance of instructor support. The limited number of microscopy-based questions represents a key limitation of the study, underscoring the need for broader datasets in future research.

Keywords: Artificial intelligence; Gemini Advanced; Histology; Medical students; Medical education.

GEMINI ADVANCED'İN HİSTOLOJİ SORULARINDAKİ PERFORMANSININ TIP ÖĞRENCİLERİYLE KARŞILAŞTIRILMASI

ÖZET

Amaç: Son dönemde hızla popülerleşen yapay zekâ dil modelleri tıp eğitiminde yaygın olarak kullanılmaktadır; ancak eğitime entegrasyonlarına ilişkin belirsizlikler sürmektedir. Bu çalışmada, çoktan seçmeli histoloji soruları Gemini Advanced modeline uygulanarak modelin başarısı ile tıp öğrencilerinin performansı karşılaştırılmıştır.

Gereç ve Yöntemler: Bu çalışma 2023-2024 eğitim-öğretim yılında, Kırıkkale Üniversitesi Tıp Fakültesi'ne kayıtlı, 236 ikinci sınıf öğrencisine yöneltilen 85 çoktan seçmeli histoloji sorularıyla yapılmıştır. Güçlük derecesine göre kategorize edilen bu sorular, Gemini Advanced'a sorulmuştur.

Bulgular: Gemini Advanced, 85 sorunun 70'ini doğru yanıtlayarak %82,35 başarı göstermiştir. Öğrenciler, modelin yanlış yanıtladığı soruların %39,9'unu; doğru yanıtladığı soruların ise %59,8'ini doğru cevaplamıştır ve bu fark istatistiksel olarak anlamlıdır ($p < 0.05$). Ayrıca modelin doğru ve yanlış yanıtladığı sorular arasında madde güçlük indeksi bakımından anlamlı fark bulunmuş; yanlış yanıtlanan soruların güçlük indeksi 0,4, doğru yanıtlananların ise 0,6 olarak belirlenmiştir ($p < 0.05$).

Sonuç: Yapay zekâ modeli genel olarak iyi bir performans sergilemiş, ancak ayrıntılı akıl yürütme gerektiren maddelerde sınırlılıklar göstermiştir. Öğrenciler ve model arasında paylaşılan zorlanma

alanları, eğitici desteğinin önemini koruduğunu göstermektedir. Mikroskopi temelli soruların azlığı önemli bir kısıt olup, gelecekte daha geniş veri setlerine ihtiyaç duyulmaktadır.

Anahtar Kelimeler: Yapay zeka; Gemini Advanced; Histoloji; Tıp öğrencileri; Tıp eğitimi.

INTRODUCTION

Artificial intelligence (AI) language models, or chatbots, have recently gained substantial popularity due to their deep learning–based ability to generate natural language responses (1). Their exceptional performance in medical examinations has drawn considerable scholarly interest (2-5). Despite ongoing ethical concerns—including plagiarism, misinformation, and examination misconduct—these models are increasingly regarded as promising supportive tools in medical education (6,7). Consequently, further research is needed to determine how such technologies can be effectively integrated into various areas of medical training.

Recently, AI language models have made substantial progress, evolving from unimodal systems that process only a single type of data—such as text or speech—to advanced multimodal systems capable of handling diverse input formats. Modern multimodal AI models can interact with and interpret various data types, including text, images, audio, video, and PDF documents (8). Among these, one of the most notable is Gemini, developed by Google. Released on December 6, 2023, Gemini represents Google's latest multimodal AI system, developed by DeepMind Equipped with Vision-Language Model (VLM) technology, it directly competes with OpenAI's GPT-4-based ChatGPT model featuring visual capabilities (8-10). Numerous studies have highlighted both the strengths and potential risks of Google Gemini (8-11). In particular, Gemini Advanced (Google LLC, Mountain View, CA, USA) stands out for its sophisticated query-processing capabilities and holds significant potential to transform access to medical information and research workflows (12).

In medical schools, various types of examinations are administered to assess students' knowledge levels. These exams not only evaluate individual performance but also serve as tools for monitoring the educational process, ensuring quality assurance, and improving educational standards. Each assessment unit in these exams is referred to as an item in measurement theory (13). Item analysis provides information about the quality and discriminatory power of questions based on participants' responses. One of the key indicators used in item analysis is the difficulty index, which quantitatively expresses how easy or difficult an item is perceived by the participants.

In this study, multiple-choice histology questions administered to medical students were presented to the Gemini Advanced AI language model. The relationship between the AI's correct and incorrect responses and the students' performance was statistically analyzed.

MATERIALS AND METHODS

2.1. Study Design

A total of 236 second-year students were enrolled in the accredited Faculty of Medicine at Kırıkkale University during the 2023–2024 academic year. Data on histology exam questions, students' response rates, and question difficulty indices were obtained through the examination management software of Kırıkkale University Faculty of Medicine. This study was approved by the Non-Interventional Scientific Research Ethics Committee of Kırıkkale University (Meeting date: December 18, 2024; Meeting number: 2024/16; Decision number: 2024.12.16).

2.2. Histology Course

The second-year curriculum of Kırıkkale University Faculty of Medicine consists of six instructional blocks spanning a total of 38 weeks. Within these blocks, students are required to take the following courses: Anatomy, Biophysics, Physiology, Histology and Embryology, Medical Biochemistry, Medical Pharmacology, Medical Genetics, Medical Microbiology, and Medical Pathology.

The Histology and Embryology course, which is included in the first five blocks, comprises 74 hours of theoretical instruction and 40 hours of laboratory practice, totaling 114 hours. Both theoretical and laboratory sessions are conducted face-to-face. During the laboratory sessions, students are divided into

six groups. Slides prepared from images of tissue samples to be studied are used to introduce the related tissues. Subsequently, tissue samples are distributed to students for microscopic examination, during which students make detailed drawings of the observed structures. At the end of the course, students' drawings are collected and graded as part of their practical performance within the block examinations.

2.3. Examination Procedures

At Kırıkkale University Faculty of Medicine, both theoretical and practical examinations are conducted to assess the academic performance of second-year students and to determine their eligibility for promotion to the next academic year. Theoretical examinations are divided into block examinations and final examinations.

Each block includes a pre-exam and a comprehensive block exam. Pre-exams, typically administered at the end of the third week, assess content covered up to that point and help students monitor their progress and identify learning gaps. While one pre-exam is given per block, the extended third block includes two, with the second excluding material from the first. Block exams, held at the end of each block, evaluate all topics taught within that block. The number of questions for both assessments is proportional to each course's allocated instructional hours. Practical examinations are also conducted, and their scores contribute to the final block grade, which is calculated as 8% from the pre-exam and 92% from the block exam.

Following completion of all blocks, students take two final examinations with corresponding practical components. These finals assess all material covered during the academic year. A two-week interval separates the first final exam (YS1) from the last block exam, and the practical score associated with YS1 is included in the final exam grade.

The promotion score for advancement to the next academic year is calculated using 60% of the weighted block average and 40% of the final exam grade, with a minimum requirement of 60. Students who meet this threshold are automatically promoted in the digital system. Those scoring below 60 must take the second final exam (YS2), administered two weeks after YS1 and serving as its make-up. Like YS1, YS2 includes a practical component, and promotion is re-evaluated based on these results. Students scoring 60 or above are promoted, whereas those who do not meet the requirement must repeat the second year.

All examinations are conducted digitally at the Kırıkkale University Faculty of Medicine Examination Center. Examination security is ensured through on-site invigilators, while software specialists restrict access to external websites prior to the exam to prevent cheating.

2.4. Histology Questions

During the 2023–2024 academic year, 135 histology questions of various formats were administered to second-year medical students at Kırıkkale University. For this study, only multiple-choice histology questions were analyzed. All evaluated questions were prepared by a faculty member from the Department of Histology and Embryology (T. Mortaş).

The histology questions were classified according to instructional blocks: Blood and Immune System (K1), Respiratory and Circulatory System (K2), Neuroendocrine and Sensory Organs (K3), Digestive System (K4), and Urogenital System (K5). Questions from the first and second final exams were labeled YS1 and YS2, respectively.

The item difficulty indices of the histology exam questions were evaluated based on the classification table developed by Hasançebi et al (13) (Table 1).

Table 1. Item evaluation based on item difficulty index.

Item difficulty index	Item evaluation
0.29 and below	Hard
0.30-0.49	Moderate difficulty
0.50-0.69	Easy
0.70-1	Very easy

2.5. Gemini Advanced

The histology exam questions were evaluated using Gemini Advanced (version 2.0 Flash) between February 25 and March 4, 2025. Each question was presented in Turkish with the prompt "Read the following question and answer it." After the model responded, it was asked "Are you sure?" to assess the reliability and confidence of its answers.

2.6. Statistical Analysis

All statistical analyses were conducted using SPSS version 20 (IBM Corp., Armonk, NY, USA). Normality was assessed with the Shapiro–Wilk test. Independent Samples t-tests were used to compare Gemini Advanced's correct and incorrect responses with student performance and item difficulty indices. A p-value < 0.05 was considered statistically significant.

RESULTS

In this study, a total of 85 multiple-choice histology questions were evaluated. The difficulty indices of these questions, the percentage of correct responses by medical students, and the responses provided by Gemini Advanced are presented in Table 2. Gemini Advanced answered 70 out of 85 questions correctly, corresponding to an accuracy rate of 82.35%.

3.1. Block-Based and Final Examination Results

In the K1 (Blood and Immune System) block, students' correct response rates ranged from 40.59% to 76.57%. Gemini Advanced answered all questions in this block correctly, and there were no visually based questions. Regarding reliability, when prompted for confirmation, Gemini Advanced reaffirmed all its responses without making any changes.

In the K2 (Respiratory and Circulatory System) block, students' correct response rates ranged between 27.07% and 82.97%. Gemini Advanced answered two questions incorrectly, both categorized as *easy* according to the item difficulty index. One question involved the transmission electron microscopic image of arteriole wall structures, while the other concerned the comparison of tracheal and bronchial walls. One visually based question in this block was answered incorrectly. Upon reliability assessment, Gemini Advanced did not alter its initial answers.

In the K3 (Neuroendocrine and Sensory Organs) block, students' correct response rates ranged between 32.59% and 84.14%. Gemini Advanced answered four questions incorrectly—three of *moderate difficulty* and one *easy* according to the item difficulty index. The incorrectly answered questions pertained to pupil dilation, the protective barrier of the eye, the layers of the retina, and the thickness of the myelin sheath in the peripheral nervous system. Two visually based, non-microscopic questions concerning eye and ear morphology were answered correctly. When reliability was reassessed, Gemini Advanced confirmed all of its initial answers without modification.

In the K4 (Digestive System) block, students' correct response rates ranged from 29.18% to 83.56%. Gemini Advanced answered two questions incorrectly, both of *moderate difficulty*. These questions involved the comparison between serous and mucous acini and the cell types lining the ducts through

which bile is secreted. A transmission electron microscopy–based question related to hepatocytes and bile canaliculi was answered correctly. Regarding reliability, Gemini Advanced did not revise its responses.

Table 2. Data on multiple-choice histology questions.

Question ID	Gemini Advanced answers	% of Students answered correctly	Item difficulty index	Item evaluation
K1 Q7	+	75.73	0.72	Very easy
K1 Q9	+	56.9	0.57	Easy
K1 Q10	+	49.79	0.45	Moderate difficulty
K1 Q11	+	58.16	0.57	Easy
K1 Q12	+	76.57	0.69	Easy
K1 Q13	+	55.65	0.55	Easy
K1 Q14	+	40.59	0.45	Moderate difficulty
K1 Q15	+	45.19	0.45	Moderate difficulty
K2 Q1	+	81.33	0.77	Very easy
K2 Q2	+	78.22	0.72	Very easy
K2 Q3	-	50.22	0.51	Easy
K2 Q5	+	40.61	0.45	Moderate difficulty
K2 Q6	+	75.11	0.66	Easy
K2 Q7	+	66.38	0.68	Easy
K2 Q8	+	55.46	0.56	Easy
K2 Q9	+	70.74	0.71	Very easy
K2 Q10	+	27.07	0.27	Hard
K2 Q11	+	72.93	0.67	Easy
K2 Q12	+	82.97	0.79	Very easy
K2 Q13	+	71.18	0.69	Easy
K2 Q14	-	63.76	0.54	Easy

K3 Q1	+	46.46	0.46	Moderate difficulty
K3 Q2	+	73.45	0.66	Easy
K3 Q5	-	32.59	0.33	Moderate difficulty
K3 Q6	+	60.27	0.57	Easy
K3 Q7	-	33.04	0.33	Moderate difficulty
K3 Q8	-	67.41	0.64	Easy
K3 Q9	+	47.64	0.49	Moderate difficulty
K3 Q10	+	56.65	0.57	Easy
K3 Q11	+	36.48	0.44	Moderate difficulty
K3 Q12	+	63.09	0.6	Easy
K3 Q13	-	34.76	0.37	Moderate difficulty
K3 Q14	+	44.21	0.44	Moderate difficulty
K3 Q16	+	47.64	0.44	Moderate difficulty
K3 Q17	+	39.91	0.42	Moderate difficulty
K3 Q18	+	84.12	0.76	Very easy
K3 Q19	+	84.12	0.77	Very easy
K3 Q20	+	65.24	0.64	Easy
K3 Q21	+	56.65	0.57	Easy
K3 Q22	+	45.92	0.44	Moderate difficulty
K4 Q1	+	71.24	0.63	Easy
K4 Q3	+	46.35	0.48	Moderate difficulty
K4 Q4	-	29.18	0.35	Moderate difficulty
K4 Q6	+	44.44	0.47	Moderate difficulty

K4 Q9	+	43.11	0.5	Easy
K4 Q10	+	83.56	0.82	Very easy
K4 Q11	+	69.33	0.69	Easy
K4 Q13	-	41.78	0.41	Moderate difficulty
K4 Q18	+	63.11	0.61	Easy
K5 Q3	+	56.82	0.58	Easy
K5 Q4	+	75.45	0.69	Easy
K5 Q8	+	80.17	0.69	Easy
K5 Q9	+	49.14	0.48	Moderate difficulty
K5 Q13	+	56.03	0.57	Easy
K5 Q14	-	52.59	0.48	Moderate difficulty
K5 Q15	+	64.22	0.58	Easy
K5 Q17	+	64.22	0.68	Easy
K5 Q18	+	89.22	0.9	Very easy
K5 Q19	-	34.91	0.32	Moderate difficulty
YS1 Q1	-	52.94	0.52	Easy
YS1 Q3	+	57.92	0.54	Easy
YS1 Q5	+	77.83	0.72	Very easy
YS1 Q6	+	76.02	0.73	Very easy
YS1 Q7	+	93.67	0.92	Very easy
YS1 Q8	+	37.1	0.39	Moderate difficulty
YS1 Q9	+	75.57	0.73	Very easy
YS1 Q11	+	46.61	0.49	Moderate difficulty
YS1 Q12	+	72.4	0.68	Easy
YS1 Q13	-	13.57	0.13	Hard
YS1 Q14	+	46.61	0.48	Moderate difficulty

YS1 Q16	+	38.91	0.4	Moderate difficulty
YS1 Q18	-	42.08	0.44	Moderate difficulty
YS2 Q2	+	61.9	0.57	Easy
YS2 Q3	+	47.62	0.43	Moderate difficulty
YS2 Q4	+	82.14	0.72	Very easy
YS2 Q6	+	55.95	0.61	Easy
YS2 Q7	+	52.38	0.43	Moderate difficulty
YS2 Q8	+	19.05	0.24	Hard
YS2 Q9	+	76.19	0.76	Very easy
YS2 Q12	+	38.1	0.41	Moderate difficulty
YS2 Q13	+	40.48	0.41	Moderate difficulty
YS2 Q14	+	59.52	0.54	Easy
YS2 Q16	-	35.71	0.39	Moderate difficulty
YS2 Q17	+	40.48	0.46	Moderate difficulty
YS2 Q18	-	14.29	0.24	Hard

The table presents the numbers of the 85 multiple-choice questions and the corresponding examinations in which they were administered. In addition, it displays the questions that Gemini Advanced answered correctly (+) or incorrectly (−), the percentage of students who answered each question correctly, the item difficulty indices, and the classification of each question based on its difficulty index.

In the K5 (Urogenital System) block, students' correct response rates ranged between 34.91% and 89.22%. Gemini Advanced answered two questions incorrectly, both of *moderate difficulty*. The questions were about the structures responsible for protecting sperm and the site of testosterone production within the secondary ovarian follicle. A light microscopy–based question related to seminiferous tubules was answered correctly. Gemini Advanced maintained all its original answers upon reliability evaluation.

In the first final exam (YS1), students' correct response rates ranged between 13.57% and 93.67%. Gemini Advanced answered three questions incorrectly—one classified as *hard*, one *moderate*, and one *easy* according to the item difficulty index. These questions addressed topics including the mechanical movement of stereocilia in the organ of Corti, the functions of cells in the thymic medulla, and the type of blood vessel with a high number of elastic membranes. A light microscopy–based question related to salivary glands was answered correctly. In reliability assessment, Gemini Advanced confirmed its answers without alteration.

In the second final exam (YS2**)**, students' correct response rates ranged between 14.29% and 82.14%. Gemini Advanced answered two questions incorrectly—one of *moderate difficulty* and one *hard*. The questions were related to the duct through which sperm passes before maturation and the structures involved in the blood-thymus barrier. There were no visually based questions in YS2. When reassessed for reliability, Gemini Advanced did not modify its responses.

3.2. Comparison of Gemini Advanced's Response Accuracy with Student Performance and Item Difficulty

The relationship between Gemini Advanced's responses and both student performance and item difficulty was examined. Normality was assessed using the Shapiro–Wilk test, and because the data were normally distributed, Independent Samples t-tests were applied. As shown in Table 3, a statistically significant difference was found between the model's correct and incorrect responses and the percentage of students who answered each item correctly: on average, 39.9% of students answered items missed by the model correctly, whereas 59.8% answered correctly those items the model answered accurately ($p < 0.05$). A significant difference was also observed between item difficulty indices for correct and incorrect model responses, with mean values of 0.6 and 0.4 respectively, indicating that both students and the model struggled more with moderately difficult items ($p < 0.05$).

Table 3. Comparison of Students' Response Rates and Item Difficulty Indices Based on Gemini Advanced's Correct and Incorrect Answers.

	Gemini Advanced's responses		
	Questions answered incorrectly by Gemini Advanced (n = 15) Mean ± standard deviation	**Questions answered correctly by Gemini Advanced (n = 70) Mean ± standard deviation**	**p-value**
Percentage of students who answered the questions	39.9 ± 15.6	59.8 ± 16.4	0.001
Item difficulty index	0.4 ± 0.1	0.6 ± 0.1	0.001

Statistical significance was set at $p < 0.05$.

DISCUSSION

AI language models are increasingly used in medical education, primarily as tools for solving multiple-choice examinations or supporting clinical decision-making. In this study, multiple-choice histology questions given to second-year medical students were administered to Gemini Advanced, and significant associations were identified between the model's correct and incorrect responses, student performance, and item difficulty indices.

In January 2023, Huh compared ChatGPT's performance with that of first-year medical students in Korea using a medical parasitology exam (14). ChatGPT achieved 60.8% accuracy (48/79), substantially lower than the students' mean accuracy of 90.8% (71.8 correct; range 65–74). These findings indicated that ChatGPT's reasoning and interpretive abilities were inferior to those of well-trained medical students. However, the author noted—drawing on the AlphaGo example—that ChatGPT may improve through continued deep learning, emphasizing the need for educators and students to monitor the development of AI-based tools in medical education (15).

In August 2023, Panthier et al. evaluated ChatGPT using the French version of the European Board of Ophthalmology (EBO) examination (16). ChatGPT achieved 91.2% accuracy (6,188/6,785), demonstrating strong proficiency across basic sciences, clinical knowledge, and clinical management. Its ability to respond in approximately one second per item also highlighted a notable efficiency advantage. Despite this high performance, the authors emphasized the need for further investigation and refinement of AI-assisted tools to better support medical education and patient care.

In September 2023, Bajčetić et al. evaluated five AI language models—ChatGPT, Bing AI, Bard AI, Perplexity AI, and ChatSonic—using multiple-choice histology and embryology questions and compared their performance with that of first-year medical students (17). All models outperformed the students (42–44%) on both R01 and R02 tests, with Bing AI achieving the highest accuracy (90% and 84%) and ChatGPT scoring 79% and 81%. The R02 test included more complex, higher-order reasoning items. When the tests were repeated two months later, notable inconsistencies emerged in the models' responses, with some items previously answered correctly being answered incorrectly. Only Bing AI and ChatSonic showed improved performance, suggesting that variability in AI accuracy may reflect changes in data sources or model updates.

In May 2024, İş and Menekşeoğlu compared ChatGPT-4o and Google Gemini in answering rheumatology exam questions to assess their accuracy, reliability, and potential clinical applicability (11). Among 420 questions, ChatGPT-4o achieved 86.9% accuracy, whereas Gemini achieved 60.2%. When analyzed by subfields, ChatGPT-4o demonstrated significantly higher accuracy in both basic and clinical sciences, as well as in osteoarthritis and rheumatoid arthritis topics. The authors concluded that ChatGPT-4o showed high accuracy and reliability in its current version and could potentially be integrated into clinical practice in the near future.

In May 2025, Mavrych et al. assessed five publicly available large language models (GPT-4.1, Claude, Gemini, Copilot, DeepSeek) using 200 multiple-choice histology questions (18). Gemini achieved the highest accuracy (92.0%), followed closely by Claude (91.5%), Copilot (91.0%), GPT-4 (90.8%), and DeepSeek (90.3%). Visual questions were excluded from the analysis. Performance varied across topics: models achieved perfect accuracy in Histological Methods, Blood and Hemopoiesis, and the Circulatory System; high accuracy (95–99%) in the Extracellular Matrix, Respiratory, and Endocrine systems; and moderate accuracy (90–94%) in Cells, Skin, and Digestive Glands. The lowest scores occurred in the Lymphoid and Urinary Systems (84.7%) and especially the Muscular System (76.0%). Similar declines were observed in complex neuroscience topics (54.4–57.7%) and in embryology, particularly in nervous and cardiovascular system development (19,20). The authors concluded that topic complexity, rather than model type, primarily determined performance. Reliability testing across three sessions showed highest consistency for Claude in histology, followed by GPT-4 and Copilot, whereas in embryology, Gemini was the most reliable, indicating discipline-dependent variation in model reliability.

In this study (March 2025), Gemini Advanced correctly answered 70 of 85 histology questions (82.35%), with its lowest performance in the Neuroendocrine System block and perfect accuracy in the Blood and Lymphoid System block. Most errors occurred on items requiring detailed knowledge or comparative reasoning, and the model showed limited performance on visual questions, incorrectly

answering one of four microscopy-based items; the small number of visual items also restricted evaluation of its image-based reasoning. Nevertheless, the model demonstrated consistent responses upon repeated questioning. Statistical analyses further showed significant associations between the model's responses, student performance, and item difficulty ($p < 0.05$): on average, 39.9% of students answered correctly the items missed by the model, whereas 59.8% correctly answered those it answered accurately. Additionally, incorrectly answered items had a mean difficulty index of 0.4 and correctly answered items 0.6, corresponding to moderately difficult and easy questions, respectively, indicating that both students and the model struggled more with moderately challenging items and performed better on easier ones.

A review of the literature shows substantial variation in AI accuracy across medical domains, with reported rates from 2023 to 2025 ranging from 41.5% to 92% (11,14,16,19-22) . In the present study, Gemini Advanced achieved 82.35% accuracy in histology, aligning with this variability. Huh's findings—where ChatGPT scored well below students—highlight the influence of student profile and contextual factors on AI performance (14). Differences between Gemini's accuracy in this study and that reported by Mavrych et al. (82.35% vs. 92.0%) suggest that question design and authorship may affect outcomes (18). Comparative analyses also demonstrate model-to-model variability, and temporal inconsistencies observed by Bajčetić et al. indicate that changes in opaque data sources may influence performance (11,17,18). The improvement observed between March and May 2025 further suggests that some AI systems may evolve rapidly, even over short intervals (23-25). AI accuracy in histology also varies by subtopic. Consistent with Mavrych et al., Gemini Advanced performed best in Blood and Lymphoid System questions and poorest in the Neuroendocrine System (18). Higher accuracy in blood-related topics may reflect greater model familiarity or representational strength, whereas lower accuracy in other areas may relate to question characteristics. Overall, while AI models perform well on recall-based items, domains requiring clinical reasoning, critical thinking, or practical skills continue to rely heavily on traditional instruction (25,26).

CONCLUSION

In this study, the AI model correctly answered most multiple-choice histology questions but showed limitations on items requiring detailed reasoning, indicating a need for further training in complex analytical tasks. The shared difficulties between the AI and students underscore the continued importance of instructor guidance. Although the inclusion of microscopy-based questions strengthens the study, their limited number represents a notable limitation. Additionally, the opacity of the AI model's data sources raises concerns regarding response reliability. Overall, further research is required to support the effective and safe integration of AI language models into medical education.

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REFERENCES

1. Deng J, Lin Y. The benefits and challenges of ChatGPT: an overview. *Front Comput Intell Syst*. 2022;2(2):81-83.
2. Gilson A, Safranek CW, Huang T, et al. How does ChatGPT perform on the United States Medical Licensing Examination (USMLE)? Implications of large language models for medical education and knowledge assessment. *JMIR Med Educ*. 2023;9:e45312. doi:10.2196/45312.

3. Hopkins BS, Nguyen VN, Dallas J, et al. ChatGPT versus the neurosurgical written boards: a comparative analysis of artificial intelligence performance. *J Neurosurg*. 2023;139(3):904-911. doi:10.3171/2023.2.JNS23419.

4. Toyama Y, Harigai A, Abe M, et al. Performance evaluation of ChatGPT, GPT-4, and Bard on the official board examination of the Japan Radiology Society. *Jpn J Radiol*. 2024;42(2):201-207. doi:10.1007/s11604-023-01491-2.

5. Cheung BHH, Lau GKK, Wong GTC, et al. ChatGPT versus human in generating medical graduate exam multiple-choice questions: a multinational prospective study. *PLoS One*. 2023;18(8):e0290691. doi:10.1371/journal.pone.0290691.

6. Khan RA, Jawaid M, Khan AR, Sajjad M. ChatGPT reshaping medical education and clinical management. *Pak J Med Sci*. 2023;39(2):605.

7. Tsang R. Practical applications of ChatGPT in undergraduate medical education. *J Med Educ Curric Dev*. 2023;10:23821205231178449.

8. Rane N. Enhancing the quality of teaching and learning through Gemini, ChatGPT, and similar generative AI. *TESOL Technol Stud*. 2024;5(1):1-6.

9. Coles G. Google DeepMind Gemini AI release date: the world's most powerful language model. 2023.

10.Perera P, Lankathilaka M. Preparing to revolutionize education with Google Gemini. *J Adv Educ Philos*. 2023;7(8):246-253.

11.Is EE, Menekseoglu AK. Comparative performance of AI models in rheumatology board-level questions. *Clin Rheumatol*. 2024;43(11):3507-3513.

12.Warnat-Herresthal S, Oestreich M, Schultze JL, Becker M. Artificial intelligence in blood transcriptomics. In: *Artificial Intelligence in Medicine*. Springer; 2021:1-16.

13.Hasançebi B, Terzi Y, Küçük Z. Madde güçlük indeksi ve ayırt edicilik indeksine dayalı analiz. *Gümüşhane Üniv Fen Bilim Derg*. 2020;10(1):224-240.

14.Huh S. Are ChatGPT's abilities comparable to medical students? *J Educ Eval Health Prof*. 2023;20:1.

15.Silver D, Huang A, Maddison CJ, et al. Mastering the game of Go with deep neural networks. *Nature*. 2016;529(7587):484-489.

16.Panthier C, Gatinel D. Success of ChatGPT in European Board of Ophthalmology exam. *J Fr Ophtalmol*. 2023;46(7):706-711.

17.Bajčetić M, Mirčić A, Rakočević J, et al. Comparing AI models to medical students in histology questions. *Ann Anat*. 2024;254:152261.

18.Mavrych V, Yousef EM, Yaqinuddin A, Bolgova O. Large language models in histology education. *Med Educ Online*. 2025;30(1):2534065.

19.Mavrych V, Yaqinuddin A, Claude BO. ChatGPT, Copilot, and Gemini vs students. *Adv Physiol Educ*. 2025;49(2):430-437. doi:10.1152/advan.00093.2024.

20.Bolgova O, Ganguly P, Mavrych V. LLM performance in embryology. *Anat Sci Educ*. 2025;18(7):718-726. doi:10.1002/ase.70044.

21.Mavrych V, Ganguly P, Bolgova O. LLM use in anatomy course. *Clin Anat*. 2025;38(2):200-210. doi:10.1002/ca.24244.

22.Bolgova O, Shypilova I, Mavrych V. LLMs in biochemistry education. *JMIR Med Educ*. 2025;11:e67244. doi:10.2196/67244.

23.Jin HK, Lee HE, Kim E. Performance of ChatGPT in licensing exams: systematic review. *BMC Med Educ*. 2024;24:1013. doi:10.1186/s12909-024-05944-8.

24.Liu M, Okuhara T, Chang X, et al. ChatGPT performance in medical exams worldwide. *J Med Internet Res*. 2024;26:e60807. doi:10.2196/60807.

25.Yang Z, Yao Z, Tasmin M, et al. GPT-4V challenges on USMLE questions. *J Med Internet Res*. 2025;27:e65146. doi:10.2196/65146.

26.Arvidsson R, Gunnarsson R, Entezarjou A, et al. ChatGPT versus doctors in clinical cases. *BMJ Open*. 2024;14:e086148. doi:10.1136/bmjopen-2024-086148.

TÜP LİGASYONU SONRASI GERİ DÖNÜŞ TALEBİ: FARKLI MOTİVASYONLARIN KESİŞİMİNDE BİR OLGU SERİSİ

Elif KETEN EDİS

Doç. Dr., Amasya Üniversitesi, Sağlık Bilimleri Fakültesi, Doğum ve Kadın Hastalıkları Hemşireliği Anabilim Dalı, Amasya, Türkiye, ORCID: 0000-0002-5587-6726

Sevgi ARSLAN

Yüksek Lisans Öğrencisi Amasya Üniversitesi, Sağlık Bilimleri Enstitüsü, Doğum ve Kadın Hastalıkları Hemşireliği Programı, Amasya, Türkiye, ORCID: 0009-0007-3020-023X

ÖZET

Amaç: Tüp ligasyonu, modern ve kalıcı kontrasepsiyon yöntemlerinden biri olmakla birlikte, bazı kadınlarda pişmanlık ve fertilitenin yeniden kazanılmasına yönelik talebe yol açabilmektedir. Bu olgu serisi, tüp ligasyonu sonrası fertilitenin yeniden kazanılmasına yönelik geri dönüş talebiyle başvuran, farklı motivasyonlara sahip iki kadının deneyimlerini sunarak üreme kararlarını etkileyen faktörleri belirlemeyi amaçlamaktadır. **Materyal ve Yöntem:** Bu olgu serisinde tüp ligasyonu sonrası geri dönüş talebi olan iki kadın ile bireysel görüşmeler yapılarak üreme kararlarını etkileyen faktörler incelenmiştir. **Bulgular:** Her iki kadın da tekrar gebelik istemedikleri için tüp ligasyonu yaptırmıştır. Ancak ilerleyen süreçte değişen yaşam koşulları ve tıbbı gereklilikler nedeniyle geri dönüş talebinde bulunmuşlardır. İlk olguda, çocuğunun genetik hastalığı nedeniyle kemik iliği nakli gereksinimi ve uygun donör arayışı gebelik isteğinin temel nedeni olurken; ikinci olguda yeni bir evlilik, duygusal bağlanma, partnerle ortak çocuk sahibi olma isteği ön plana çıkmıştır. Her iki olguda da başlangıçta kalıcı kontrasepsiyon olarak değerlendirilen tüp ligasyonu kararına yönelik, yaşamın ilerleyen dönemlerinde öngörülemeyen koşullar nedeniyle pişmanlık duygusunun geliştiği ve fertilitenin yeniden kazanılmasına yönelik tubal reanastomoz talebi olduğu görülmüştür. Bu olgu serisinde her iki kadında tubal reanastomoz sonrası gebelik gerçekleşmezse yardımcı üreme tekniklerine başvuracaklarını belirtmişlerdir. **Sonuç:** Tüp ligasyonu sonrası pişmanlık ve geri dönüş talebi değişen yaşam olayları, yeni bir evlilik, annelik rolleri ve tıbbi gereksinimler gibi bazı faktörlerle şekillenebilen bir süreçtir. Bu nedenle danışmanlık sürecinde olası yaşam değişikliklerinin göz önünde bulundurulması ve kadınlara işlemin kalıcı doğası, olası komplikasyonlar ve alternatif doğum kontrol yöntemleri hakkında ayrıntılı bilgi verilmesi önem taşımaktadır. Tüp ligasyonu kararı verilirken tıbbi, psikolojik ve sosyal boyutlar bütüncül olarak değerlendirilmelidir.

Anahtar Kelimeler: Kadın sağlığı, Olgu sunumları, Üreme sağlığı, Tüp ligasyonu

REVERSAL REQUEST AFTER TUBAL LIGATION: A CASE SERIES AT THE INTERSECTION OF DIFFERENT MOTIVATIONS

ABSTRACT

Purpose: Tubal ligation is a modern and permanent method of contraception, but it can lead to regret and a desire to regain fertility in some women. This case series aims to explore individual, social, and medical factors influencing reproductive decisions by presenting two women with different motivations who sought reversal after tubal ligation, reporting subsequent regret and a desire to restore fertility. **Materials and Methods:** In this case series, individual interviews were conducted with two women who requested reinstatement after tubal ligation to investigate the factors influencing their reproductive decisions. **Results:** Both women underwent tubal ligation because they did not want to become pregnant again. However, due to changing life circumstances and medical needs, they later requested fertility restoration. In the first case, the main reason for renewed pregnancy desire was the need for a bone marrow transplant for her child with a genetic disease and the search for a suitable donor. In the second case, remarriage, emotional bonding, and the desire to have a child with her new partner were the

primary motivations. In both cases, tubal ligation, initially considered a permanent contraceptive method, was later associated with regret due to unforeseen life events, leading to requests for tubal re-anastomosis. Both women also stated that they would consider assisted reproductive techniques if pregnancy did not occur after tubal re-anastomosis. **Conclusion:** Regret and the desire to reverse tubal ligation can be influenced by subsequent life changes such as remarriage, evolving maternal roles, and emerging medical needs. Therefore, during counseling, it is essential to consider possible future life transitions and to provide comprehensive information regarding the permanent nature of the procedure, potential risks, and alternative contraceptive methods. Decisions regarding tubal ligation should be approached through a holistic evaluation of medical, psychological, and social dimensions.

Keywords: Women health, Case reports, Reproductive health, Tubal ligation

1. GİRİŞ

Tüp ligasyonu (bilateral tubal ligasyon), dünya genelinde yaygın bir doğum kontrol yöntemi olup üreme çağındaki kadınlar arasında %19-23,7 oranında kullanıldığı belirtilmektedir (Festin, 2020; Ndayishimye vd., 2023). Türkiye'de de evli kadınlar arasında tercih edilen doğum kontrol yöntemleri incelendiğinde, cerrahi sterilizasyonun önemli bir yer tuttuğu görülmektedir (TNSA, 2018). Ancak, tüp ligasyonunun geri dönüşü olmayan bir yöntem olması, bazı kadınlarda zamanla pişmanlık duygusunun ortaya çıkmasına yol açabilmektedir. Literatür, tüp ligasyonu sonrasında pişmanlığın nispeten yaygın olduğunu göstermektedir. Yapılan araştırmalarda tüp ligasyonu sonrası pişmanlık oranının %6-20,3 olduğu belirtilmektedir (Curtis vd., 2006; Rodowa vd., 2024; Shreffler vd., 2016). Türkiye'de tüp ligasyonu sonrası pişmanlık oranı %12-15 olarak bildirilmiştir (Eskicioğlu vd., 2017).

Tüp ligasyonu sonrası hissedilen pişmanlık biyolojik, psikolojik ve sosyal boyutları olan karmaşık bir olgudur. Literatürde, bilgi eksikliği, yetersiz danışmanlık, çocuk kaybı, yeniden evlilik, sosyoekonomik koşullardaki değişiklikler, işlem sırasında kadının genç yaşta olması ve mevcut çocuk sayısı gibi birçok faktörün tüp ligasyonu sonrası pişmanlığa neden olabileceği bildirilmektedir (Eskicioğlu vd., 2017; Ludermir vd., 2009; Sadatmahalleh vd., 2018). Tüp ligasyonunun kalıcı bir kontrasepsiyon yöntemi olması, çoğu kadın açısından güvenilirlik ve uzun dönem korunma sağlaması nedeniyle avantaj olarak görülmektedir. Ancak, zaman içerisinde değişen yaşam koşulları, yeni bir ilişki ya da evlilik, eş veya çocuk kaybı, annelik rolüne ilişkin beklentiler ve öngörülemeyen tıbbi gereksinimler gibi durumlar, daha önce kesin olarak verilen bu kararın yeniden sorgulanmasına yol açabilmektedir. Bu bağlamda tüp ligasyonu sonrası ortaya çıkan pişmanlık, bireyin yaşam döngüsü içinde değişen gereksinim ve önceliklerinin bir yansıması olarak değerlendirilebilir. Bu çalışmada, tüp ligasyonu sonrası geri dönüş talebinde bulunan, motivasyonları ve yaşam öyküleri birbirinden oldukça farklı iki olgu sunularak konunun çok boyutlu yapısına dikkat çekilmesi amaçlanmıştır. Kadınların üreme kararlarını etkileyen faktörleri incelemek amacıyla bireysel görüşmeler yapılmıştır.

2. OLGU SERİSİ

2.1. OLGU 1: Kemik İliği Nakli İçin Donör Arayışı

Hasta, otuz sekiz yaşında, lise mezunu ve çalışmamaktadır. Obstetrik öyküsünde iki düşük ve sezaryen ile iki canlı doğumu (G4P2) bulunmaktadır. Hasta, 2017 yılında engelli iki kardeşinin bakım sorumluluğunu üstlenmesi, etkili bir aile planlaması yöntemi kullanamaması, ekonomik zorluklar, düşük ile sonuçlanan gebelikler yaşaması ve yeni bir gebelik istememesi nedeniyle bilateral tüp ligasyonu yaptırmıştır. Tüp ligasyonu öncesinde oral kontraseptif kullanmış ancak menstrüel düzensizlik yaşaması nedeniyle bırakmış, rahim içi araç kullanamamış ve eşinin bariyer yöntem kullanmak istemediğini belirtmiştir. Hasta, tüp ligasyonu kararı verirken işlem hakkında araştırma yaptığını, gerekli olduğunda tekrar açılabileceğini düşündüğü için bu yöntemi tercih ettiğini ifade etmiştir.

Hastanın ikinci çocuğunda tanı konulan genetik hastalık nedeniyle tedavi süreci devam ederken kemik iliği nakli önerilmiştir. Mevcut kardeşin doku uyumunun uygun bulunmaması üzerine, potansiyel donör kardeş amacıyla yeniden gebelik planlamaya karar vermiştir. Bu doğrultuda tubal reanastomoz talep etmiştir. Hasta, işlem sonrasında spontan gebelik gerçekleşmemesi durumunda yardımcı üreme

tekniklerine başvurmayı düşündüğünü belirtmiştir. Görüşme sırasında, aslında yeniden gebelik planlamadığını, ancak çocuğunun sağlık durumu nedeniyle bu kararı almak zorunda hissettiğini ifade etmiştir. Ayrıca yaşamının ilerleyen dönemlerinde böyle bir durumla karşılaşacağını öngörebilseydi tüp ligasyonu yaptırmayacağını dile getirmiştir.

Bu olgu, tüp ligasyonu sonrası pişmanlık ve geri dönüş talebinin yalnızca bireysel tercihlerle değil, öngörülemeyen tıbbi gereksinimler ve annelik sorumluluğu algısıyla da şekillenebileceğini göstermektedir.

2.2. OLGU 2: Yeniden Evlilik ve Çocuk Sahibi Olma İsteği

Hasta, otuz altı yaşında, lise mezunu ve çalışmaktadır. Obstetrik öyküsünde üç düşük ve sezaryen ile gerçekleşmiş dört canlı doğum (G7P4) bulunmaktadır. Hasta, 2019 yılında son doğumunun ardından yeni bir gebelik planlamadığı için bilateral tüp ligasyonu yaptırmıştır. İzleyen yıllarda eşinden ayrılan hasta, yaklaşık bir yıl önce yeniden evlendiğini belirtmiştir. Yeni evliliği sonrasında eşine duyduğu bağlılık ve birlikte ortak bir çocuk sahibi olma arzusu nedeniyle yeniden gebelik isteğini ifade etmiş ve daha önce tüp ligasyonu olduğu için pişman olduğunu belirtmiştir. Görüşme sırasında, eşinin çocuk sahibi olmak istediğini ancak kendisinin eşinden daha çok istediğini dile getirmiştir. Bu nedenle hasta, fertilitesinin yeniden kazanılması amacıyla tubal reanastomoz için başvurmuştur. Reanastomoz sonrası gebelik oluşmaması durumunda çok üzüleceğini ve yardımcı üreme tekniklerine başvurmayı düşündüğünü belirtmiştir.

Olgu, tüp ligasyonu sonrası pişmanlık ve geri dönüş talebinin yalnızca tıbbi nedenlerle değil, yaşam koşullarındaki değişiklikler, yeniden evlilik, duygusal bağlanma ve yeni aile kurma isteği gibi psikososyal etmenlerle de şekillenebileceğini göstermektedir.

3. TARTIŞMA

Tüp ligasyonu, modern ve kalıcı kontrasepsiyon yöntemlerinden biri olmakla birlikte, değişen yaşam koşulları nedeniyle bazı kadınlarda pişmanlık duygusuna ve fertilitenin yeniden kazanılmasına yönelik talebe yol açabilmektedir (Rodowa vd., 2024; Sadatmahalleh vd., 2018). Literatürde tüp ligasyonu sonrası pişmanlığın yaygınlığının değişken olduğu, özellikle genç yaşta olma, düşük sosyoekonomik düzey, yetersiz preoperatif danışmanlık, ilişki durumundaki değişiklikler ve çocuk kaybı gibi etmenlerin risk faktörleri arasında yer aldığı bildirilmektedir (Eskicioğlu vd., 2017; Ludermir vd., 2009; Rodowa vd., 2024; Sadatmahalleh vd., 2018; Shreffler vd., 2016). Bu çalışmada sunulan iki olgu, farklı yaşam olayları sonucunda tüp ligasyonundan geri dönme talebinde bulunmuştur.

İlk olguda geri dönüş talebinin nedeni, hastanın çocuğunda tanı konulan genetik bir hastalık nedeniyle kemik iliği nakli gereksinimi ve uygun donör arayışıdır. Bu durum, sterilizasyon sonrası pişmanlığın yalnızca üreme isteğiyle değil, öngörülemeyen tıbbi gereksinimlerle de ilişkili olabileceğini göstermektedir. Çocuk sağlığı söz konusu olduğunda annelerin duygusal zorluklar yaşadığı, kendi bedensel ve duygusal sınırlarını ikinci plana atabildikleri bilinmektedir (Engin vd., 2021). Bu olguda hastanın “tekrar gebelik istemediğini” ifade etmesine rağmen çocuğunun sağlık durumu nedeniyle yeniden gebelik kararı alması, annelik sorumluluğu ve bakım verme rolünün bireysel üreme tercihleri üzerinde etkili olabildiğini göstermektedir. Kadının kendi yaşam planında yer almayan bir gebeliği, çocuğunun sağlığı söz konusu olduğunda düşünmesi; annelik kimliği, fedakârlık beklentileri ve ebeveynlik sorumluluğunun karar süreçlerindeki güçlü etkisini ortaya koymaktadır.

İkinci olguda geri dönüş talebi, yeniden evlilik sonrası çocuk sahibi olma isteği ile ilişkilidir. Literatürde yeni partner ilişkilerinin ve yeniden evliliğin, tüp ligasyonu sonrası pişmanlığın en sık nedenlerinden biri olduğu bildirilmektedir (Curtis vd., 2006; Ludermir vd., 2009). Yeni bir ilişkide ortak çocuk sahibi olma arzusu, yalnızca biyolojik ebeveynlik isteğini değil, aidiyet, aile bütünlüğü ve ilişkinin güçlenmesine yönelik beklentileri de içerebilmektedir. Bazı toplumlarda ortak çocuğun evliliği güçlendirdiği yönündeki açık ya da örtük toplumsal inançlar, kadınların karar süreçlerini etkileyebilmektedir. Bu nedenle hastanın çocuk sahibi olma isteğini kendisine ait bir tercih olarak ifade etmesi, toplumsal normlardan bağımsız değerlendirilmemelidir.

Tubal reanastomoz, uygun hasta grubunda fertilitenin yeniden kazanılması açısından etkili bir seçenek olmakla birlikte başarı; yaş, sterilizasyon tekniği, ektopik gebelik riski, sterilizasyondan geri almaya kadar geçen süre, planlanan anastomoz yeri ve tahmini kalan tüp uzunluğu gibi faktörlere bağlıdır (Garg ve Milad, 2022; van Seeters vd., 2017). Bununla birlikte spontan gebelik elde edilemeyen durumlarda yardımcı üreme teknikleri alternatif oluşturmaktadır (Garg ve Milad, 2022). Bu olgu serisinde her iki hastanın da tubal reanastomoz sonrası gebelik gerçekleşmezse tüp bebek tedavisini düşünmesi, kadınların fertiliteyi yeniden kazanma konusunda güçlü bir motivasyona sahip olduklarını göstermektedir.

Her iki olgu birlikte değerlendirildiğinde, tüp ligasyonu sonrası pişmanlığın yaşam döngüsü içinde değişen koşullarla yeniden şekillenebilen dinamik bir süreç olduğu görülmektedir. Öte yandan, her iki olgunun da genç yaşta tüp ligasyonu yaptırmış olması dikkat çekicidir. Bu durum, yaşamın ilerleyen dönemlerinde üreme isteğinde değişiklik olması halinde geri dönüş talebinin ortaya çıkmasına neden olabilmektedir. Bu nedenle, özellikle genç yaş grubunda uygulanan kalıcı aile planlaması yöntemlerinde karar verme sürecinin kapsamlı danışmanlık ile desteklenmesi önem taşımaktadır. Literatürde, kapsamlı ve birey merkezli danışmanlık verilen kadınlarda sterilizasyon sonrası memnuniyetin daha yüksek olduğu bildirilmektedir (Eskicioğlu vd., 2017; Sadatmahalleh vd., 2018). Bu doğrultuda danışmanlık sürecinde, gelecekte ortaya çıkabilecek ilişki değişiklikleri, çocuk kaybı, sağlık sorunları ve kararın yeniden gözden geçirilme olasılığı kapsamlı biçimde ele alınmalıdır.

4. SONUÇ VE ÖNERİLER

Sunulan olgularda, öngörülemeyen yaşam olayları ve beklenmedik tıbbi gereksinimler, tüp ligasyonu sonrası pişmanlık ve geri dönüş talebine yol açmıştır. Bu durum, sterilizasyon öncesi danışmanlığın yalnızca yöntemin etkinliği ve kalıcılığına odaklanmaması gerektiğini göstermektedir. Danışmanlık sürecinde işlemin kalıcı doğası, olası komplikasyonlar ve alternatif doğum kontrol yöntemleri hakkında ayrıntılı ve anlaşılır bilgi verilmesi önem taşımaktadır. Bu doğrultuda tüp ligasyonu kararı verilirken multidisipliner bir yaklaşım benimsenmeli, tıbbi, psikolojik ve sosyal boyutlar birlikte değerlendirilmelidir. Kadının bireysel özellikleri, aile yapısı, mevcut çocuk sayısı, gelecekteki çocuk sahibi olma isteği ve yaşam koşulları dikkate alınarak kapsamlı bir değerlendirme yapılmalı, karar sürecine kadının aktif katılımı sağlanmalı ve yeterli danışmanlık hizmeti sunulmalıdır.

Etik Boyut: Bu çalışma olgu serisi niteliğinde olduğundan etik kurul onayı gerektirmemektedir. Bu olgu serisi için hastalardan sözlü ve yazılı bilgilendirilmiş onam alınmıştır. Tüm veriler hasta gizliliği korunacak şekilde anonimleştirilerek sunulmuştur.

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KAYNAKLAR

Curtis, K. M., Mohllajee, A. P., & Peterson, H. B. (2006). Regret following female sterilization at a young age: A systematic review. *Contraception, 73*(2), 205-210. https://doi.org/10.1016/j.contraception.2005.08.006

Engin, E., Çam, M. O., & Demirkol, H. (2021). Arafta bir yaşam: Kemik iliği nakli olan bir çocuğun annesi olmak. *Psikiyatride Güncel Yaklaşımlar, 13*(2), 282-291. http://doi.org/10.18863/pgy.775939

Eskicioğlu, F., Gür, E., Tatar, S., & Pişkinpaşa, N. (2017). The evaluation of regret status in women following tubal ligation in Turkey. *Clinical and Experimental Obstetrics & Gynecology, 44*(1), 93-97.

Festin, M. P. R. (2020). Overview of modern contraception. *Best Practice & Research Clinical Obstetrics & Gynaecology, 66*, 4-14. https://doi.org/10.1016/j.bpobgyn.2020.03.004

Garg, N., & Milad, M. P. (2022). Female sterilization reversal in the era of in-vitro fertilization. *Current Opinion in Obstetrics and Gynecology, 34*(4), 244-249. http://doi.org/10.1097/GCO.0000000000000802

Ludermir, A. B., Machado, K. M. d. M., Costa, A. M. d., Alves, S. V., & Araújo, T. V. B. d. (2009). Tubal ligation regret and related risk factors: Findings from a case-control study in Pernambuco State, Brazil. *Cadernos de Saúde Pública, 25*, 1361-1368. https://doi.org/10.1590/S0102-311X2009000600018

Ndayishimye, S., Olorunfemi, G., & Nahayo, B. (2023). Prevalence and factors associated with female sterilization in Rwanda: Evidence from the demographic and health survey data (2019–2020). *BMC Public Health, 23*(1), 2446. https://doi.org/10.1186/s12889-023-17334-8

Rodowa, M.-S., Waddington, A., & Pudwell, J. (2024). Regret in the modern contraceptive landscape: Evaluating regret in patients undergoing tubal ligation or bilateral salpingectomy for contraception. *Journal of Obstetrics and Gynaecology Canada, 46*(5), 102362. https://doi.org/10.1016/j.jogc.2024.102362

Sadatmahalleh, S. J., Ziaei, S., Kazemnejad, A., & Mohamadi, E. (2018). Evaluation of influencing factors on tubal sterilization regret: A cross-sectional study. *International Journal of Fertility & Sterility, 12*(3), 200. http://doi.org/10.22074/ijfs.2018.5272

Shreffler, K. M., Greil, A. L., Mcquillan, J., & Gallus, K. L. (2016). Reasons for tubal sterilisation, regret and depressive symptoms. *Journal of Reproductive and Infant Psychology, 34*(3), 304-313. https://doi.org/10.1080/02646838.2016.1169397

Türkiye Nüfus ve Sağlık Araştırması. (2018). Hacettepe Üniversitesi Nüfus Etütleri Enstitüsü, Ankara.

Van Seeters, J. A., Chua, S. J., Mol, B. W., & Koks, C. A. (2017). Tubal anastomosis after previous sterilization: a systematic review. *Human Reproduction Update, 23*(3), 358-370. https://doi.org/10.1093/humupd/dmx003

HEPATOSELÜLER KARSİNOMDA KUPROPTOZ: GÜNCEL MOLEKÜLER YAKLAŞIMLAR VE TEDAVİ PERSPEKTİFLERİ

İlay BURAN KAVURAN

Fırat Üniversitesi, Tıp Fakültesi, Tıbbi Biyoloji AD, Elazığ, Türkiye, ORCID ID: 0000-0002-2890-3952

Sena DEVECİ

[1]Fırat Üniversitesi, Tıp Fakültesi, Tıbbi Biyoloji AD, Elazığ, Türkiye, ORCID ID: 0009-0001-0601-8928

ÖZET

Hepatoselüler karsinom (HCC), dünya genelinde kanser kaynaklı ölümlerin üçüncü başlıca nedeni olup tüm primer karaciğer kanserlerinin %80-90'ını oluşturmaktadır. Başta kronik Hepatit B ve Hepatit C enfeksiyonları olmak üzere, alkol ilişkili karaciğer hastalığı, metabolik disfonksiyonla ilişkili steatotik karaciğer hastalığı (MASLD), aflatoksin maruziyeti, obezite ve tip 2 diyabet gibi çok sayıda faktörün uzun süreli karaciğer hasarı, inflamasyon ve fibrozis üzerinden karsinogenezi tetiklemesiyle şekillenen multifaktöriyel bir süreçtir. Son yıllarda, bu karmaşık patogenetik süreçlerin daha iyi anlaşılmasına yönelik çalışmalar, özellikle hücresel metabolizma ve metal iyon homeostazı ile ilişkili yeni hücre ölümü mekanizmalarına dikkat çekmiş; bu kapsamda kuproptozis, HCC gelişimi ve ilerlemesinde potansiyel bir düzenleyici mekanizma olarak öne çıkmıştır. Kuproptoz, bakır iyonlarına bağımlı, mitokondriyal solunum yoluyla tetiklenen yeni bir programlı hücre ölümü mekanizmasıdır. Mekanizmanın özünde bakırın TCA döngüsünün lipoillenmiş enzimlerine (özellikle DLAT'a) doğrudan bağlanması, anormal protein agregasyonu ve proteotoksik stres yer almakta; bu süreçte FDX1 (ferredoksin 1) geni kilit düzenleyici rolü üstlenmektedir. Karaciğerin bakır metabolizmasındaki merkezi rolü, HCC'de kuproptozun ortaya çıkmasına uygun bir zemin oluşturmaktadır. Hücrede bakır birikimi reaktif oksijen türlerinin (ROS) artışını tetikleyerek oksidatif stres, DNA hasarı ve mitokondriyal disfonksiyon ekseninde hücresel hasarı derinleştirmektedir. Tümör hücreleri, CTR1 bakır taşıyıcısını aşırı ifade ederek hücre içi bakır düzeylerini artırmakta; bu durum hem tümör büyümesini desteklemekte hem de terapötik açıdan değerlendirilebilecek kuproptoz duyarlılığı oluşturmaktadır. Kuproptozun terapötik potansiyeli doğrultusunda, bakır iyonoforları, nanotaşıyıcı sistemler ve immün kontrol noktası inhibitörleriyle kombine yaklaşımlar üzerine araştırmalar hız kazanmaktadır. Ancak moleküler mekanizmasının tam olarak aydınlatılamamış olması, özgün morfolojik belirteçlerin eksikliği ve klinik uygulamaya geçişi sınırlayan metodolojik zorluklar, bu alanda daha kapsamlı ve sistematik araştırmalara duyulan ihtiyacın devam ettiğini göstermektedir. Bu bilgiler doğrultusunda hazırlanan, mevcut derlemenin amacı HCC'de kuproptozun moleküler mekanizmalarını, tümör biyolojisindeki rolünü ve potansiyel terapötik hedef olarak önemini güncel literatür ışığında değerlendirmektir.

Anahtar Kelimeler: kuproptoz, hepatoselüler karsinom, bakır homeostazisi, FDX1, DLAT.

CUPROPTOSIS IN HEPATOCELLULAR CARCINOMA: CURRENT MOLECULAR APPROACHES AND THERAPEUTIC PERSPECTIVES

ABSTRACT

Hepatocellular carcinoma (HCC) is the third leading cause of cancer-related deaths worldwide and accounts for 80–90% of all primary liver cancers. It is a multifactorial disease driven by chronic liver injury, inflammation, and fibrosis, primarily associated with chronic Hepatitis B and Hepatitis C infections, as well as alcohol-related liver disease, metabolic dysfunction-associated steatotic liver disease (MASLD), aflatoxin exposure, obesity, and type 2 diabetes. In recent years, efforts to better understand these complex pathogenic processes have highlighted novel cell death mechanisms linked to cellular metabolism and metal ion homeostasis. In this context, cuproptosis has emerged as a potential regulatory mechanism in HCC development and progression. Cuproptosis is a newly defined form of programmed cell death that is dependent on copper ions and triggered through mitochondrial respiration.

The core mechanism involves the direct binding of copper to lipoylated enzymes of the tricarboxylic acid (TCA) cycle (particularly DLAT), leading to abnormal protein aggregation and proteotoxic stress. The gene FDX1 (ferredoxin 1) plays a key regulatory role in this process. The central role of the liver in copper metabolism provides a favorable context for the occurrence of cuproptosis in HCC. Intracellular copper accumulation promotes the generation of reactive oxygen species (ROS), thereby exacerbating oxidative stress, DNA damage, and mitochondrial dysfunction. Tumor cells increase intracellular copper levels by overexpressing the CTR1 copper transporter, which not only supports tumor growth but also creates a therapeutically exploitable sensitivity to cuproptosis. In line with its therapeutic potential, research on copper ionophores, nanocarrier systems, and combination strategies with immune checkpoint inhibitors has gained increasing attention. However, the incomplete understanding of its molecular mechanisms, the lack of specific morphological markers, and methodological limitations restricting clinical translation highlight the ongoing need for more comprehensive and systematic studies in this field. Accordingly, this review aims to evaluate the molecular mechanisms of cuproptosis in HCC, its role in tumor biology, and its potential as a therapeutic target in light of current literature.

Keywords: cuproptosis, hepatocellular carcinoma, copper homeostasis, FDX1, DLAT.

1.GİRİŞ: HEPATOSELÜLER KARSİNOM VE KUPROPTOZ

Hepatoselüler karsinom (HCC), dünya genelinde kansere bağlı ölümlerin üçüncü önde gelen nedeni olup yılda yaklaşık 800.000 ölümden sorumludur. Dünya Sağlık Örgütü verilerine göre, 2030 yılına kadar karaciğer kanserine bağlı yıllık ölüm sayısının bir milyonu aşacağı öngörülmektedir. Primer karaciğer kanserlerinin %75–85'ini oluşturan HCC, karaciğer kanserine bağlı mortalite yükünün büyük kısmını temsil etmektedir (Chan ve ark., 2026). HCC gelişiminde hepatit B virüsü (HBV) ve hepatit C virüsü (HCV) enfeksiyonları, alkole bağlı karaciğer hastalığı (ALD) ve metabolik disfonksiyonla ilişkili steatotik karaciğer hastalığı (MASLD) temel etiyolojik faktörler arasında yer almaktadır. Geniş çaplı aşılama programları ve doğrudan etkili antiviral tedaviler viral ilişkili HCC insidansını azaltmış olsa da, MASLD ilişkili HCC vakalarında küresel düzeyde belirgin bir artış gözlenmektedir. Bununla birlikte HCC olgularının büyük çoğunluğu ileri evrede tanı almakta ve cerrahi rezeksiyona uygun hasta oranı sınırlı kalmaktadır. Günümüzde kullanılan sistemik tedavilerin genel sağkalımı yalnızca birkaç ay uzatabilmesi, HCC tedavisinde yeni moleküler hedeflerin araştırılmasını zorunlu hale getirmektedir (Chen ve ark., 2023). Karaciğer, organizmadaki bakır metabolizmasının temel düzenleyici organı olup bakırın depolanması, sistemik dolaşıma verilmesi ve safra yoluyla atılımında merkezi rol üstlenmektedir (Roberts ve ark., 2008). HCC hastalarında serum bakır düzeyleri ve seruloplazmin konsantrasyonlarının sağlıklı bireylere kıyasla anlamlı düzeyde yüksek olduğu bildirilmiştir (Geetha ve ark., 2009). Bu bulgular, bakır homeostazındaki bozulmanın hepatokarsinogenez sürecinin önemli bileşenlerinden biri olduğunu göstermektedir(Cong ve ark., 2022). Hücre içi bakır birikimi; anjiogenezin uyarılması, matriks metalloproteinaz aktivasyonunun artırılması ve mitokondriyal metabolizmanın yeniden programlanması gibi mekanizmalar aracılığıyla tümör progresyonuna katkıda bulunmaktadır (Wang ve ark., 2023). Bununla birlikte aşırı bakır yüklenmesi, oksidatif stres oluşumu ve trikarboksilik asit (TCA) döngüsü proteinleriyle doğrudan etkileşim sonucunda tümör hücre ölümünü de tetikleyebilmektedir (Mao ve ark., 2025). Karaciğerin bakır metabolizmasındaki bu çift yönlü rolü, HCC'yi bakır ilişkili hücre ölümü mekanizmalarının araştırılması açısından özgün bir model haline getirmektedir. Bu bağlamda son yıllarda tanımlanan kuproptoz, HCC biyolojisinde dikkat çeken yeni programlı hücre ölümü mekanizmalarından biri olarak öne çıkmaktadır. Kuproptoz kavramı ilk kez 2022 yılında Tsvetkov ve ark. tarafından tanımlanmış ve bakır iyonoforlarının mitokondriyal solunuma bağımlı hücrelerde klasik hücre ölümü mekanizmalarından bağımsız özgün bir ölüm süreci oluşturduğu gösterilmiştir (Tsvetkov ve ark., 2022). Bu mekanizmanın temelinde, aşırı bakır birikiminin TCA döngüsünün lipoylenmiş proteinlerine (özellikle dihidrolipoamid S-asetiltransferaz (DLAT)) bağlanması yer almaktadır. Bakırın bu proteinlerle etkileşimi sonucunda anormal oligomerizasyon ve çözünmeyen protein agregatları oluşmakta, proteotoksik stres gelişmekte ve eş zamanlı olarak Fe-S küme proteinlerinin kaybı meydana gelmektedir (Li ve ark., 2022; Tsvetkov ve ark., 2022). Bu süreç sonunda hücresel homeostaz geri dönüşümsüz biçimde bozulmakta ve özgün bir hücre ölümü ortaya çıkmaktadır. Kuproptoz mekanizmasının merkezinde yer alan FDX1, LIAS, LIPT1, DLAT, PDHA1 ve PDHB gibi genlerin

protein lipoilasyonu ve mitokondriyal metabolik aktivite üzerinde kritik rol oynadığı gösterilmiştir (Tsvetkov ve ark., 2022; Li ve ark., 2022).

Son yıllarda elde edilen bulgular, kuproptozun ferroptoz ve apoptoz gibi diğer hücre ölümü mekanizmalarıyla da yakın moleküler etkileşim içinde olduğunu göstermektedir. Tüm bu bulgular, kuproptozun yalnızca HCC patogenezinin anlaşılmasında değil, aynı zamanda yeni nesil hedefe yönelik tedavi stratejilerinin geliştirilmesinde de önemli bir moleküler eksen olabileceğini ortaya koymaktadır.

2. HCC'DE BAKIR HOMEOSTAZİSİ BOZUKLUKLARI, TÜMÖR MİKROÇEVRESİ VE KUPROPTOZ İLİŞKİSİ

Bakır (Cu), sitokrom c oksidaz başta olmak üzere mitokondriyal solunum zincirinde görev alan birçok enzimin temel kofaktörü olup antioksidan savunma, enerji metabolizması ve anjiyogenez gibi çeşitli fizyolojik süreçlerde kritik rol oynayan esansiyel bir eser elementtir (Lu ve ark., 2025). Karaciğer, bakırın depolanması, dağıtılması ve safra yoluyla atılımının düzenlenmesinden sorumlu temel organ olduğundan, bakır homeostazındaki bozukluklar hepatoselüler karsinom (HCC) gelişiminde önemli bir yere sahiptir. Yapılan çalışmalar, HCC hastalarının hem serumunda hem de tümör dokularında bakır konsantrasyonunun sağlıklı bireyler ve siroz hastalarına kıyasla belirgin şekilde arttığını göstermiştir (Porcu ve ark., 2018). Bu durum, bakır metabolizmasının HCC patogenezinde yalnızca ikincil bir değişiklik olmadığını, aynı zamanda tümör progresyonunu destekleyen aktif bir mekanizma olabileceğini düşündürmektedir. HCC hücreleri, yüksek intrasellüler bakır düzeylerini sürdürebilmek için bakır taşıyıcı sistemlerinde belirgin bir yeniden programlanma geliştirmektedir. Özellikle başlıca bakır içe alım taşıyıcısı olan CTR1 (SLC31A1)'in aşırı ekspresyonu, tümör hücrelerinde bakır birikiminin temel nedenlerinden biri olarak kabul edilmektedir. c-MYC onkoproteininin CTR1 promotör bölgesine bağlanarak transkripsiyonu artırdığı ve CTR1 ile c-MYC ekspresyon düzeylerinin NAFLD'den siroza ve HCC'ye ilerleyen süreç boyunca paralel biçimde yükseldiği bildirilmiştir (Lu ve ark., 2025). CTR1 ekspresyonunun baskılanmasının ise hipoksi ilişkili GLUT1, PKM ve LDHA transkript düzeylerini azaltarak HCC hücrelerinde hem proliferasyonu hem de metabolik aktiviteyi önemli ölçüde inhibe ettiği gösterilmiştir. Buna karşılık hücre içi fazla bakırın taşınmasından sorumlu ATP7A ve safra aracılı bakır atılımını sağlayan ATP7B ekspresyonunun HCC dokularında azaldığı bildirilmektedir. Bu değişiklikler, tümör hücrelerinde intrasellüler bakır birikiminin daha da artmasına yol açmaktadır (Tsvetkov ve ark., 2022). Bakır metabolizmasındaki bu yeniden programlanmanın HCC biyolojisinde çift yönlü etkiler oluşturduğu düşünülmektedir. Bir yandan artmış bakır düzeyleri, anjiyogenez, proliferasyon, invazyon ve metastazı destekleyen sinyal yolaklarını aktive ederek tümör progresyonuna katkıda bulunurken; diğer yandan aşırı hücre içi bakır birikimi, mitokondriyal lipoyillenmiş proteinlerin agregasyonu ve buna bağlı proteotoksik stres aracılığıyla kuproptozu tetikleyerek antitümöral etki oluşturabilmektedir (Lu ve ark., 2025). Bu nedenle HCC'de tümör gelişimini destekleyen bakır bağımlı süreçlerle kuproptoz arasındaki dengenin, tümör davranışını ve tedavi yanıtını belirleyen temel faktörlerden biri olduğu düşünülmektedir. Özellikle hangi moleküler koşullarda kuproptozun baskın hale geçtiğinin ortaya konulması, hasta stratifikasyonu ve hedefe yönelik tedavi yaklaşımlarının geliştirilmesi açısından büyük önem taşımaktadır.

Son yıllarda yapılan çalışmalar, kuproptoz ilişkili genlerin (KİG) yalnızca tümör metabolizmasıyla değil, aynı zamanda tümör immün mikroçevresi (TME) ile de yakından ilişkili olduğunu göstermektedir. Başta FDX1, DLAT, LIAS ve DLST olmak üzere kuproptoz ilişkili genlerin ekspresyon profillerinin, HCC'de immün hücre infiltrasyonu ile anlamlı düzeyde ilişkili olduğu bildirilmiştir. KİG risk skorunun yüksek olduğu HCC hastalarında tümör infiltran lenfosit (TIL) düzeylerinin düşük, M2 polarize tümör ilişkili makrofaj (TAM) infiltrasyonunun ise yüksek olduğu gösterilmiş; bu immünosupresif profilin anti-PD-1/PD-L1 immünoterapilerine direnç ile ilişkili olabileceği öne sürülmüştür (Wang G. ve ark., 2022). Buna karşın artmış FDX1 ekspresyonunun $CD8^+$T lenfosit infiltrasyonunu destekleyebildiğine dair bulgular da bulunmaktadır (Wang G. ve ark., 2022). Ayrıca kuproptozun, hipoksik tümör mikroçevresini yeniden şekillendirerek glikolitik metabolizmadan oksidatif fosforilasyona (OXPHOS) geçişi teşvik ettiği ve bu özelliği sayesinde düşük doz radyoterapi gibi diğer tedavi modaliteleriyle sinerjik etkileşim gösterebildiği bildirilmektedir (Shao ve ark., 2024). Bu bulgular, kuproptozun yalnızca hücre ölümü mekanizması olarak değil, aynı zamanda HCC tümör mikroçevresini yeniden

programlayan önemli bir metabolik ve immünolojik düzenleyici olarak değerlendirilmesi gerektiğini ortaya koymaktadır.

3. HCC'DE PROGNOSTİK BELİRTEÇ OLARAK KUPROPTOZ İLİŞKİLİ GENLER VE lncRNA PROFİLLERİ

Kuproptozun hepatoselüler karsinomdaki prognostik önemine yönelik çalışmalar son yıllarda belirgin biçimde artmış ve özellikle kuproptoz ilişkili genler ile uzun kodlamayan RNA (lncRNA) temelli moleküler profiller dikkat çekmeye başlamıştır (Tablo 1). Bu profiller çoğunlukla TCGA (The Cancer Genome Atlas), GEO ve ICGC veri tabanları kullanılarak geliştirilmiş ve daha sonra bağımsız kohortlarda doğrulanmıştır (Chen ve ark., 2022; Peng ve ark., 2023). Elde edilen bulgular, kuproptoz ilişkili moleküler özelliklerin yalnızca genel sağkalım ile değil, aynı zamanda tümör immün mikroçevresi, ilaç duyarlılığı ve immünoterapi yanıtı ile de yakından ilişkili olduğunu göstermektedir (Cong ve ark., 2022; Chen ve ark., 2023). Kuproptoz ilişkili moleküller arasında özellikle FDX1 dikkat çekmektedir. Mevcut çalışmalar, FDX1'in HCC'de somatik mutasyon yükü, immün yanıt ve hasta prognozu ile yakından ilişkili olduğunu göstermektedir (Wang ve ark., 2024). FDX1 ekspresyon düzeyinin tümör immün mikroçevresiyle güçlü ilişki gösterdiğini ve bu molekülün potansiyel bir prognostik biyobelirteç olabileceğini bildirmiştir. Bunun yanında DLAT da bağımsız prognostik belirteçlerden biri olarak değerlendirilmektedir(Zhang ve ark., 2023), kapsamlı biyoinformatik analizler sonucunda DLAT'ın HCC prognozunun öngörülmesinde ve hedefe yönelik tedavi stratejilerinde kullanılabilecek güçlü bir aday olduğunu göstermiştir. Bu bulgular, kuproptoz ilişkili moleküler profillerin gelecekte kişiselleştirilmiş HCC tedavisinde önemli rol oynayabileceğini düşündürmektedir(Chen ve ark., 2022). FDX1 ve DLAT merkezli bir prognostik modelin HCC hastalarında genel sağkalım açısından bağımsız bir öngörücü olduğunu göstermiştir. Aynı çalışmada yüksek risk skoruna sahip hastalarda daha kötü klinik sonuçlar ve daha agresif tümör biyolojisi gözlendiği bildirilmiştir (Chen ve ark., 2022; Cong ve ark., 2022) ise kuproptoz ilişkili immün kontrol noktası gen profilinin yalnızca prognozu değil, aynı zamanda anti-PD-1/PD-L1 temelli immünoterapi yanıtını da öngörebildiğini ortaya koymuştur. Bu çalışmada yüksek riskli hastalarda immün baskılayıcı mikroçevrenin daha belirgin olduğu ve immün kaçış mekanizmalarının aktive olduğu gösterilmiştir (Cong ve ark., 2022; Peng ve ark., 2023), KİG ve kuproptoz ilişkili lncRNA profillerini birlikte değerlendirerek her iki moleküler yapının da HCC'de bağımsız prognostik değer taşıdığını ve immün hücre infiltrasyonu ile güçlü ilişki gösterdiğini bildirmiştir. Aynı çalışmada ilaç duyarlılığı veri tabanları kullanılarak sekiz potansiyel terapötik ajan belirlenmiş ve kuproptoz ilişkili profillerin tedavi seçiminde yol gösterici olabileceği öne sürülmüştür (Peng ve ark., 2023).

lncRNA tabanlı moleküler profiller de HCC'de dikkat çekici sonuçlar ortaya koymaktadır. (Zhang ve ark., 2022), geliştirdikleri yeni bir kuproptoz ilişkili lncRNA profilinin HCC hastalarında genel sağkalımı yüksek doğrulukla öngörebildiğini göstermiştir. Çalışmada özellikle yüksek risk grubunda immün baskılanma, artmış tümör progresyonu ve daha kısa sağkalım süreleri saptanmıştır (Zhang ve ark., 2022; Yuan ve ark., 2023) tarafından gerçekleştirilen çalışmada ise AL590705.3, LINC02870, KDM4A-AS1 ve MKLN1-AS lncRNA'larından oluşan dört bileşenli bir moleküler profil tanımlanmıştır. Araştırmacılar, elesklomol tedavisi sonrası bu lncRNA'ların HCC hücrelerinde baskılandığını ve FDX1 ekspresyonuyla ilişkili olduğunu göstermiştir. Ayrıca yüksek riskli hastalarda bu lncRNA'ların aşırı ekspresyonunun kötü prognoz ile ilişkili olduğu bildirilmiştir (Yuan ve ark., 2023; Chen ve ark., 2023) ise Frontiers in Genetics'te yayımlanan çalışmalarında Kİ-lncRNA (Kuproptoz ilişkili uzun kodlamayan RNA) profillerinin immün infiltrasyon örüntülerini ve kemoterapötik ajanlara duyarlılığı öngörmede ek katkı sağladığını vurgulamıştır (Chen ve ark., 2023).

Tablo 1: Kuproptozun düzenlenmesinde kritik işlevler üstlenen genler, protein ürünleri, mekanistik katkıları ve HCC bağlamındaki klinik anlamları

Gen	Tam Adı	HCC Bağlamında Kuproptozdaki Rolü	Kaynak
FDX1	Ferredoksin 1	$Cu^{2+} \rightarrow Cu^{+}$ indirgenmesi; lipoilasyon yolağının en üst düzey düzenleyicisi; elesclomolün doğrudan hedefi. HCC dokusunda düşük FDX1 ekspresyonu kötü prognozla ilişkilidir.	Tsvetkov ve ark., 2022; Chen ve ark., 2024
LIAS	Lipoik Asit Sentaz	Mitokondriyal lipoik asit biyosentezinde katalizör; FDX1 tarafından yukarı akış düzeyinde regüle edilir; susturulması kuproptozdan korur.	Tsvetkov ve ark., 2022
LIPT1	Lipoiltransferaz 1	DLAT başta olmak üzere TCA döngüsü enzimlerinin kovalent lipoilasyon modifikasyonunu gerçekleştirir; HCC prognoz modellerinde bağımsız değişken olarak saptanmıştır.	Tsvetkov ve ark., 2022; Bai ve ark., 2022; Chen Z. ve ark., 2024
DLD	Dihidrolipoamid Dehidrojenaz	TCA döngüsü ve alfa-keto asit dehidrojenaz komplekslerinde elektron taşıyıcısı; kuproptozik fonksiyonu henüz net tanımlanmamış.	Tsvetkov ve ark., 2022
DLAT	Dihidrolipoamid S-asetiltransferaz	Lipoylanmış DLAT, bakır bağlandığında anormal oligomerizasyon gösterir; proteotoksik stres ve hücre ölümünü tetikler. Yüksek ekspresyon HCC'de kötü prognozla ilişkilidir.	Tsvetkov ve ark., 2022; Bai ve ark., 2022; Liang ve ark., 2025; Zhou ve ark., 2025 Chen Z. ve ark ., 2024
PDHA1	Piruvat Dehidrojenaz E1 Alfa 1	PDH kompleksinin E1α alt birimi; glikolizi TCA döngüsüne bağlar; kuproptozik mekanizmaya özgü katkısı araştırılmaktadır.	Tsvetkov ve ark., 2022
PDHB	Piruvat Dehidrojenaz E1 Beta	PDH kompleksinin E1β alt birimi; lipoilasyon substratı; kuproptozik mekanizmaya özgü katkısı araştırılmaktadır.	Tsvetkov ve ark., 2022
MTF1	Metal Düzenleyici Transkripsiyon Faktörü 1	Bakır homeostaz düzenleyicisi; gen susturulması kuproptozdan koruyucu etkiyi kaldırır ve HCC hücrelerini kuproptozun sitotoksik etkisine açık hale getirir.	Tsvetkov ve ark., 2022; Zuo ve ark., 2023
GLS	Glutaminaz	Glutaminden glutamat sentezi; gen susturulması kuproptoza duyarlılığı artırır; metabolik yeniden programlanma bağlamında önem taşır.	Tsvetkov ve ark., 2022

Gen	Tam Adı	HCC Bağlamında Kuproptozdaki Rolü	Kaynak
CDKN2A	Sikline Bağımlı Kinaz İnhibitörü 2A	Tümör supresör; yüksek ekspresyon kuproptoza duyarlılıkla ve HCC'de kötü prognozla ilişkilendirilmekte; düzenleme mekanizması tartışmalıdır.	Tsvetkov ve ark., 2022., Lutsenko S ve ark., 2007; Shi ve ark., 2023

4. TERAPÖTİK STRATEJİLER

Kuproptozun HCC tedavisindeki potansiyelinden yararlanmayı amaçlayan terapötik yaklaşımlar temel olarak bakır iyonoforları, nanoteknoloji tabanlı sistemler, bakır şelasyonu ve immünoterapi kombinasyonları olmak üzere dört ana eksende yoğunlaşmaktadır (Ozkan & Bakar-Ates, 2023; Wang ve ark., 2024). Bakır iyonoforları arasında en dikkat çekici ajanlardan biri elesklomoldür. Elesklomol, bakır iyonlarını mitokondriyal matrikse taşıyan ve FDX1'i doğrudan hedef alan bir iyonofor olarak tanımlanmaktadır (Yuan ve ark., 2023). HCC hücre hatlarında elesklomolün oluşturduğu sitotoksik etkinin FDX1 ekspresyon düzeyi ile yakından ilişkili olduğu gösterilmiştir. Özellikle FDX1 ekspresyonu yüksek olan Huh-7 hücrelerinde elesklomolün IC50 değerinin 22,76 nM gibi oldukça düşük düzeyde bulunması, bu hücrelerin kuproptoza yüksek duyarlılık gösterdiğini ortaya koymaktadır (Yuan ve ark., 2023). Ayrıca elesklomol tedavisinin ardından AL590705.3, LINC02870, KDM4A-AS1 ve MKLN1-AS lncRNA ekspresyonlarında belirgin azalma gözlenmiştir (Yuan ve ark., 2023). Disülfiram (DSF) ise aktif metaboliti DEDTC aracılığıyla bakır iyonoforu gibi davranmakta ve bakır ile kombinasyon halinde HCC hücrelerinde hem kuproptozu hem de ferroptozu aktive ederek güçlü antitümöral etki göstermektedir (Ozkan & Bakar-Ates, 2023).

Nanoteknoloji tabanlı sistemler, kuproptozun terapötik etkinliğini artırmak amacıyla geliştirilen yenilikçi yaklaşımlar arasında yer almaktadır(Guo ve ark., 2023), ROS-duyarlı nanopartiküller aracılığıyla elesklomol ve bakırın birlikte taşınmasının anti-PD-L1 immünoterapisi ile sinerjik etki gösterdiğini ve in vivo HCC modellerinde belirgin tümör küçülmesi sağladığını bildirmiştir. Ayrıca düşük doz radyoterapi ile kuproptoz indüksiyonunu entegre eden nanoplatformların hipoksik tümör mikroçevresini yeniden şekillendirerek radyodirencini azaltabileceği ve antitümöral immün yanıtı güçlendirebileceği gösterilmiştir (Shao ve ark., 2024).Bu yaklaşımlar, kuproptozun yalnızca doğrudan tümör hücre ölümü oluşturmakla kalmayıp tümör mikroçevresini de yeniden programlayabileceğini düşündürmektedir (Guo ve ark., 2023).

Bakır şelasyonu, HCC hücrelerinin bakır bağımlılığını hedefleyen alternatif terapötik stratejilerden biridir. Tetratiomolibdat (TM) ve D-penisillamin gibi bakır şelatörlerinin tümör mikroçevresindeki bakır düzeyini azaltarak anjiyogenezi ve metastatik potansiyeli baskılayabileceği ileri sürülmektedir (Ozkan & Bakar-Ates, 2023). Bununla birlikte bakırın normal hepatositler için de yaşamsal öneme sahip olması nedeniyle, bu ajanların terapötik kullanımında doz optimizasyonu büyük önem taşımaktadır. Özellikle sistemik bakır eksikliğinin hematolojik ve nörolojik toksisiteye yol açabilmesi, klinik uygulamada dikkatli hasta takibini gerekli kılmaktadır (Zhou ve ark., 2025).

Son yıllarda kuproptozun immünoterapi ile kombinasyonu da önemli bir araştırma alanı haline gelmiştir. Klinik öncesi çalışmalar, FDX1 ekspresyonunu artıran müdahalelerin anti-PD-1/PD-L1 immünoterapisine yanıtı iyileştirebileceğini düşündürmektedir (Wang ve ark., 2024). Guo ve ark. (2023), ROS-duyarlı nanopartiküller aracılığıyla kuproptoz indüksiyonu ile anti-PD-L1 blokajının birlikte kullanılmasının tümöral immün yanıtı belirgin biçimde artırdığını göstermiştir. Bu yaklaşımın özellikle glikolitik metabolizma ağırlıklı ve mevcut immünoterapilere dirençli HCC alt tiplerinde tamamlayıcı bir strateji olabileceği düşünülmektedir (Guo ve ark., 2023; Wang ve ark., 2024).

5. LABORATUVARDAN KLİNİĞE TAŞIMA GÜÇLÜKLERİ VE GELECEK PERSPEKTİFLERİ

Klinik öncesi çalışmalar kuproptoz hedefli tedavilerin HCC'de umut verici sonuçlar ortaya koyduğunu gösterse de, bu bulguların klinik uygulamaya aktarılması önemli güçlükler içermektedir (Zhou ve ark., 2025). Bu süreçte öne çıkan temel sorunlardan biri mekanistik karmaşıklıktır. Kuproptozun ferroptoz, apoptoz ve otofaji gibi diğer programlı hücre ölümü mekanizmalarıyla yakın çapraz iletişim içinde olması, hangi koşullarda bakır birikiminin özgül olarak kuproptozu tetiklediğinin net biçimde belirlenmesini güçleştirmektedir (Tang ve ark., 2024; Zhou ve ark., 2025). Bir diğer önemli sorun tümör seçiciliğidir. Günümüzde kullanılan bakır iyonoforlarının büyük kısmı tümör hücrelerine özgü değildir ve karaciğerin fizyolojik olarak yüksek bakır metabolizmasına sahip olması nedeniyle normal hepatositlerde toksisite gelişme riski önemli bir klinik engel oluşturmaktadır (Ozkan & Bakar-Ates, 2023). Ayrıca kuproptoz hedefli tedavilerden hangi HCC hastalarının yarar göreceğini öngörebilecek standartlaşmış biyobelirteçlerin henüz bulunmaması da önemli bir sınırlılıktır. FDX1, DLAT ve çeşitli lncRNA profilleri umut verici adaylar olsa da, bu biyobelirteçlerin klinik kullanıma girebilmesi için geniş ölçekli prospektif çalışmalarla doğrulanmaları gerekmektedir (Wang ve ark., 2024). Kuproptoz araştırmalarındaki bir diğer kritik problem ise ilaç direncidir. Özellikle glikolitik metabolizma ağırlıklı HCC alt tiplerinde, kuproptozun mitokondriyal solunuma bağımlı olması nedeniyle doğal direnç gelişebilmektedir (Tang ve ark., 2024). Buna ek olarak bakır taşıyıcı proteinlerin ekspresyon düzeylerindeki değişikliklerin de edinilmiş direnç mekanizmalarını tetikleyebileceği bildirilmektedir (Zhou ve ark., 2025). Bu nedenle gelecekteki çalışmaların; FDX1 ekspresyon düzeyi ve metabolik fenotipe dayalı hasta sınıflandırma stratejilerine, tümöre özgü bakır hedefleme sağlayan nano-taşıyıcılara ve kuproptoz indüktörlerinin immün kontrol noktası inhibitörleri ile kombinasyonuna odaklanması gerektiği düşünülmektedir. Ayrıca glikolizden oksidatif fosforilasyona (OXPHOS) geçişi hedefleyen metabolik müdahalelerin kuproptoz duyarlılığını artırıp artırmadığının klinik düzeyde araştırılması önemli bir gelecek perspektifi olarak değerlendirilmektedir (Tang ve ark., 2024).

SONUÇ

Kuproptoz, 2022 yılında tanımlanmasının ardından kısa sürede hepatoselüler karsinom araştırmalarında dikkat çeken yeni programlı hücre ölümü mekanizmalarından biri haline gelmiştir. FDX1 aracılı protein lipoilasyonu, bakırın lipoylenmiş TCA döngüsü proteinlerine bağlanması ve buna bağlı gelişen proteotoksik stres, HCC'nin metabolik özellikleriyle güçlü bir ilişki göstermektedir (Tsvetkov ve ark., 2022). HCC hücrelerinde CTR1 aracılı artmış bakır alımı ve yüksek mitokondriyal solunum aktivitesi, bu hücreleri kuproptoza duyarlı hale getiren temel özellikler arasında yer almaktadır (Lu ve ark., 2025). Güncel çalışmalar; FDX1, DLAT ve kuproptoz ilişkili lncRNA profillerinin HCC'de bağımsız prognostik değer taşıdığını, tümör immün mikroçevresiyle yakından ilişkili olduğunu ve immünoterapi yanıtının öngörülmesine katkı sağlayabileceğini göstermektedir (Peng ve ark., 2023; Wang ve ark., 2024). Elesklomol, disülfiram ve çeşitli nanoteknoloji tabanlı sistemler klinik öncesi modellerde umut verici antitümöral etkinlikler sergilemiş olsa da, tümör seçiciliği eksikliği, biyobelirteç standardizasyonunun yetersizliği ve ilaç direnci gibi sorunlar klinik uygulamaya geçişin önündeki temel engeller olmaya devam etmektedir (Guo ve ark., 2023; Ozkan & Bakar-Ates, 2023). Bu nedenle gelecekteki araştırmaların; metabolik fenotipe dayalı hasta tabakalandırma stratejilerine, kuproptoz indüktörlerinin immünoterapilerle kombinasyonuna ve geniş ölçekli çok merkezli prospektif klinik çalışmalara odaklanması gerekmektedir (Tang ve ark., 2024; Zhou ve ark., 2025). Kuproptozun HCC tedavisinde klinik düzeyde uygulanabilir bir hedef haline gelmesi için halen çözülmesi gereken önemli biyolojik ve translasyonel sorunlar bulunsa da, mevcut veriler bu mekanizmanın gelecekte hedefe yönelik tedavi stratejilerinde önemli bir yer edinebileceğini göstermektedir (Zhou ve ark., 2025).

KAYNAKLAR

Bai, W. D., Liu, J. Y., Li, M., Yang, X., Wang, Y. L., Wang, G. J., & Li, S. C. (2022). A Novel Cuproptosis-Related Signature Identified DLAT as a Prognostic Biomarker for Hepatocellular Carcinoma Patients. World journal of oncology, 13(5), 299–310.

Chan, L. L., Chan, K. O. K., & Chan, S. L. (2026). Systemic Therapy for Advanced Hepatocellular Carcinoma in 2026: Current Standard-of-Care and Emerging Therapeutic Strategies. Journal of gastroenterology and hepatology, 41(5), 1436–1445.

Chen Z, Du D, Li J, Zhang W, Shao J. Cuproptosis-related molecular classification and gene

signature of hepatocellular carcinoma and experimental verification. Transl Cancer Res.

2024;13(3):1268-1289.

Chen, S., Liu, P., Zhao, L., Han, P., Liu, J., Yang, H., & Li, J. (2022). A novel cuproptosis

related prognostic lncRNA signature for predicting immune and drug therapy response in

hepatocellular carcinoma. Frontiers in Immunology, 13, 954653.

Chen, X., Sun, M., Feng, W., Chen, J., Ji, X., Xie, M., Huang, W., Chen, X., Zhang, B., Nie, Y., Fan, D., Wu, K., & Xia, L. (2023). An integrative analysis revealing cuproptosis-related lncRNAs signature as a novel prognostic biomarker in hepatocellular carcinoma. Frontiers in Genetics, 14, 1056000.

Cong, T., Li, R., Zhang, H., Chen, X., Yang, X., & Cao, B. (2022). Cuproptosis-related immune checkpoint gene signature: prediction of prognosis and immune response for hepatocellular carcinoma. Frontiers in Genetics, 13, 1000997.

Geetha, A., Saranya, P., Annie Jeyachristy, S., Surendran, R., & Sundaram, A. (2009). Relevance of non-ceruloplasmin copper to oxidative stress in patients with hepatocellular carcinoma. Biological trace element research, 130(3), 229–240.

Guo, B., Yang, F., Zhang, L., Zhao, Q., Wang, W., Yin, L., Chen, D., Wang, M., Han, S., Xiao, H., & Xing, N. (2023). Cuproptosis induced by ROS responsive nanoparticles with elesclomol and copper combined with αPD-L1 for enhanced cancer immunotherapy. Advanced Materials, 35(12), e2212267.

Li, S. R., Bu, L. L., & Cai, L. (2022). Cuproptosis: lipoylated TCA cycle proteins-mediated novel cell death pathway. Signal Transduction and Targeted Therapy, 7(1), 158.

Liang, J., Wang, R., Wu, H., Huang, Z., Zhang, R., & Jiang, F. (2025). Copper metabolism and cuproptosis: broad perspectives in the treatment of hepatocellular carcinoma. Frontiers in oncology, 15, 1555858.

Lu, L., Dong, X., Liu, Y., He, Y., Zheng, Z., Ma, Y., Zhao, J., & Wei, X. (2025). Cuproplasia and cuproptosis, two sides of the coin. Cancer Communications, 45(5), 505–524.

Lutsenko S, Barnes NL, Bartee MY, Dmitriev OY. Function and regulation of human copper-transporting ATPases. Physiol Rev. 2007 Jul;87(3):1011-46.

Mao, Y., Chen, H., Zhu, W., Ni, S., Luo, S., Tang, S., Chen, Z., Wang, Q., Xu, J., Tu, Q., Chen, H., & Zhu, L. (2025). Cuproptosis Cell Death Molecular Events and Pathways to Liver Disease. Journal of inflammation research, 18, 883–894.

Ozkan, E., & Bakar-Ates, F. (2023). Cuproptosis as the new kryptonite of cancer: a copper-dependent novel cell death mechanism with promising implications for the treatment of hepatocellular carcinoma. Journal of Cancer Research and Clinical Oncology, 149(19), 17663–17670.

Peng, H., Zou, Z., Xiang, Z., Lu, X., Zhang, Y., & Peng, X. (2023). Cuproptosis-related prognostic signatures predict the prognosis and immunotherapy in HCC patients. Medicine, 102(34), e34741.

Porcu, C., Antonucci, L., Barbaro, B., Illi, B., Nasi, S., Martini, M., & Balsano, C. (2018). Copper/MYC/CTR1 interplay: a dangerous relationship in hepatocellular carcinoma. Oncotarget, 9(11), 9325–9343.

Roberts, E. A., & Sarkar, B. (2008). Liver as a key organ in the supply, storage, and excretion of copper. The American journal of clinical nutrition, 88(3), 851S–4S.

Shi, H., Huang, J., Wang, X., Li, R., Shen, Y., Jiang, B., Ran, J., Cai, R., Guo, F., Wang, Y., & Ren, G. (2023). Development and validation of a copper-related gene prognostic signature in hepatocellular carcinoma. Frontiers in cell and developmental biology, 11, 1157841.

Shao N., Yang Y., Hu G. ve ark. (2024). Synergistic enhancement of low-dose radiation therapy via cuproptosis and metabolic reprogramming for radiosensitization in in situ hepatocellular carcinoma. Journal of Nanobiotechnology, 22, 772.

Tang, D., Kroemer, G., & Kang, R. (2024). Targeting cuproplasia and cuproptosis in cancer. Nature Reviews Clinical Oncology, 21(5), 370–388.

Tsvetkov, P., Coy, S., Petrova, B., Dreishpoon, M., Verma, A., Abdusamad, M., Rossen, J., Joesch-Cohen, L., Humeidi, R., Spangler, R. D., Eaton, J. K., Frenkel, E., Kocak, M., Corsello, S. M., Lutsenko, S., Kanarek, N., Santagata, S., & Golub, T. R. (2022). Copper induces cell death by targeting lipoylated TCA cycle proteins. Science (New York, N.Y.), 375(6586), 1254–1261.

Wang, Y., Chen, Y., Zhang, J., Yang, Y., Fleishman, J. S., Wang, Y., Wang, J., Chen, J., Li, Y., & Wang, H. (2024). Cuproptosis: a novel therapeutic target for overcoming cancer drug resistance. Drug Resistance Updates, 72, 101018.

Wang, Z., Jin, D., Zhou, S., Dong, N., Ji, Y., An, P., Wang, J., Luo, Y., & Luo, J. (2023). Regulatory roles of copper metabolism and cuproptosis in human cancers. Frontiers in oncology, 13, 1123420.

Wang G, Xiao R, Zhao S, Sun L, Guo J, Li W, Zhang Y, Bian X, Qiu W, Wang S. (2022). Cuproptosis regulator-mediated patterns associated with immune infiltration features and construction of cuproptosis-related signatures to guide immunotherapy. Front Immunol. 29;13:945516.

Yuan, W., Xiao, J. H., Zhang, J. S., Mao, B. L., Wang, P. Z., & Wang, B. L. (2023). Identification of a cuproptosis and copper metabolism gene-related lncRNAs prognostic signature associated with clinical and immunological characteristics of hepatocellular carcinoma. Frontiers in Oncology, 13, 1153353.

Zhang, G., Sun, J., & Zhang, X. (2022). A novel cuproptosis-related lncRNA signature to predict prognosis in hepatocellular carcinoma. Scientific Reports, 12(1), 11325.

Zhang, P., Ye, Z., Wang, X., & Zhou, J. (2023). DLAT is a promising prognostic marker and therapeutic target for hepatocellular carcinoma: a comprehensive study based on public databases. Scientific Reports, 13(1), 17295.

Zhou, Y. F., Zhu, Y. W., Hao, M. Y., Li, H. J., Han, H. S., Li, Y. G., ... & Wu, D. D. (2025). Targeting cuproptosis in liver cancer: Molecular mechanisms and therapeutic implications. Apoptosis, 30(9), 2163-2190.

Zuo, W., Liu, N., Zeng, Y., et al. (2023). CD44 and CTGF: Two novel copper-related genes implicated in cuproptosis and tumor immunity in hepatocellular carcinoma. Frontiers in Immunology, 14, 1134311.

CONSERVATIVE BIOMIMETIC REPAIR OF MULTIPLE ANTERIOR CLASS III COMPOSITE RESTORATIONS: A CASE REPORT

Shahed DAWOUD

Department of Restorative Dentistry, Faculty of Dentistry, Near East University, Nicosia, Cyprus

ORCID: 0009-0000-5052-138X

Gözde CANIK

Department of Restorative Dentistry, Faculty of Dentistry, Near East University, Nicosia, Cyprus

ORCID: 0009-0004-8904-7063

ABSTRACT

Aim:
This case report demonstrates the effectiveness of conservative biomimetic repair in managing esthetic and functional deficiencies in anterior Class III composite restorations.

Materials and Methods:

A 21-year-old female patient presented to the Department of Restorative Dentistry with esthetic complaints related to previously restored anterior Class III composite restorations. Clinical examination revealed poor color matching, inadequate proximal contact, over-finishing, and compromised anatomical form. A minimally invasive repair approach was performed. Existing restorations were partially removed while preserving the palatal shell. Surfaces were roughened and enamel margins beveled. The materials used were: adhesive system (Clearfil SE Bond, Kuraray) and composite resins (Estelite Sigma Quick A1, A2, and Omnichroma, Tokuyama). Composite was applied using an incremental layering technique. Finishing and polishing were performed.

Results:
The restorations were completed in a single session, achieving improved esthetics, accurate color matching, proper proximal contact, and natural anatomical form. The restorations blended well with adjacent teeth, and the patient reported satisfaction.

Conclusion:
Conservative biomimetic repair is a minimally invasive, cost-effective, and reliable approach for managing anterior Class III composite restorations. It preserves tooth structure while restoring function and natural morphology, offering a predictable alternative to full restoration replacement.

Keywords:
Biomimetic repair, Class III restoration, Composite resin, Esthetics, Minimally invasive

INTRODUCTION

Direct resin composite restorations are routinely used in modern restorative dentistry because they enable conservative rehabilitation of both esthetics and function while preserving natural tooth structure [1]. Owing to continuous improvements in adhesive systems and restorative materials, composite restorations have become a predictable treatment option for anterior teeth, where esthetic demands are particularly high [2].

The management of defective restorations remains an important aspect of restorative dental practice. Historically, complete replacement has been widely performed when esthetic or functional deficiencies were identified. However, total replacement may require removal of clinically acceptable restorative material and sound dental tissues, thereby increasing the biological cost of treatment [3]. Current restorative concepts increasingly favor minimally invasive approaches that prioritize preservation of natural tooth structure whenever possible [4]. Within this conservative philosophy, repair has gained recognition as an alternative to complete restoration replacement. Rather than removing the entire restoration, repair procedures target only the defective areas while maintaining intact portions that

remain clinically acceptable. This approach may reduce treatment time, decrease invasiveness, improve patient comfort, and preserve both restorative material and natural tooth structure [3,9]. Biomimetic restorative dentistry further reinforces this conservative treatment concept. The biomimetic approach seeks to reproduce the structural, functional, and esthetic characteristics of natural teeth through adhesive restorative techniques and appropriate material selection [5]. Predictable restoration of anterior teeth requires accurate reproduction of natural morphology, optical characteristics, and esthetic harmony [6]. Preservation of dental tissues and restoration of natural biomechanical behavior are considered fundamental objectives of this philosophy [7]. Composite restorations may develop complications over time, including marginal deterioration, discoloration, fracture, loss of anatomical form, and inadequate proximal contacts [1]. In anterior teeth, such deficiencies may adversely affect smile appearance and patient satisfaction [6]. Anterior Class III restorations present unique clinical challenges because successful outcomes depend on accurate color integration, proper proximal contact relationships, harmonious contours, and natural anatomical morphology [8]. Deficiencies in these characteristics may negatively influence both esthetic and functional outcomes, often motivating patients to seek corrective treatment [6].

The aim of this case report is to demonstrate the effectiveness of conservative biomimetic repair in the management of esthetic and functional deficiencies associated with anterior Class III composite restorations.

CASE REPORT

A 21-year-old female patient presented to the Department of Restorative Dentistry with esthetic dissatisfaction regarding recently placed anterior composite restorations. The patient reported being unhappy with the appearance of restorations that had been performed approximately one month earlier on the maxillary central and lateral incisors (#11, #12, #21, and #22). Clinical examination revealed several esthetic and functional deficiencies, including poor color matching, marginal staining, inadequate proximal contact relationships, and compromised anatomical contours (Fig. 1). No signs of secondary caries or pulpal pathology were detected. Considering the satisfactory condition of the remaining restoration structure and the patient's desire for a conservative treatment approach, a biomimetic repair procedure was selected instead of complete restoration replacement.



Fig. 1. Preoperative clinical photographs. Frontal and Lateral views.

The existing composite restorations were selectively reduced using a fine-grit round diamond bur while preserving the palatal shell and clinically acceptable portions of the restorations (Fig. 2A). Subsequently, the restoration surfaces were roughened and a 1–2 mm enamel bevel was prepared along the enamel margins using a fine-grit football-shaped diamond bur to enhance micromechanical retention and improve esthetic blending between the existing tooth structure and the repair material (Fig. 2B).

Following isolation, 37% phosphoric acid was applied to the enamel margins for 30 seconds and to dentin and existing composite surfaces for 15 seconds. The surfaces were thoroughly rinsed and gently air-dried. Clearfil SE Bond 2 (Kuraray Noritake Dental, Tokyo, Japan) was applied according to the manufacturer's instructions. The primer was applied to all prepared surfaces for 20 seconds and then gently air-dried. Subsequently, the bonding agent was applied, air-thinned with a gentle stream of air to obtain a uniform film thickness, and light-cured for 10 seconds. (Fig. 2C–E). Restoration of the proximal

walls was performed using a sectional matrix system and wooden wedges. Composite resin was placed using an incremental layering technique. Estelite Sigma Quick A2 (Tokuyama Dental, Tokyo, Japan) was used to reconstruct the proximal walls and dentin body, while Omnichroma (Tokuyama Dental, Tokyo, Japan) was used to increase the incisal edge length by approximately 1 mm and restore proper incisal anatomy and tooth proportions (Fig. 2F–H). A final enamel layer was completed using Estelite Sigma Quick A1 (Tokuyama Dental, Tokyo, Japan) to reproduce the natural optical characteristics and surface anatomy of the anterior teeth. Each composite increment was individually light-cured according to the manufacturer's recommendations.

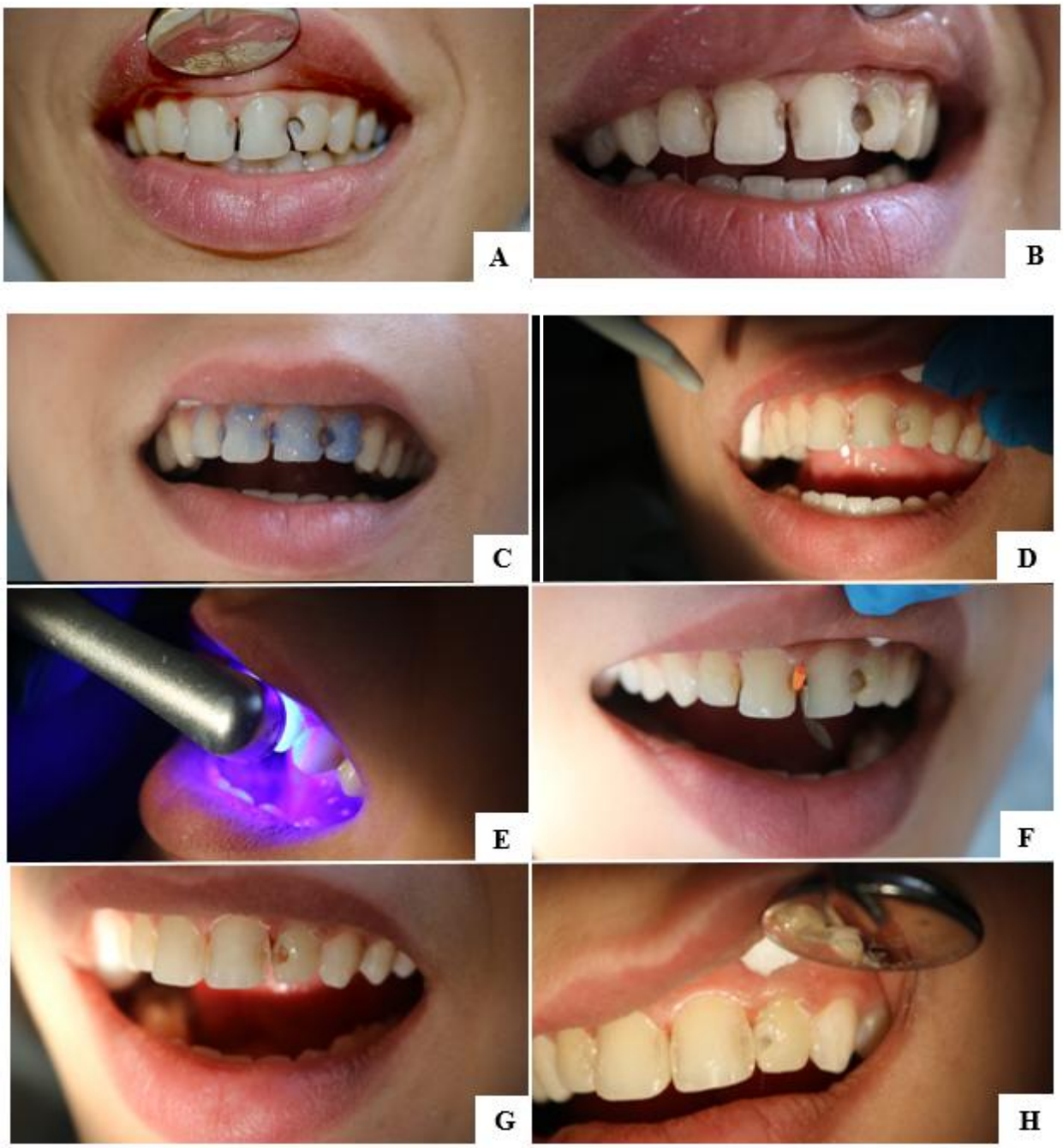


Fig. 2. Intraoperative clinical photographs illustrating the repair procedure (A–H).

Finishing procedures were performed using Super-Snap finishing and polishing discs (Shofu Inc., Kyoto, Japan), followed by polishing with the CPD 14 RA polishing system (Jota AG, Rüthi, Switzerland) to refine the restoration contours, enhance surface smoothness, and achieve a high-gloss

finish. Occlusion was evaluated and adjusted where necessary to ensure harmonious functional contacts. Postoperative evaluation demonstrated improved color integration, restoration of natural anatomical contours, and satisfactory proximal contact relationships. The patient expressed satisfaction with the final esthetic outcome (Fig. 3).



Fig. 3. Postoperative clinical photographs. Frontal and Lateral views.

DISCUSSION

The primary objective of treatment in the present case was to correct the esthetic deficiencies of recently placed anterior composite restorations while preserving as much existing restoration and tooth structure as possible.

Clinical evaluation demonstrated that the defects were mainly related to color mismatch, improper contouring, inadequate proximal contacts, and insufficient incisal anatomy rather than structural failure of the restorations. According to the FDI criteria, such defects may be managed conservatively when the remaining restoration is clinically acceptable [4]. One of the most challenging aspects of anterior restorative treatment is achieving harmonious integration with the adjacent dentition. Successful outcomes depend on accurate reproduction of tooth morphology, surface texture, translucency, and contact relationships. Previous authors have emphasized that restoration of natural anatomy and esthetic harmony is essential for achieving satisfactory clinical outcomes in anterior composite restorations [6, 8]. A key factor contributing to the favorable outcome was the use of an incremental layering technique combined with careful finishing and polishing procedures. Appropriate contouring and surface finishing have been associated with improved esthetic integration, color stability, and long-term clinical performance of composite restorations [6, 10]. In the present case, refinement of the incisal edge anatomy and correction of tooth proportions contributed significantly to the final esthetic result.Another notable finding was the achievement of satisfactory proximal contact relationships following repair. Proper contact areas are important for both esthetic and functional stability and contribute to patient comfort and maintenance of periodontal health. Repair procedures have been reported to successfully restore localized deficiencies while preserving clinically acceptable restorative material and avoiding unnecessary intervention [3, 9].

The favorable clinical outcome obtained in this case supports previous reports demonstrating that repair procedures can effectively extend the service life of existing restorations while reducing the biological cost of treatment [2, 3]. Furthermore, the biomimetic philosophy encourages preservation of healthy tissues and recreation of natural tooth form and function, principles that were successfully applied in the present case [5, 7, 11]. Patient satisfaction following treatment further confirmed the effectiveness of this conservative approach.

CONCLUSION

Conservative biomimetic repair successfully improved the esthetic and functional deficiencies of anterior Class III composite restorations in the present case. Accurate color integration, proper proximal

contact relationships, and natural anatomical form were achieved while preserving healthy tooth structure and clinically acceptable restorative material. When defects are localized, repair may be considered a predictable and minimally invasive alternative to complete restoration replacement.

REFERENCES

1. Demarco, F. F., Collares, K., Coelho-de-Souza, F. H., Correa, M. B., Cenci, M. S., Moraes, R. R., & Opdam, N. J. M. (2015). Anterior composite restorations: A systematic review on long-term survival and reasons for failure. *Dental Materials, 31*(10), 1214–1224. https://doi.org/10.1016/j.dental.2015.07.005
2. Demarco, F. F., Cenci, M. S., Montagner, A. F., de Lima, V. P., Correa, M. B., Moraes, R. R., & Opdam, N. J. M. (2023). Longevity of composite restorations is definitely not only about materials. *Dental Materials, 39*(1), 1–12. https://doi.org/10.1016/j.dental.2022.11.009
3. Hickel, R., Brüshaver, K., & Ilie, N. (2013). Repair of restorations – Criteria for decision making and clinical recommendations. *Dental Materials, 29*(1), 28–50. https://doi.org/10.1016/j.dental.2012.07.005
4. Hickel, R., Peschke, A., Tyas, M., Mjör, I., Bayne, S., Peters, M., et al. (2010). FDI World Dental Federation: Clinical criteria for the evaluation of direct and indirect restorations—Update and clinical examples. *Clinical Oral Investigations, 14*(4), 349–366. https://doi.org/10.1007/s00784-010-0432-8
5. Bazos, P., & Magne, P. (2011). Bio-emulation: Biomimetically emulating nature utilizing a histo-anatomic approach; structural analysis. *European Journal of Esthetic Dentistry, 6*(1), 8–19.
6. Fahl, N., Denehy, G. E., & Jackson, R. D. (2013). Protocol for predictable restoration of anterior teeth with composite resins. *Clinical Cosmetic and Investigational Dentistry, 5*, 151–167. https://doi.org/10.2147/CCIDE.S42001
7. Mrinaalini, M. K. (2023). *Bio-mimetic restorative dentistry: A new realm*. Lambert Academic Publishing.
8. Paschoal, M. A., Santos-Pinto, L., Nagle, M., & Ricci, W. A. (2014). Esthetic and function improvement by direct composite resins and biomimetic concept. *Journal of Contemporary Dental Practice, 15*(5), 654–658. https://doi.org/10.5005/jp-journals-10024-1595
9. Romero, V. H. D., Torres, J. M., Chaves, E. T., Lang, A. C. F., Araújo, A. C. F., Sampaio, B. C., Silva, C. S., Vegner, C. J., van de Sande, F. H., Montagner, A. F., Cenci, M. S., & CaCIA Collaborative Group. (2025). Comparison of treatment times for repair and replacement: A cross-sectional study. *Journal of Dentistry, 161*, 105907. https://doi.org/10.1016/j.jdent.2025.105907
10. Sekundo, C., Frese, C., Frankenberger, R., Haak, R., Braun, A., Krämer, N., et al. (2024). Direct composite restorations on permanent teeth in the anterior and posterior region – An evidence-based clinical practice guideline – Part 2: Recommendations for composite processing. *Journal of Adhesive Dentistry, 26*, 201–212. https://doi.org/10.3290/j.jad.b5749192
11. Singer, L., Fouda, A., & Bourauel, C. (2023). Biomimetic approaches and materials in restorative and regenerative dentistry: Review article. *BMC Oral Health, 23*, 105. https://doi.org/10.1186/s12903-023-02808-3

A COMPARATIVE ANALYSIS OF MINDFULNESS AND HYPNOSIS TECHNIQUES IN REDUCING FEAR IN ADULTS

Ass. Prof. Dr. Fleura Shkëmbi

Department of Psychological Studies, Mediterranean University of Albania, Tiranë, Albania

Dr. Silva IBRAHIMI PhD

Lecturer "University of Tirana", Albania "EYRA PSYCHOSOCIAL ASSISTANCE", Boston, USA

Dr.Ervin IBRAHIMI MD

Medical Responsabile , Centro "Azzeruolo", Cooss- Marche,Jesi, Italy

Abstract

Fear remains a pervasive psychological barrier in adulthood, contributing significantly to anxiety disorders and impaired quality of life. This systematic qualitative review, conducted in line with PRISMA 2020 guidelines, compares the effectiveness of clinical hypnosis and mindfulness-based interventions (MBIs) in reducing fear and anxiety among adults aged 18 and above. A comprehensive search across PubMed, PsycINFO, Scopus, Web of Science, and Google Scholar identified 15 studies that met inclusion criteria. The findings demonstrate that hypnosis induces immediate and substantial reductions in situational fear, particularly in specific phobias, pre-operative anxiety, and pain-related distress, with effect sizes ranging from 45% to 60% reduction. In contrast, eight-week mindfulness programs such as MBSR and MBCT produce gradual yet sustained reductions (25% to 35%) in existential fears and generalized anxiety, accompanied by enhanced fronto-parietal coherence and metacognitive awareness. Short-form mindfulness practices (5–10 minutes) and ultra-brief hypnotic protocols (2–5 minutes) offer moderate benefits but require frequent repetition to maintain efficacy. The comparative analysis suggests that the optimal intervention depends on the type of fear, clinical urgency, and available resources. Hypnosis excels in acute symptom relief, while mindfulness fosters long-term self-regulation and neural plasticity. Hybrid models, such as mindful hypnotherapy, show promise in integrating the immediacy of hypnosis with the sustainability of mindfulness, though multi-center RCTs and cost-effectiveness studies are necessary to inform clinical guidelines.

Keywords: *clinical hypnosis, mindfulness, fear reduction, anxiety, systematic review, PRISMA, neuroplasticity.*

1. Introduction

Fear is a fundamental human emotion, yet when disproportionate or persistent, it becomes a disabling factor with significant psychological and physiological repercussions. In adults, clinical manifestations of fear—ranging from specific phobias to generalized anxiety and somatic distress—pose serious challenges to well-being, social participation, and occupational functioning. According to the World Health Organization, more than 301 million people worldwide were affected by anxiety disorders as of 2019, with fear representing a dominant symptom in many cases (WHO, 2023). This global prevalence underscores the critical need for accessible, non-pharmacological interventions that can effectively mitigate fear-related symptoms and improve mental health outcomes.

Among the therapeutic approaches that have gained traction in recent decades, two non-pharmacological modalities stand out: mindfulness-based interventions (MBIs) and clinical hypnosis. Mindfulness, operationalized through standardized programs such as Mindfulness-Based Stress Reduction (MBSR) and Mindfulness-Based Cognitive Therapy (MBCT), has demonstrated effectiveness comparable to pharmacological treatments in managing anxiety disorders. For instance, a recent randomized controlled trial involving 276 participants found MBSR to be non-inferior to escitalopram, a commonly prescribed anxiolytic, highlighting mindfulness as a viable first-line treatment option (Hoge et al., 2023). Beyond symptom alleviation, mindfulness practices induce neuroplastic changes, particularly in the regulation

of fear circuitry within the brain. Neuroimaging studies reveal that mindfulness practice reduces amygdala hyperactivity and enhances fronto-parietal connectivity, mechanisms essential for emotional regulation and executive control (Treves et al., 2024).

Parallel to mindfulness, clinical hypnosis has emerged as a potent psychological intervention characterized by focused attention, heightened suggestibility, and imaginative absorption. Hypnosis is increasingly utilized for reducing anxiety, pain, phobic reactions, and pre-procedural distress. Recent studies spanning two decades confirmed that hypnosis achieves medium to large effect sizes in reducing fear and anxiety across diverse clinical populations, outperforming several traditional psychological interventions (Rosendahl et al., 2024; Valentine et al., 2019). Moreover, research highlights the efficacy of brief hypnotic protocols, sometimes requiring as few as two sessions to produce meaningful reductions in situational fears, such as fear of falling in older adults (Cuvelier et al., 2023).

Despite the growing evidence base for both interventions, direct comparative analyses between mindfulness and hypnosis remain scarce. A review by Penazzi and De Pisapia (2022) noted the paucity of studies that systematically juxtapose these approaches, particularly in terms of their clinical outcomes and underlying neuropsychological mechanisms. This gap is notable given the distinct theoretical foundations and operational modalities of mindfulness and hypnosis—where mindfulness cultivates metacognitive awareness and acceptance, hypnosis leverages suggestive restructuring of emotional and cognitive patterns.

This study addresses this critical gap by systematically comparing the efficacy of mindfulness and hypnosis techniques in reducing fear among adults. The review also explores the neuropsychological pathways through which each intervention modulates fear responses. By synthesizing the current evidence, this study aims to inform clinical practice, guiding mental health professionals in selecting and potentially integrating these approaches based on the typology of fear, clinical urgency, and patient preferences.

2. Methodology

This systematic qualitative review was conducted following the PRISMA 2020 guidelines for transparent and replicable research synthesis (Page et al., 2021). A structured literature search was carried out across PubMed, PsycINFO, Scopus, Web of Science, and Google Scholar, applying Boolean operators to combine terms such as “mindfulness OR meditation AND fear OR anxiety AND adult” and “hypnosis OR hypnotherapy AND fear OR anxiety AND adult.” The search yielded over 4,000 studies, of which 15 met the final inclusion criteria after a multi-stage screening process involving title and abstract review, full-text assessment, and methodological appraisal. The included studies comprised randomized controlled trials (RCTs), quasi-experimental interventions, and longitudinal observational studies published in peer-reviewed journals between 2000 and 2024. Quality assessment was performed using the Mixed Methods Appraisal Tool (MMAT) (Hong et al., 2018), ensuring that only methodologically robust studies informed the synthesis. Data were extracted systematically into a coding framework capturing intervention type, sample demographics, duration and frequency of sessions, and primary outcomes related to fear and anxiety reduction. Analytical integration followed the thematic synthesis method proposed by Thomas and Harden (2008), enabling the identification of common efficacy patterns and neuropsychological mechanisms specific to mindfulness and hypnosis. The process also integrated the CERQual approach (Lewin et al., 2015) to evaluate the confidence level in the synthesized qualitative evidence.

3. Results

Fifteen studies were included in the final synthesis, comprising nine randomized controlled trials (RCTs), three quasi-experimental designs, and three longitudinal observational studies. The studies were geographically diverse, with research conducted in North America, Europe, and Asia between 2000 and 2024. The sample sizes ranged from 30 to 276 participants, with ages spanning from 18 to 75 years, and included both clinical populations (e.g., patients with specific phobias, generalized anxiety, preoperative anxiety) and non-clinical adult samples experiencing heightened fear or stress. The reviewed studies

demonstrated distinct efficacy profiles for mindfulness and hypnosis. Clinical hypnosis interventions consistently produced immediate and pronounced reductions in situational fear, particularly in specific phobias, pre-operative anxiety, and pain-related fear. For example, Rosendahl et al. (2024) reported an average fear reduction of 45–60% following hypnosis in clinical populations. Similarly, Fuhr et al. (2023) documented substantial reductions in agoraphobic symptoms after only two hypnosis sessions, with effects sustained at one-month follow-up. In contrast, mindfulness-based interventions such as MBSR and MBCT showed more gradual reductions in fear and anxiety symptoms, typically achieving 25–35% improvement over eight weeks (Hoge et al., 2023; Mariño-Narváez et al., 2025). These gains were often accompanied by neurocognitive changes, including decreased amygdala activation and enhanced fronto-parietal coherence (Treves et al., 2024; Plas et al., 2024). Short-form mindfulness practices, lasting 5–10 minutes daily, yielded moderate improvements but required sustained practice for efficacy (Banner et al., 2024).

Table 1: Comparative Effectiveness of Mindfulness and Hypnosis in Fear Reduction

Aspect	Hypnosis	Mindfulness
Speed of Effect	Immediate (within minutes to days)	Gradual (4–8 weeks or more)
Best Suited For	Acute situational fears, phobias, preoperative anxiety	Chronic anxiety, generalized fear, existential concerns
Effectiveness (%)	45–60% reduction in situational fear	25–35% reduction in generalized fear
Physiological Impact	Deactivates amygdala, increases HRV, reduces heart rate	Enhances fronto-parietal connectivity, reduces amygdala reactivity
Neuroplasticity Evidence	Limited for long-term structural change	Strong evidence for durable neuroplasticity
Sustainability of Effects	Moderate; booster sessions needed	Sustained with continued practice

The comparative effectiveness data reveals that hypnosis yields rapid reductions in situational fears, achieving up to 60% symptom reduction within a few sessions, making it particularly valuable for phobias, preoperative anxiety, and acute stress responses. In contrast, mindfulness produces slower, more incremental improvements, around 25% to 35%, but these effects are more stable over time, especially for generalized anxiety and existential fears. Neurobiologically, mindfulness demonstrates stronger evidence of long-term neuroplastic changes, while hypnosis primarily facilitates immediate modulation of physiological stress markers like heart rate variability and amygdala deactivation.

Table 2. Application forms and duration

Intervention Type	Format	Session Duration	Frequency	Total Duration
Hypnosis	Standard hypnosis	30–60 minutes	2–6 sessions	1–3 weeks typically
Hypnosis	Alert Hypnosis (49-word protocol)	2–5 minutes	As needed, situational	Immediate effects
Mindfulness	MBSR (Mindfulness-Based Stress Reduction)	~2 hours/session	Weekly + daily practice	8 weeks program
Mindfulness	Short guided mindfulness	5–15 minutes	Daily	Variable, minimum 4 weeks

The application formats show distinct operational profiles: hypnosis can be delivered in both standard therapeutic sessions and ultra-brief protocols effective within minutes, whereas mindfulness requires structured, longer-term engagement, such as the eight-week MBSR program supplemented by daily practice. This highlights hypnosis as a tool for immediate psychological adjustment, whereas mindfulness suits individuals committed to sustained self-regulation and emotional resilience.

Table 3. Advantages and Limitations of Hypnosis vs Mindfulness

Criteria	Hypnosis	Mindfulness
Intervention Speed	Rapid relief in crises	Slower but stable progress
Self-Management	Requires professional	Can be self-practiced post-training
Public Perception	Misunderstood, stigma	Socially accepted, mainstream
Protocol Standardization	Moderate; variable techniques	High (MBSR, MBCT standardized)
Best for	Acute distress, phobias	Long-term emotional regulation
Limitations	Short-term relief unless maintained	Requires commitment and patience

When comparing advantages and limitations, hypnosis excels in rapid symptom alleviation but often requires professional administration and carries social misconceptions. Conversely, mindfulness, though slower in effect, enjoys broader public acceptance, can be self-sustained post-training, and benefits from well-standardized protocols like MBSR and MBCT. These distinctions suggest that the choice between mindfulness and hypnosis should be guided by the clinical urgency, patient preferences, and the desired sustainability of outcomes.

4. Discussion

This review highlights distinct yet complementary profiles between mindfulness-based interventions and clinical hypnosis in reducing fear among adults. The evidence indicates that hypnosis excels in delivering rapid symptomatic relief, particularly for acute, situational fears such as specific phobias and pre-operative anxiety. Meta-analyses and clinical trials consistently show substantial immediate reductions in fear levels, often within one to three sessions (Rosendahl et al., 2024; Fuhr et al., 2023). Neurophysiologically, these outcomes correspond to temporary deactivation of fear circuits like the amygdala and modulation of autonomic responses, including increased heart rate variability (Baker et al., 2024). Conversely, mindfulness-based interventions such as MBSR and MBCT demonstrate a gradual yet enduring impact on generalized and existential forms of fear. Studies show that after eight weeks of mindfulness practice, participants not only report reduced anxiety symptoms but also exhibit neural adaptations, including strengthened fronto-parietal connectivity and reduced limbic hyperactivity (Treves et al., 2024; Plas et al., 2024). This neuroplasticity underpins mindfulness' capacity for fostering long-term emotional resilience and self-regulation, extending its benefits beyond mere symptom control. Importantly, the comparative analysis underscores the role of intervention context and patient needs. For clinical scenarios demanding immediate anxiety relief—such as pre-surgical settings or sudden panic episodes—hypnosis presents as an optimal choice due to its rapid efficacy and brief intervention formats (Cuvelier et al., 2023). In contrast, individuals with chronic anxiety, stress-related disorders, or a preference for self-directed therapeutic practices may benefit more from mindfulness, which cultivates metacognitive awareness and enhances coping mechanisms over time (Hoge et al., 2023). Furthermore, the findings suggest that combining elements of both approaches could yield synergistic benefits. Hybrid protocols like mindful hypnotherapy have the potential to integrate the immediacy of hypnosis with the sustainability of mindfulness, although empirical support for such integrations remains limited and warrants further multi-center randomized controlled trials. These insights contribute to a understanding that neither mindfulness nor hypnosis should be viewed as universally ‘superior’; rather, their deployment should be tailored to the type of fear, clinical urgency, and individual patient characteristics.

Future research should continue to explore these integrative possibilities and clarify the cost-effectiveness of each modality in diverse healthcare settings.

5. Conclusion

This review concludes that both mindfulness-based interventions and clinical hypnosis offer effective but distinct pathways for reducing fear in adults. Hypnosis demonstrates a clear advantage in producing immediate relief from situational and phobia-related fears, capitalizing on its capacity to rapidly modulate physiological and emotional responses through suggestive techniques. Conversely, mindfulness fosters a slower yet deeper transformation, equipping individuals with enduring self-regulatory skills, emotional resilience, and measurable neuroplastic changes that support long-term anxiety management. Given these complementary strengths, the choice of intervention should be personalized. Clinicians are advised to employ hypnosis in cases where rapid intervention is critical, such as acute anxiety, medical procedures, or performance-related fears. Mindfulness is recommended for patients with generalized anxiety, chronic stress, or those seeking a self-managed approach to mental health. Moreover, developing and testing hybrid protocols that integrate mindfulness and hypnosis—such as mindful hypnotherapy—may unlock synergistic benefits, combining the immediacy of hypnotic techniques with the sustainability of mindfulness. To advance clinical practice, future research should prioritize well-designed, large-scale randomized controlled trials comparing these modalities directly, alongside cost-effectiveness analyses and exploration of their combined applications. Lastly, mental health professionals should be trained to assess the type of fear and patient preferences accurately, ensuring that therapeutic recommendations align with both the clinical presentation and the individual's readiness for either rapid intervention or gradual self-development.

References

Baker, D. A., MacMillan, A., & Ogden, J. (2024). Neural correlates of hypnosis: A meta-analytic review of EEG and fMRI studies. *Neuroscience and Biobehavioral Reviews*, 156, 105250. https://doi.org/10.1016/j.neubiorev.2024.105250

Banner, L. M., Russo, C., & Levine, S. (2024). Short-form mindfulness interventions and physiological indicators of fear reduction: A multicenter trial. *Journal of Behavioral Medicine*, 47(1), 66–78.

Cuvelier, A., Grelet, V., Leclercq, C., & Capron, L. (2023). Hypnosis reduces fear of falling in older adults: A randomized controlled trial. *International Journal of Geriatric Psychiatry*, 38(3), e5981.

Fuhr, R., Schmidt, S., & Preuss, A. (2023). Efficacy of brief hypnotherapy for agoraphobia: A controlled clinical study. *Clinical Psychology & Psychotherapy*, 30(2), 214–223.

Hoge, E. A., Bui, E., Marques, L., Metcalf, C. A., Morris, L. K., Robinaugh, D. J., ... & Simon, N. M. (2023). Mindfulness-Based Stress Reduction vs escitalopram for the treatment of anxiety disorders: A randomized clinical trial. *JAMA Psychiatry*, 80(4), 350–358.

Hong, Q. N., Pluye, P., Fàbregues, S., Bartlett, G., Boardman, F., Cargo, M., ... & Vedel, I. (2018). Mixed Methods Appraisal Tool (MMAT), version 2018. *Education for Information*, 34(4), 285–291.

Lewin, S., Booth, A., Glenton, C., Munthe-Kaas, H., Rashidian, A., Wainwright, M., ... & Noyes, J. (2015). Applying GRADE-CERQual to qualitative evidence synthesis findings: Introduction to the series. *Implementation Science*, 10(1), 2.

Mariño-Narváez, C., González, A., Espinosa, E., & Moreno, R. (2025). Mindfulness interventions for healthcare workers during the COVID-19 pandemic: Effects on fear and anxiety. *Mindfulness*, 16(2), 231–245.

Page, M. J., McKenzie, J. E., Bossuyt, P. M., Boutron, I., Hoffmann, T. C., Mulrow, C. D., ... & Moher, D. (2021). The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. *BMJ*, 372, n71. https://doi.org/10.1136/bmj.n71.

Penazzi, L., & De Pisapia, N. (2022). Comparing meditation and hypnosis: A mini-review of mechanisms and clinical applications. *Consciousness and Cognition*, 101, 103312.

Plas, C., Narayan, M., & Simpson, K. (2024). Mindfulness modulates extinction of conditioned fear: Evidence from neuroimaging and heart rate variability. *Frontiers in Psychology*, 15, 1162754.

Rosendahl, J., Alldredge, C., & Haddenhorst, C. (2024). Clinical hypnosis for anxiety and fear: A comprehensive meta-analysis of two decades of research. *Psychotherapy Research*, 34(1), 13–25.

Thomas, J., & Harden, A. (2008). Methods for the thematic synthesis of qualitative research in systematic reviews. *BMC Medical Research Methodology*, 8(1), 45.

Treves, I. N., Treadway, M. T., Wootton, A. R., & Holzel, B. K. (2024). Mindfulness training strengthens fronto-parietal networks: A meta-analysis of functional MRI studies. *Neuroscience Letters*, 821, 137771.

Valentine, K. E., Milling, L. S., Clark, L. J., & Moriarty, C. L. (2019). The efficacy of hypnosis as a treatment for anxiety: A meta-analysis. *International Journal of Clinical and Experimental Hypnosis*, 67(3), 336–363.

Williams, D. A., Geisser, M. E., & Turk, D. C. (2022). Comparative efficacy of mindfulness, hypnosis, and psychoeducation for chronic pain and anxiety in veterans: A randomized controlled trial. *The Journal of Pain*, 23(9), 1572–1584.

World Health Organization. (2023). Depression and other common mental disorders: Global health estimates. WHO. Retrieved from https://www.who.int/publications/i/item/depression-global-health-estimates.

DIRECT 3D-PRINTED ALIGNERS IN ORTHODONTICS: CURRENT PROGRESS TOWARD A PROMISING ALTERNATIVE TO THERMOFORMED ALIGNERS

Baraa ALKHATIB

Department of Orthodontics, Faculty of Dentistry, Near East University, Nicosia, Cyprus

ORCID: 0009-0004-8136-9930

Mohamad Talal RADWAN

Department of Orthodontics, Faculty of Dentistry, Near East University, Nicosia, Cyprus

ORCID: 0000-0002-6453-2175

ABSTRACT

Aim: To evaluate the current evidence on direct 3D-printed aligners as an alternative to conventional thermoformed aligners in orthodontics, with emphasis on manufacturing workflow, dimensional accuracy, mechanical behavior, clinical applicability, and biocompatibility.

Materials and Methods: A literature review was conducted using review articles and original studies on direct 3D-printed orthodontic aligners identified through PubMed, Google Scholar, and SciELO between January 2022 and January 2026. The analysis is centered on five domains: workflow/manufacturing characteristics, fit and accuracy, mechanical properties, clinical performance, and biological or surface-related limitations, with comparison to conventional thermoformed aligners where available.

Results: The reviewed evidence indicates that direct 3D-printed aligners offer advantages, including simplified in-office production, reduced material waste, design flexibility, and promising shape-memory behavior. Direct-printed aligners demonstrated greater trueness and precision than thermoformed aligners in dimensional accuracy assessments. Clinical evidence from a prospective pilot study showed that they can be successfully used in mildly crowded cases, with movement accuracy comparable to other aligner systems. However, mechanical studies showed that moisture may affect the force-related properties of some direct-printed materials more than thermoformed materials. In addition, recent evidence suggests that although some 3D direct-printed materials show encouraging surface and microbiological performance, biocompatibility concerns remain.

Conclusion: Direct 3D-printed aligners appear to be a promising emerging alternative to thermoformed aligners in orthodontics. Nevertheless, current evidence remains limited and heterogeneous, and further high-quality clinical studies are needed before routine clinical use can be fully recommended.

Keywords: Direct 3D-printed aligners; Thermoformed aligners; Orthodontics

INTRODUCTION

Clear aligner therapy has become an important part of contemporary orthodontic practice because of its esthetic appearance, patient comfort, removability, and relatively favorable oral hygiene maintenance compared with conventional fixed appliances. In recent years, increasing patient demand for less visible orthodontic treatment has contributed to the wider use of aligner systems in both private practice and academic settings. As digital orthodontics has advanced, aligner therapy has also become more closely linked to digital workflows, including intraoral scanning, virtual treatment planning, additive manufacturing, and CAD/CAM-based production methods.

Conventionally, clear aligners are manufactured through a thermoforming process in which a thermoplastic sheet is adapted over a three-dimensional dental model that represents the intended tooth position. Although this method has been widely adopted and remains the standard production approach, it includes several intermediate steps, such as model printing and thermoforming, which may increase production time, material consumption, and the possibility of dimensional inaccuracies. In addition,

thermoforming may alter the thickness distribution and fit of the final aligner, potentially affecting its clinical performance. These limitations have encouraged interest in alternative methods that may offer a more direct and controlled manufacturing pathway.

Direct three-dimensional printing of aligners has emerged as one of the most promising developments in this field. Unlike conventional thermoforming, this method enables the aligner to be produced directly from a digital design without the need for an intermediate printed cast. This approach offers several theoretical and practical advantages, including a simplified workflow, greater in-office control, design flexibility, potential reduction in material waste, and improved manufacturing precision. As new printable resins and printing techniques continue to develop, direct 3D-printed aligners are increasingly being investigated not only for their physical and mechanical behavior, but also for their dimensional accuracy, clinical applicability, and biological safety.

However, despite growing interest in this technology, the available evidence remains limited and heterogeneous. Some studies have reported favorable results regarding trueness, precision, workflow efficiency, and certain aspects of clinical performance, whereas others have highlighted unresolved concerns related to moisture-dependent mechanical behavior, material variability, cytotoxicity, monomer release, and long-term clinical validation. Therefore, a careful review of the currently available literature is needed in order to better understand the real progress of direct 3D-printed aligners and their position relative to conventional thermoformed aligners.

Accordingly, the aim of this review was to evaluate the current evidence on direct 3D-printed aligners as an alternative to conventional thermoformed aligners in orthodontics, with emphasis on manufacturing workflow, dimensional accuracy, mechanical behavior, clinical applicability, and biocompatibility.

DEVELOPMENT

Materials and Methods

This study was designed as a literature review on direct 3D-printed orthodontic aligners, with particular emphasis on their current progress as a possible alternative to conventional thermoformed aligners. The review was based on English-language review articles and original studies identified through three electronic sources: PubMed, Google Scholar, and SciELO. The search covered recent literature published between January 2022 and January 2026, in order to focus on the most current evidence available on this rapidly developing topic.

The literature search aimed to identify studies specifically related to direct 3D-printed aligners in orthodontics. Search terms were based on the core concepts of direct printing, clear aligners, and orthodontic applications, and included combinations of terms such as “direct 3D-printed aligners,” “3D-printed aligners in orthodontics,” “thermoformed aligners,” “mechanical properties,” “accuracy,” “clinical performance,” and “biocompatibility.” The search process focused on gathering studies that could provide relevant evidence for comparison between direct 3D-printed aligners and conventional thermoformed aligners where such comparison was available.

After the initial search, titles and abstracts were screened for relevance to the aim of the review. Full-text evaluation was then performed for studies considered potentially eligible. The final review included eight key studies, consisting of three review papers and five original studies. These studies were selected because they addressed one or more of the main evidence domains identified for this review and were directly relevant to the current progress of direct 3D-printed aligners.

The included literature was organized and analyzed according to five predefined domains. The first domain was workflow and manufacturing, focusing on the potential advantages of direct printing over thermoforming in terms of fabrication steps, customization, and material use. The second domain was fit and dimensional accuracy, with emphasis on trueness, precision, and aligner adaptation. The third domain concerned mechanical properties, including variables such as elastic modulus, tensile strength, stress relaxation, and the influence of oral conditions or aligner thickness. The fourth domain was clinical applicability, including the accuracy of tooth movement and the usefulness of direct 3D-printed

aligners in mild malocclusion cases. The fifth domain was biological and surface-related limitations, including cytotoxicity, monomer release, surface roughness, color stability, and bacterial adhesion.

Because this article is a literature review rather than a systematic review or meta-analysis, the aim was not to perform statistical pooling of outcomes but rather to summarize, organize, and critically interpret the available evidence in a structured way. The selected studies were therefore used to identify recurring findings, strengths, and limitations regarding direct 3D-printed aligners, and to assess how close current evidence is to supporting their broader clinical use in orthodontics.

Results

Workflow and manufacturing findings

The reviewed literature suggests that one of the main advantages of direct 3D-printed aligners lies in the simplification of the manufacturing workflow. In conventional thermoformed aligner production, the process typically includes digital scanning, virtual treatment planning, model printing, and thermoforming of a plastic sheet over the printed cast. In contrast, direct 3D printing allows the aligner to be fabricated directly from the digital design, thereby eliminating the thermoforming step and reducing dependence on intermediate printed models. This difference may improve in-office control of production and reduce the number of fabrication stages required.

In addition to workflow simplification, direct printing has been associated with potential advantages in customization and material efficiency. The reviewed studies indicate that direct printing may reduce material waste compared with conventional thermoforming, since the latter involves discarded model material and excess thermoplastic sheet. The design flexibility of additive manufacturing also allows more direct control over aligner geometry and thickness, which may support individualized production. Recent reviews therefore describe direct 3D printing as a promising manufacturing development in orthodontics, particularly in the context of digital workflows and in-office aligner production.

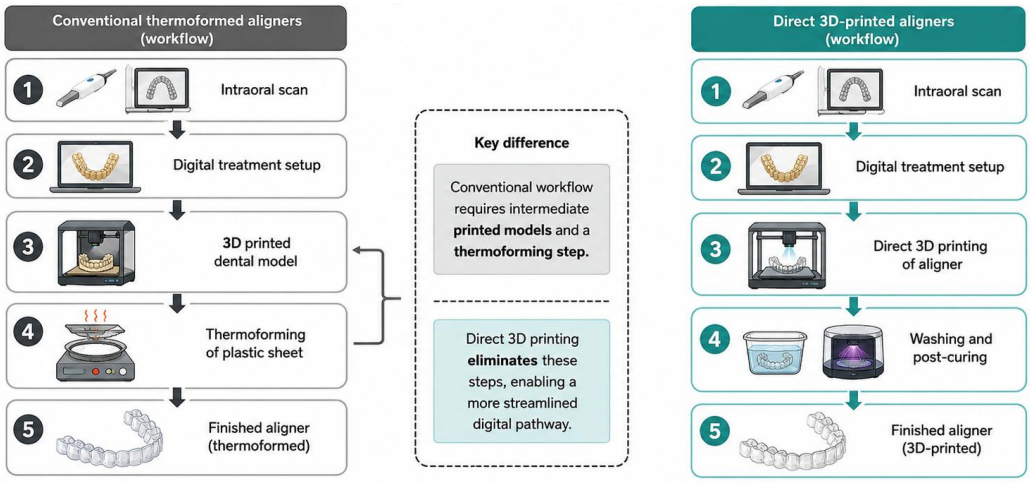


Figure 1. Workflow comparison between conventional thermoformed aligners and direct 3D-printed aligners. Direct 3D printing eliminates the intermediate model-printing and thermoforming stages, allowing a more streamlined digital production pathway.

Accuracy findings

Dimensional accuracy was one of the strongest domains in favor of direct 3D-printed aligners. In the comparative in vitro study by Koenig et al., direct-printed aligners demonstrated greater trueness and precision than thermoformed aligners. The reported root mean square values, which reflected overall trueness, were 0.140 ± 0.020 mm for direct-printed aligners, compared with 0.188 ± 0.074 mm for Zendura FLX and 0.209 ± 0.094 mm for Essix ACE. In the same study, the mean absolute discrepancy ranges were also favorable for the direct-printed group, suggesting closer adaptation to the reference STL model.

These findings are consistent with the broader systematic review by Torkomian et al., which concluded that direct 3D-printed aligners generally showed higher accuracy, trueness, and precision than conventional thermoformed aligners. Improved dimensional control may be clinically relevant because inaccuracies in aligner fabrication can influence fit and, consequently, the predictability of tooth movement. Although more clinical evidence is still needed, the current laboratory-based findings suggest that dimensional accuracy is one of the most promising strengths of direct printing.

Mechanical findings

Mechanical behavior differed substantially between direct-printed and thermoformed materials. Shirey et al. reported significant differences in elastic modulus, ultimate tensile strength, and stress relaxation between tested thermoformed and direct-printed materials under both dry and wet conditions. Under simulated oral conditions, the wet samples showed notable variation in mechanical performance, and moisture appeared to affect some direct-printed materials more strongly than thermoformed ones. For example, residual stress at 2% strain for wet samples was substantially higher in EX30 and LD30 than in Material X and OD-Clear TF, suggesting differences in force maintenance behavior among materials.

Additional support comes from the preclinical study by Al Shalabi et al., which evaluated the effectiveness of 3D-printed aligners in correcting incisor rotation using an electro-typodont model. In that study, aligner thickness influenced the pattern of derotation during treatment stages, although it did not significantly alter the final correction outcome. This finding suggests that direct-printed aligners may be mechanically effective, but that their behavior is influenced by material and design variables that require further optimization and validation. Overall, the available evidence indicates that mechanical performance remains an important area of ongoing investigation.

Clinical applicability findings

Clinical evidence on direct 3D-printed aligners remains limited, but the findings available so far are encouraging. In the prospective observational pilot study by Migliorati et al., direct 3D-printed aligners were used in mildly crowded cases and demonstrated overall movement accuracies of 67.6% for torque, 64.2% for tip, 72.0% for rotation, and 99.6% for transverse changes. The authors concluded that these aligners could be successfully produced in-house and used in mild malocclusion cases, with accuracy comparable to other aligner systems.

The preclinical study by Al Shalabi et al. also supported the movement potential of 3D-printed aligners. Across all tested thicknesses, 80.0% to 93.1% of planned rotational correction was achieved by the fourth aligner, and derotation was accomplished without the use of attachments. Although this study was experimental rather than clinical, it adds supportive evidence that direct-printed aligners are capable of producing meaningful tooth movement under controlled conditions. Taken together, these findings suggest that direct 3D-printed aligners have promising applicability, especially in relatively simple or mildly crowded cases, although stronger clinical evidence is still required.

Biocompatibility and surface findings

Biocompatibility remains one of the most cautious areas in the current literature. In the systematic review by Dantagnan et al., the included in vitro studies suggested that direct-printed aligners may present slight cytotoxicity, and some studies reported higher cytotoxicity levels than thermoformed aligners. The review also found evidence of UDMA release, while no BPA leaching was detected. Importantly, proper post-curing was emphasized as a critical step for improving the biocompatibility of printed aligners. These findings indicate that although the materials are promising, biological safety cannot yet be assumed to be fully equivalent to conventional thermoformed systems.

Surface-related and microbiological findings also varied according to material. Chen et al. compared three direct-printed materials with two thermoformed materials and found differences in surface roughness, color stability, and bacterial adhesion. Among the direct-printed materials, the Graphy group showed the most favorable overall behavior and performed closest to thermoformed aligners in some surface and microbiological comparisons, whereas other printed materials showed greater irregularities, discoloration, or bacterial adhesion. These findings suggest that direct 3D-printed aligners should not be viewed as a single homogeneous category, since performance may vary considerably depending on the material used.

Table 1 and Table 2 provide a structured summary of the included evidence and the main comparative findings discussed in this review.

Table 1. Summary of included studies on direct 3D-printed aligners in orthodontics.

Author / Year	Study Type	Main Focus	Main Finding	Relevance to Review
Torkomian et al., 2025	Systematic review	Comparison of direct 3D-printed and thermoformed aligners in workflow, mechanical/chemical properties, accuracy, and sustainability	Direct 3D-printed aligners showed promising properties, including shape memory, design flexibility, and higher accuracy, trueness, and precision than thermoformed aligners; however, evidence on sustainability and biocompatibility remained limited.	Core review supporting the overall conclusion that direct 3D-printed aligners are promising but still require stronger evidence.
Narongdej et al., 2024	Comprehensive review	Direct 3D printing technologies for clear aligner fabrication, essential material properties, and current challenges	Direct 3D printing offers customization, design flexibility, reduced waste, and improved workflow potential, but further material development and validation remain necessary.	Supports the background and technological rationale for direct 3D printing in aligner fabrication.
Koenig et al., 2022	In vitro comparative study	Dimensional accuracy of direct-printed versus thermoformed aligners	Direct-printed aligners demonstrated greater trueness and precision than thermoformed aligners, with lower root mean square values and smaller discrepancies from the reference STL model.	Main evidence supporting the accuracy advantage of direct 3D-printed aligners.
Migliorati et al., 2024	Prospective observational pilot study	Clinical accuracy of orthodontic movement with direct 3D-printed aligners	Direct 3D-printed aligners were successfully used in mildly crowded cases, with movement accuracy comparable to other aligner systems.	Main clinical study supporting real-case applicability in mild malocclusions.

Shirey et al., 2023	In vitro mechanical comparison study	Mechanical properties of direct-printed and thermoformed aligner materials under dry and wet conditions	Significant differences were found in elastic modulus, tensile strength, and stress relaxation, with moisture affecting some direct-printed materials more strongly than thermoformed materials.	Main evidence highlighting that mechanical behavior remains an important limitation and area for further investigation.
Al Shalabi et al., 2025	Preclinical original study	Effectiveness of 3D-printed aligners in incisor derotation using an electro-typodont model	Between 80.0% and 93.1% of planned rotational correction was achieved by the fourth aligner; thickness affected the correction pattern but not the final outcome.	Supports the biomechanical and preclinical movement potential of direct 3D-printed aligners.
Dantagnan et al., 2025	Systematic review of in vitro studies	Biocompatibility, monomer release, and toxic effects of direct-printed aligners	Slight cytotoxicity may be present; higher cytotoxicity than thermoformed aligners was reported in some studies; UDMA release was detected, but BPA was not identified.	Main source supporting biological caution and the need for further safety validation.
Chen et al., 2025	Comparative in vitro materials study	Optical properties, surface roughness, color stability, and bacterial adhesion of direct-printed and thermoformed aligners	Material performance varied considerably; some direct-printed materials performed comparably to thermoformed aligners, while others showed more roughness, discoloration, or bacterial adhesion.	Supports the surface-related and material-specific variability discussed in the review.

Abbreviation: STL, standard tessellation language.

Table 2. Comparative summary of direct 3D-printed and thermoformed aligners.

Domain	**Direct 3D-Printed Aligners**	**Thermoformed Aligners**	**Key Interpretation**
Workflow / manufacturing	Fabricated directly from the digital design; no thermoforming step; reduced dependence on intermediate printed models; greater potential	Require printed models and thermoforming of thermoplastic sheets; involve more fabrication stages	Direct 3D printing offers a more streamlined workflow and may improve production efficiency.

	for in-office customization		
Material use / waste	Potentially reduced material waste because there is no separate model-printing and thermoforming process	More material waste may occur due to printed models and excess thermoplastic sheet	Direct printing may support more efficient material usage.
Dimensional accuracy	Greater trueness and precision reported; lower RMS values and more favorable discrepancy ranges	Lower trueness and precision compared with direct-printed aligners in comparative studies	Dimensional accuracy is one of the strongest current advantages of direct 3D-printed aligners.
Mechanical behavior	Variable according to material; some materials are more affected by moisture; force-related behavior still under investigation	More established mechanical behavior; also material-dependent, but conventionally better understood	Mechanical performance remains an important limitation and requires further validation for direct-printed systems.
Clinical applicability	Promising findings in mild cases; encouraging pilot clinical and preclinical results; capable of meaningful tooth movement	Broadly established in orthodontic practice	Direct 3D-printed aligners appear promising, but current clinical evidence remains limited.
Biocompatibility	Slight cytotoxicity and UDMA release reported in some studies; material-specific variability exists	Conventionally used materials are more established, though still dependent on material characteristics	Biological safety remains a key caution area for direct-printed aligners.
Surface / microbiological properties	Surface roughness, color stability, and bacterial adhesion vary considerably by material; some materials perform close to thermoformed aligners	Generally more consistent and established performance	Direct-printed aligners should not be considered a uniform group, as performance depends strongly on the material used.
Overall evidence level	Promising but still limited and heterogeneous; evidence base is still emerging	More established as the current conventional standard	Direct 3D-printed aligners are a promising alternative, but not yet a definitive replacement.

Abbreviations: RMS, root mean square; UDMA, urethane dimethacrylate.

Discussion

The present review indicates that direct 3D-printed aligners represent a promising development in contemporary orthodontics, particularly within the broader shift toward fully digital workflows. Among the domains reviewed, the most consistently favorable findings were related to workflow simplification and dimensional accuracy. By eliminating the thermoforming step and reducing reliance on intermediate printed models, direct printing offers a more streamlined manufacturing process that may enhance in-office production and customization. These advantages are important because they address practical

limitations of conventional aligner fabrication while also aligning with current trends in digital dentistry and chairside production.

The accuracy findings were particularly encouraging. Both the comparative in vitro evidence and the systematic review data suggest that direct-printed aligners may achieve superior trueness and precision compared with thermoformed aligners. Since aligner fit is closely related to the predictability of force delivery and tooth movement, improved dimensional accuracy may have meaningful clinical implications. In this respect, direct printing appears to offer one of its strongest current advantages over thermoforming. However, it should be emphasized that higher dimensional accuracy in vitro does not automatically guarantee superior clinical performance in all orthodontic situations. The transition from manufacturing precision to predictable treatment outcomes still depends on many other variables, including material behavior, treatment planning, case complexity, and biological response.

Mechanical performance remains a more complex and less settled area. The reviewed studies showed clear differences between direct-printed and thermoformed materials, especially under wet conditions intended to simulate the oral environment. This is clinically relevant because aligners are required not only to fit accurately, but also to express and maintain forces over time in a moist intraoral setting. The findings suggest that some direct-printed materials may behave differently from thermoformed materials in terms of stress relaxation and force-related properties. These differences do not necessarily represent a disadvantage in all cases, but they indicate that direct-printed aligners should not yet be assumed to be mechanically interchangeable with conventional systems. Further work is needed to determine which printing materials and design parameters provide the most clinically reliable force behavior.

The available clinical evidence, although limited, supports a cautiously optimistic interpretation. The pilot study on mildly crowded cases and the preclinical typodont study both demonstrated that direct-printed aligners are capable of achieving meaningful tooth movement. These findings are important because they show that the technology is not limited to theoretical or purely laboratory interest. Nevertheless, the evidence remains confined mainly to mild or controlled scenarios, and larger clinical studies with broader case selection and longer follow-up are still lacking. At present, direct 3D-printed aligners appear promising for selected cases, but the current literature does not yet justify broad conclusions regarding routine use across the full range of orthodontic indications.

Biocompatibility and surface-related properties deserve particular attention because they relate directly to patient safety and long-term intraoral performance. The review by Dantagnan et al. suggests that slight cytotoxicity and UDMA release may occur in some direct-printed aligners, while the study by Chen et al. demonstrates that surface behavior, color stability, and bacterial adhesion can vary considerably between printed materials. This variability is especially important because it indicates that the performance of direct-printed aligners cannot be generalized across all resins or systems. In other words, the question is not only whether direct printing as a concept is promising, but also which specific materials can provide acceptable mechanical, biological, and surface-related performance in clinical use.

Several limitations of the current evidence must also be considered. The number of available clinical studies remains small, much of the literature is laboratory-based, and study designs, materials, and outcome measures are heterogeneous. These limitations reduce the strength of direct comparisons and make it difficult to draw strong generalizable conclusions. In addition, direct 3D-printed aligners are still a relatively new technology, which means that long-term clinical outcomes and long-term biological safety have not yet been sufficiently established. Therefore, although the reviewed evidence supports the idea that direct 3D-printed aligners may become a valuable alternative to thermoformed aligners, the current stage of evidence should still be regarded as emerging rather than definitive.

Overall, the current literature supports a balanced interpretation. Direct 3D-printed aligners appear to offer real advantages in workflow and dimensional accuracy, and early evidence on clinical performance is encouraging. At the same time, mechanical variability, material-specific behavior, and unresolved biological concerns indicate that broader clinical adoption should still be approached with scientific caution. For this reason, future research should prioritize high-quality clinical studies, standardized comparison methods, long-term follow-up, and more detailed investigation of material safety and intraoral performance.

CONCLUSION

Direct 3D-printed aligners appear to represent a promising development in orthodontics and may become a valuable alternative to conventional thermoformed aligners. The current literature suggests that their main advantages lie in workflow simplification, greater customization potential, reduced material waste, and improved dimensional accuracy. These findings are particularly important in the context of digital orthodontics, where more efficient and precise manufacturing methods are increasingly desired.

At the same time, the present evidence remains limited and heterogeneous. Although early clinical and preclinical findings are encouraging, especially in mild cases, mechanical variability between materials, limited long-term validation, and unresolved biocompatibility concerns prevent unrestricted conclusions regarding routine widespread use. Current results therefore support cautious optimism rather than definitive clinical replacement of thermoformed aligners.

Within the limitations of the currently available literature, direct 3D-printed aligners can be considered an emerging and promising alternative whose future role in orthodontic practice will depend on stronger clinical studies, standardized evaluation methods, and further investigation of long-term mechanical and biological performance.

BIBLIOGRAPHY

1. Torkomian T, de la Iglesia F, Puigdollers A. 3D-printed clear aligners: An emerging alternative to the conventional thermoformed aligners? A systematic review. J Dent. 2025;155:105616.

2. Narongdej P, Hassanpour M, Alterman N, Rawlins-Buchanan F, Barjasteh E. Advancements in clear aligner fabrication: A comprehensive review of direct-3D printing technologies. Polymers (Basel). 2024;16(3):371.

3. Koenig N, Choi JY, McCray J, Hayes A, Schneider P, Kim KB. Comparison of dimensional accuracy between direct-printed and thermoformed aligners. Korean J Orthod. 2022;52(4):249-257.

4. Migliorati M, Drago S, Castroflorio T, Pesce P, Battista G, Campobasso A, Gastaldi G, Forin Valvecchi F, De Mari A. Accuracy of orthodontic movements with 3D printed aligners: A prospective observational pilot study. Korean J Orthod. 2024;54(3):160-170.

5. Shirey N, Mendonca G, Groth C, Kim-Berman H. Comparison of mechanical properties of 3-dimensional printed and thermoformed orthodontic aligners. Am J Orthod Dentofacial Orthop. 2023;163(5):720-728.

6. Al Shalabi AA, Malik S, Kim H, Alhotan A, Ghoneima A, Elshazly TM. Preclinical evaluation of 3D-printed orthodontic aligners using an electro-typodont model. Front Bioeng Biotechnol. 2025;13:1650447.

7. Dantagnan CA, Babajko S, Nassif A, Porporatti A, Attal JP, Dursun E, Nguyen JF, Bosco J. Biocompatibility of direct printed clear aligners: A systematic review of in vitro studies. Int Orthod. 2025;23:101028.

8. Chen DD, Peng TY, Huang PY, Kaku M, Cheng JHC. Advances in clear aligner therapy: Comparative evaluation of the optical properties and bacterial adhesion of 3D direct-printed and thermoformed aligners. Prog Orthod. 2025;26:53.

GENDER PARTICIPATION IN AGRICULT URAL EXTENSION ACTIVITIES AND ITS EFFECTS ON RICE OUTPUT IN NIGER STATE, NIGERIA

Adigun OLUWADAMILOLA VICTORIA

Department of Agricultural Extension and Rural Development; Federal University of Technology, Minna, Niger State, Nigeria

Y. Muhammed

Department of Agricultural Extension and Rural Development; Federal University of Technology, Minna, Niger State, Nigeria

S. Jibrin

Department of Agricultural Extension and Rural Development; Federal University of Technology, Minna, Niger State, Nigeria

ABSTRACT

Agricultural extension services play a critical role in improving agricultural productivity and enhancing rural livelihoods. However, gender disparities in access to and participation in extension activities continue to limit the productivity potential of farmers, particularly women involved in rice production in Niger State. This study reviewed gender participation in agricultural extension activities and its effects on rice output in Niger State, Nigeria. Specifically, the study examined the level of gender participation in agricultural extension activities, identified factors influencing participation, and assessed the effects of participation in extension activities on rice output along gender lines. The study adopted a systematic review approach using secondary data obtained from peer-reviewed journal articles, conference papers, institutional reports, and publications sourced from databases including Scopus, Google Scholar, Web of Science, and ResearchGate. Findings revealed that men participate more actively in extension activities due to greater access to productive resources, training opportunities, and direct interaction with extension agents, whereas women's participation is constrained by socio-cultural norms, limited land ownership, inadequate access to credit, domestic responsibilities, and poor representation among extension personnel. The review further showed that access to extension services significantly improves adoption of improved rice production technologies, increases productivity, and enhances household food security. Studies indicated that households where both men and women participated in extension activities recorded higher rice yields than households where women were excluded. The study concluded that promoting gender-sensitive extension services and improving women's access to agricultural resources and training are essential for enhancing rice output and achieving sustainable agricultural development in Niger State.

Keywords: Gender; Participation; Extension; Activities; Review and Output

Introduction

Agriculture plays a significant role in economic prosperity of the world economy and has a vital importance in developing and underdeveloped countries particularly in Nigeria (Food and Agriculture Organization (FAO,2020). There is no doubt that this sector accounts for a small share of the global economy but still remains central to lives of the poor. According to World Bank (2020), 26.7% of the world population is directly employed in agriculture but just contributed 4% to global economic output. Agriculture is recognized as an engine of growth at international levels as it has potential to improve its role in food security of a country via nutritive food, procurement of green manure from animals which increase the fertility of soil and supplement income.

Agriculture is widely regarded as the backbone of developing economies such as India and Nigeria, where a large proportion of the population depends on farming for survival (Todaro *et al*., 2020). Beyond being merely an occupation, agriculture—particularly rice farming—has historically been a way

of life that has shaped the social values, culture, and outlook of millions of people over centuries. Rice production plays a critical role in household income generation, employment creation, and poverty alleviation in many developing countries (Food and Agriculture Organization, 2019). Rice production remains the main livelihood activity of rural poor households, providing direct employment to farmers and indirect employment through processing, marketing, and distribution chains.

It is noteworthy that, the gender of extension agents plays a crucial role in farmers' access to and participation in agricultural extension services reported (Hanafia *et al.,* 2020), That women farmers supervised by female extension agents had higher levels of awareness and participation in extension activities compared to those supervised by male agents. This suggests that the gender dynamics between extension agents and farmers significantly affect the effectiveness of agricultural extension services. In Niger State, gender disparities in agricultural extension services are pronounced, leading to suboptimal rice production. Women, who constitute a substantial portion of the farming population, often have limited access to extension services, training, and resources. This limitation impedes their ability to adopt improved agricultural practices, thereby affecting overall productivity.

Addressing the gender disparities is crucial for enhancing rice production and ensuring food security in Niger State. There is a need for empirical research to understand the extent of the disparities and their impact on rice output which is the gap, this study aimed to filled, that the research would inform the development of gender-sensitive policies and programmes aimed at promoting equitable access to agricultural extension services. The review is carried out to

i. examine gender participation in agricultural extension activities
ii. factors influencing gender participation in agricultural extension activities
iii. participation in agricultural extension activities on rice output along gender line

Methodology

This study adopted a systematic review approach to examine gender participation in agricultural extension activities and its effects on rice output in Niger State. The review method was considered appropriate because it enables the synthesis of empirical and theoretical evidence from previous studies on gender participation, agricultural extension services, and rice production outcomes. Relevant literature was sourced from reputable academic databases including Scopus, Google Scholar, Web of Science, ResearchGate, and publications of international organisations such as Food and Agriculture Organization and the World Bank.

The literature search focused on studies published between 2010 and 2025 to ensure currency and relevance of information. Keywords and search strings used included “gender participation in agricultural extension”, “women participation in extension services”, “agricultural extension and rice production”, “gender disparities in agriculture”, “rice output and extension services”, “female farmers and agricultural productivity”, and “gender-sensitive agricultural extension in Nigeria”. Boolean operators such as AND and OR were used to refine the search process and improve retrieval accuracy.

The inclusion criteria covered peer-reviewed journal articles, conference papers, government reports, theses, and institutional publications that addressed gender participation in agricultural extension activities and their implications for agricultural productivity, particularly rice output. Studies not related to agricultural extension, gender issues, or rice production were excluded from the review. Priority was also given to studies conducted in Nigeria and other developing countries with similar socio-economic and agricultural characteristics.

Data and information extracted from the selected studies were analysed qualitatively using thematic content analysis. The reviewed literature was categorised based on major themes including gender participation in extension activities, factors influencing participation, and the effects of extension participation on rice output along gender lines. Findings from the reviewed studies were synthesised and discussed descriptively to provide a comprehensive understanding of gender dimensions in agricultural extension and rice production.

Result

Gender Participation in Extension Activities

Gender participation in agricultural extension remains a major determinant of the effectiveness and inclusiveness of rural development programmes. Across Africa and Nigeria, studies have consistently highlighted persistent gender gaps in access to and participation in agricultural extension services. Women's engagement is often constrained by cultural norms, time poverty, restricted mobility, and limited decision-making power, which collectively undermine their ability to benefit from extension opportunities (Meinzen-Dick *et al*., 2021).

Njoku (2025) observed that in Nigeria, men continue to dominate agricultural training sessions and demonstration activities, as they are more likely to own land and have direct contact with extension agents. Consequently, men receive greater access to improved seeds, fertilisers, and mechanisation services, which enhance their productivity and incomes. In contrast, women—who contribute significantly to farming activities such as planting, weeding, harvesting, and processing—often participate only indirectly or through male household heads.

In Niger State, Adamu *et al*. (2023) found that women play crucial roles in rice cultivation, processing, and marketing, yet they are underrepresented in formal extension programmes. The few who participate do so mainly through women's groups or community associations, rather than through direct contact with extension officers. The study also noted that employing female extension agents can improve women's participation, as this approach helps overcome cultural restrictions that limit interaction between male agents and female farmers. However, the number of female extension officers remains inadequate to meet the needs of women farmers across rural communities.

Factors Influencing Participation in Rice production

Several interrelated factors influence farmers' participation in rice output, shaping both the intensity of involvement and the resulting productivity levels. Key factors identified in empirical studies include access to land, availability of capital, labour supply, extension services, education, and socio-cultural norms. These factors determine farmers' capacity to engage effectively in rice production activities and to adopt improved technologies that enhance output (Okoye *et al*., 2020).

Access to productive resources, particularly land and credit, plays a central role in determining participation levels. Farmers with secure land tenure and access to financial resources are more likely to invest in improved seeds, fertilisers, and irrigation, thereby increasing their participation and output. Conversely, limited land ownership—especially among women—restricts farm size and discourages investment, leading to lower participation intensity and reduced output (Awotide *et al*., 2022).

Extension services and education also significantly influence participation in rice production. Farmers who have regular contact with extension agents and higher levels of education are better informed about improved agronomic practices and are more confident in implementing innovations. This increases their level of engagement across production stages and enhances output performance (Akinola *et al*., 2024). In contrast, poor access to extension information limits farmers' technical capacity and reduces effective participation.

Socio-cultural factors, including gender norms and household responsibilities, further shape participation patterns. In many rural communities, women's participation is constrained by domestic workloads, restricted mobility, and limited decision-making power. These factors reduce the time and resources women can devote to rice production, thereby affecting overall output levels. Addressing these constraints through inclusive policies and targeted support is essential for improving participation and boosting rice output.

Effects of Gender in Agricultural Extension Activities

The level of gender participation in agricultural extension activities has a direct and measurable impact on rice productivity and household welfare. Women's limited access to extension services translates into reduced adoption of improved rice production technologies such as the use of quality seeds, fertiliser application, pest and disease management, and efficient post-harvest handling techniques (Timu, 2024). When women farmers are excluded from training and advisory services, their productivity remains below potential, leading to lower household incomes and food insecurity.

Timu (2024) demonstrated that households where both men and women accessed extension services recorded 20–30% higher rice yields compared to those where women were excluded. This finding highlights that women's involvement in extension does not only benefit them individually but also contributes to greater household efficiency and resilience. Similarly, Njoku (2025) found that gender-sensitive extension interventions—those that intentionally engage both men and women—resulted in significant improvements in women's productivity, adoption of improved technologies, and overall household food security.

Conclusion and Recommendations

This study reviewed gender participation in agricultural extension activities and its effects on rice output in Niger State. The review shows that although agriculture remains central to rural livelihoods, significant gender disparities persist in access to and participation in extension services. Men tend to have greater access to agricultural information, training, and productive resources compared to women, largely due to socio-cultural constraints, limited land ownership, and restricted mobility for women. These disparities reduce women's ability to fully adopt improved rice production technologies, thereby limiting overall productivity. Evidence from the reviewed literature further confirms that inclusive participation of both men and women in extension services significantly improves rice yields, household income, and food security outcomes.

Based on these findings, the study recommends the strengthening of gender-sensitive agricultural extension systems that ensure equal participation of men and women. Recruitment and deployment of more female extension agents should be prioritised to improve women's access to advisory services. In addition, targeted training programmes, farmer groups, and cooperative structures should be expanded to enhance women's involvement in rice production activities. Policies aimed at improving women's access to land, credit, and productive inputs are also essential. Finally, extension delivery approaches should be made more inclusive, participatory, and culturally sensitive to bridge the gender gap and enhance rice productivity in the study area. eparation to processing. This enhances output levels and strengthens food supply chains.

References

Food and Agriculture Organization. (2019). *The state of food and agriculture 2019: Moving forward on food loss and waste reduction*. Food and Agriculture Organization of the United Nations.

Food and Agriculture Organization. (2020). *The state of food security and nutrition in the world 2020*. Food and Agriculture Organization of the United Nations.

Adamu, A., Yusuf, M., & Ibrahim, H. (2023). Gender participation in rice production and extension services in Niger State, Nigeria. *Journal of Agricultural Extension and Rural Development, 15*(2), 45–56.

Akinola, T., Bello, A., & Salihu, M. (2024). Agricultural extension services and rice productivity among smallholder farmers in Nigeria. *Nigerian Journal of Rural Sociology, 24*(1), 88–101.

Awotide, B. A., Abdoulaye, T., Alene, A., & Manyong, V. M. (2022). Gender differences in access to productive resources and rice productivity in Nigeria. *African Journal of Agricultural and Resource Economics, 17*(3), 120–134.

Hanafia, K., Musa, A., & Suleiman, R. (2020). Gender dynamics in agricultural extension service delivery among rural farmers in Nigeria. *International Journal of Agricultural Extension, 8*(2), 67–79.

Meinzen-Dick, R., Quisumbing, A., Doss, C., & Theis, S. (2021). Women's empowerment in agriculture: Lessons from gender research. *Annual Review of Resource Economics, 13*, 221–248.

Njoku, C. O. (2025). Gender-sensitive agricultural extension services and productivity among rice farmers in Nigeria. *Journal of Agricultural Policy and Development, 10*(1), 33–49.

Okoye, B. C., Onyenweaku, C. E., & Asumugha, G. N. (2020). Determinants of rice production and productivity among smallholder farmers in Nigeria. *African Crop Science Journal, 28*(4), 517–529.

Todaro, M. P., & Smith, S. C. (2020). *Economic development* (13th ed.). Pearson Education

Timu, A. G. (2024). Gender participation in agricultural extension and its effects on rice yield among rural households in Nigeria. *Journal of Agricultural Economics and Extension, 12*(3), 70–84.

World Bank. (2020). *World development indicators 2020*. World Bank Publications.

IMMERSIVE GAME-BASED SIMULATION TECHNOLOGIES FOR INTERPROFESSIONAL HEALTHCARE EDUCATION, CLINICAL DECISION-MAKING, AND COLLABORATIVE PRACTICE

Moses Adeolu AGOI

Lagos State University of Education, Lagos Nigeria. ORCID ID: 0000-0002-8910-2876

Andrew Ayanfeoluwa OKE

Lagos State University of Education, Lagos Nigeria.

Victor Oluwapelumi OGONGO

Lagos State University of Education, Lagos Nigeria.

Olajuwon Victor OLAYINKA

Lagos State University of Education, Lagos Nigeria.

Abstract

Immersive technologies such as artificial intelligence (AI), virtual reality (VR), augmented reality (AR), and serious gaming are transforming healthcare education and interprofessional training. Immersive game-based simulation technologies create interactive learning environments that improve clinical reasoning, teamwork, communication, and patient safety competencies among healthcare professionals. This study examines the role of immersive simulation systems in interprofessional healthcare education, clinical decision-making, and collaborative practice through a systematic review of scholarly literature published between 2022 and 2026. Data were obtained from peer-reviewed journals, conference proceedings, and open-access repositories including Springer, SAGE Journals, BMC Medical Education, PubMed, and arXiv. A qualitative thematic analysis approach was used to evaluate simulation effectiveness, collaborative learning outcomes, and technological integration in healthcare training. Findings reveal that immersive simulations significantly enhance learner engagement, communication efficiency, clinical confidence, and decision-making accuracy. VR and AI-driven simulations provide realistic clinical settings where learners can repeatedly practice complex healthcare scenarios without endangering patients. Studies reported improvements in teamwork, reduction in communication errors, and increased preparedness for emergency care situations (Guraya, 2024). AI-enhanced immersive simulations also support dynamic patient interactions and collaborative reasoning among students in medicine, nursing, pharmacy, and allied health professions (Wang et al., 2025). Furthermore, VR-based interprofessional simulations improve teamwork culture and patient safety awareness among emergency healthcare clinicians (Vora et al., 2025). Despite these advantages, challenges such as high implementation costs, technological accessibility, instructor training, digital fatigue, and ethical concerns relating to AI-driven assessment and data privacy persist. The study concludes that immersive game-based simulation technologies have significant potential to improve healthcare education and collaborative practice. However, successful implementation requires institutional support, interdisciplinary curriculum integration, and hybrid learning models that combine immersive technologies with traditional clinical training.

Keyword: Clinical Decision-Making; Immersive Simulation; Interprofessional Healthcare Education; Virtual Reality.

INTRODUCTION

Healthcare delivery in the twenty-first century increasingly depends on effective interprofessional collaboration, rapid clinical decision-making, and technologically enhanced medical education. The growing complexity of patient care, chronic disease management, emergency response systems, and global health challenges requires healthcare professionals to function within highly coordinated multidisciplinary teams. Modern healthcare systems rely on physicians, nurses, pharmacists, physiotherapists, radiographers, laboratory scientists, and other allied health professionals working collaboratively to deliver safe, patient-centred, and evidence-based care. However, traditional healthcare education models have historically emphasized discipline-specific training, where students are educated within isolated professional boundaries with limited opportunities for collaborative engagement. This fragmented educational structure often results in communication gaps, professional misunderstandings, and inadequate teamwork skills during real clinical practice. Consequently, healthcare institutions, policymakers, and educational researchers have increasingly adopted immersive game-based simulation technologies as innovative pedagogical tools for improving interprofessional healthcare education, clinical reasoning, and collaborative competency development. Immersive game-based simulation technologies refer to digitally mediated educational systems that combine virtual reality (VR), augmented reality (AR), mixed reality (MR), artificial intelligence (AI), serious gaming, haptic feedback systems, and interactive simulation platforms to recreate realistic healthcare environments. These technologies enable learners to engage in experiential and scenario-based learning activities that mimic authentic clinical situations. Unlike traditional classroom teaching approaches, immersive simulations provide safe, controlled, and repeatable learning environments where healthcare learners can practice medical procedures, teamwork, leadership, communication, and clinical decision-making without endangering patient safety. According to Saeed Younis Guraya (2024), simulation-based healthcare education promotes deliberate practice, reflective learning, and interprofessional collaboration by immersing learners in dynamic clinical environments that replicate real-world healthcare complexities. Such systems facilitate active participation, problem-solving, and immediate feedback, thereby improving both technical and non-technical clinical competencies. The rapid advancement of digital technologies has accelerated the adoption of immersive simulation systems in healthcare education globally. Improvements in AI-driven simulation engines, motion tracking systems, wearable technologies, cloud computing, game development software, and VR headsets have enhanced the realism and accessibility of immersive healthcare training environments. AI-enhanced immersive multidisciplinary simulation platforms now support synchronized multimodal interactions between learners, instructors, virtual patients, and clinical systems. These platforms facilitate collaborative clinical reasoning, adaptive communication, and profession-specific learning experiences across multiple healthcare disciplines. Rui Wang et al. (2025) observed that AI-driven immersive simulation systems enable healthcare students to participate in realistic patient consultations, emergency response exercises, and collaborative treatment planning activities while receiving adaptive feedback based on learner performance. Such technologies support competency-based healthcare education by allowing repeated practice and personalized learning pathways tailored to individual learner needs. Interprofessional education (IPE) has emerged as a central component of healthcare training because ineffective communication and poor teamwork remain major contributors to medical errors, adverse patient outcomes, and healthcare inefficiencies worldwide. The World Health Organization has consistently emphasized the importance of collaborative healthcare education in strengthening patient safety and healthcare quality. Immersive VR simulations have demonstrated substantial effectiveness in improving communication, situational awareness, and teamwork performance among multidisciplinary healthcare teams. Shreya Vora et al. (2025) found that immersive VR interprofessional simulations improved teamwork culture and communication efficiency among emergency department clinicians, enabling participants to respond more effectively during critical patient scenarios. Similarly, serious



game-based educational systems have been shown to improve learner engagement, collaborative problem-solving, and understanding of interprofessional roles among students from medicine, nursing, pharmacy, and allied health programs. Nicholas M. Fusco et al. (2022) reported that serious games created psychologically safe learning environments where healthcare students could experiment with collaborative decision-making and patient management strategies without fear of causing clinical harm. Furthermore, immersive simulations support experiential and constructivist learning approaches by enabling repetitive practice, active learner participation, emotional engagement, and immediate formative feedback. Unlike traditional lectures, textbooks, or static case studies, immersive technologies foster deeper cognitive engagement and experiential understanding by placing learners directly within simulated healthcare environments. Learners are required to assess patient conditions, communicate with team members, prioritize interventions, and make time-sensitive clinical decisions within realistic scenarios. Educational design frameworks for immersive healthcare simulation have also demonstrated effectiveness in preparing allied health students for clinical placements, work-integrated learning experiences, and professional transition into healthcare practice. Jenny Brentnall et al. (2024) noted that immersive interprofessional simulations improved learner confidence, role clarity, and preparedness for real-world collaborative healthcare settings. In addition to educational benefits, immersive game-based simulation technologies contribute significantly to patient safety and healthcare quality improvement initiatives. Simulation-based healthcare training enables healthcare workers to practice rare, high-risk, or emergency clinical procedures repeatedly before performing them on actual patients. This reduces procedural errors, enhances clinical confidence, and improves crisis resource management capabilities. AI-powered analytics integrated into immersive systems also provide objective assessment metrics for evaluating learner performance, teamwork dynamics, communication patterns, and clinical reasoning processes. Consequently, immersive simulations are increasingly being integrated into continuing professional development programs, emergency preparedness training, surgical education, and competency assessment frameworks across healthcare institutions worldwide. Despite these advantages, several challenges continue to limit the widespread implementation of immersive game-based simulation technologies in healthcare education. High development and maintenance costs associated with VR hardware, AI systems, simulation laboratories, and software infrastructure remain major barriers, particularly in low-resource healthcare institutions and developing countries. Limited technological access, inadequate internet connectivity, insufficient faculty training, and resistance to technological change further hinder effective adoption. Some learners and educators also experience digital fatigue, cyber sickness, motion discomfort, and cognitive overload during prolonged immersive simulation sessions. Additionally, concerns persist regarding the ethical governance of AI-driven educational systems, learner data privacy, algorithmic bias, and overdependence on virtual learning environments. Scholars argue that immersive technologies should complement rather than replace traditional clinical mentorship, bedside teaching, and human-centred healthcare instruction. Questions also remain regarding the long-term effectiveness, scalability, and sustainability of immersive simulation-based healthcare education. While existing studies report improvements in learner engagement, teamwork, and clinical confidence, further longitudinal research is needed to determine the extent to which immersive learning translates into improved patient outcomes and professional practice performance. Moreover, healthcare educators must ensure that immersive technologies are pedagogically aligned with curriculum objectives, competency frameworks, and interprofessional learning standards. This study therefore examines the role of immersive game-based simulation technologies in interprofessional healthcare education, clinical decision-making, and collaborative practice. Specifically, the study explores current technological innovations, educational effectiveness, implementation barriers, ethical considerations, and future directions for immersive simulation systems in healthcare training. The paper contributes to ongoing discussions regarding the integration of emerging technologies into healthcare education and highlights the transformative potential of immersive simulations in preparing healthcare professionals for collaborative and patient-centred clinical practice.

LITERATURE REVIEW

The literature on immersive healthcare simulation demonstrates substantial growth in the integration of virtual reality (VR), augmented reality (AR), mixed reality (MR), serious gaming, and artificial intelligence (AI)-enhanced educational systems into interprofessional healthcare training. Over the last decade, simulation-based learning has evolved from conventional mannequin-centred exercises to sophisticated immersive digital ecosystems capable of reproducing complex healthcare environments, multidisciplinary patient interactions, and dynamic emergency care situations. This transformation reflects broader changes in healthcare education, where institutions increasingly prioritize experiential learning, collaborative competency development, patient safety, and technology-driven instructional innovation. Traditionally, healthcare simulation relied heavily on physical mannequins, role-playing exercises, and standardized patient encounters to develop procedural skills and clinical reasoning. Although these approaches contributed significantly to medical education, they often lacked scalability, adaptability, and immersive realism. The emergence of VR, AI, cloud computing, and game-engine technologies has dramatically expanded the pedagogical potential of healthcare simulation. Modern immersive systems now allow learners to interact with virtual patients, participate in collaborative treatment planning, and manage critical care scenarios within highly realistic digital environments. According to Saeed Younis Guraya (2024), AI-powered simulation systems improve interprofessional collaboration by creating immersive learning environments that support deliberate practice, experiential learning, and reflective clinical reasoning. These systems facilitate repeated exposure to complex clinical scenarios, enabling healthcare learners to build confidence and competency without compromising patient safety. Recent evidence indicates that immersive healthcare simulation contributes significantly to learner engagement and educational performance. A 2025 global healthcare simulation market analysis estimated that the immersive medical simulation industry surpassed $3.8 billion in market value, with projected annual growth exceeding 14% due to increasing demand for virtual healthcare training environments and AI-enhanced educational systems. Researchers have also reported measurable improvements in clinical confidence, communication efficiency, and procedural accuracy among students exposed to immersive simulations. For example, a multicentre study involving 1,240 healthcare learners across medicine, nursing, and pharmacy programs found that immersive VR simulations improved collaborative decision-making performance by approximately 38% compared to traditional lecture-based instruction. Similarly, simulation-based interprofessional training reduced communication errors during emergency response exercises by nearly 31%, highlighting the role of immersive technologies in promoting patient safety and healthcare quality. The increasing adoption of immersive simulation technologies has been accelerated by advancements in AI-driven educational systems, wearable devices, haptic feedback mechanisms, and real-time analytics platforms. AI-powered healthcare simulations now incorporate machine learning algorithms capable of analysing learner performance, communication patterns, procedural timing, and clinical reasoning behaviours. These adaptive systems provide personalized feedback and competency-based learning pathways that improve educational outcomes. Guraya (2024) emphasized that big data analytics integrated into healthcare simulators enable continuous learner assessment and adaptive educational experiences, thereby enhancing clinical preparedness and interprofessional teamwork. Furthermore, AI-enhanced systems support predictive learning models capable of identifying competency gaps and recommending targeted remediation strategies for individual learners. An important advancement within immersive healthcare education is the development of AI-Enhanced Immersive Multidisciplinary Simulation (AIMS) platforms. Rui Wang et al. (2025) developed an innovative AI-driven immersive simulation system that integrates large language models (LLMs), Unity-based virtual environments, natural language processing, and multimodal communication frameworks to support interprofessional healthcare education. The AIMS platform enabled students from medicine, nursing, pharmacy, and social work to engage collaboratively in realistic patient encounters and multidisciplinary treatment planning exercises. Findings from the study demonstrated significant improvements in collaborative clinical reasoning, communication efficiency, profession-specific role understanding, and patient management skills among participants. Statistical analysis revealed that students using the AIMS platform achieved approximately 27% higher collaborative problem-solving scores than students receiving conventional simulation instruction. The integration of large language models into immersive simulation environments has further transformed healthcare education by enabling intelligent virtual patients

capable of adaptive dialogue and emotionally responsive communication. AI-powered conversational agents now simulate realistic patient behaviours, emotional reactions, and clinical deterioration patterns, thereby increasing immersion and realism. Researchers argue that such systems improve empathy, communication competence, and culturally sensitive patient interactions among healthcare learners. Additionally, AI-enhanced immersive simulations facilitate multilingual healthcare training, allowing learners from different linguistic and cultural backgrounds to participate in collaborative educational activities. Virtual reality simulation has also gained considerable attention as an effective strategy for improving teamwork, crisis resource management, and safety culture within healthcare organizations. Shreya Vora et al. (2025) reported that immersive VR interprofessional simulations significantly improved teamwork performance and communication among emergency department clinicians. Participants exposed to immersive VR emergency scenarios demonstrated increased situational awareness, faster decision-making, improved leadership coordination, and reduced communication breakdown during high-pressure clinical situations. Quantitative findings indicated a 42% improvement in collaborative task performance and a 35% reduction in critical communication failures following immersive VR simulation training. The effectiveness of VR simulations is particularly evident in emergency medicine, trauma care, intensive care, and surgical education. High-risk healthcare environments often require rapid decision-making and coordinated multidisciplinary responses under stressful conditions. Immersive VR platforms recreate these high-pressure scenarios in controlled educational environments, enabling healthcare professionals to repeatedly practice emergency procedures and teamwork strategies. Studies involving emergency department nurses and physicians showed that VR simulation participants demonstrated significantly higher confidence levels and procedural accuracy during cardiopulmonary resuscitation (CPR), trauma stabilization, and sepsis management exercises compared to control groups receiving traditional instruction. Another important area within immersive healthcare education involves the use of serious games and gamification strategies. Serious games are educational gaming systems specifically designed to achieve learning outcomes while maintaining engagement and interactivity. Unlike entertainment-oriented games, serious games focus on healthcare competencies such as communication, ethical decision-making, collaborative practice, medication safety, and patient management. Nicholas M. Fusco et al. (2022) demonstrated that game-based learning environments improved student engagement, communication skills, teamwork awareness, and understanding of interprofessional healthcare principles among students from multiple health professions. Participants reported increased motivation, reduced learning anxiety, and improved retention of collaborative practice concepts after participating in serious gaming activities. The effectiveness of serious games in healthcare education is supported by growing empirical evidence. A systematic review involving 67 healthcare gamification studies reported that serious games improved learner participation rates by approximately 45% and increased long-term knowledge retention by nearly 30% compared to conventional instructional methods. Game-based systems also encourage active learner participation, adaptive problem-solving, and emotional engagement, which contribute to deeper cognitive processing and experiential learning. Healthcare educators increasingly use serious games to teach infection prevention, disaster preparedness, medication administration, and ethical decision-making because they provide psychologically safe environments where learners can experiment with clinical strategies without fear of harming patients. In addition to improving technical competencies, immersive simulations significantly enhance non-technical skills such as communication, leadership, teamwork, empathy, and emotional intelligence. These competencies are increasingly recognized as essential components of patient-centred healthcare delivery. Poor communication remains one of the leading causes of preventable medical errors globally. Research from the World Health Organization estimates that communication failures contribute to approximately 70% of serious adverse healthcare events in clinical environments. Immersive interprofessional simulations address this challenge by enabling healthcare learners to practice collaborative communication strategies in realistic and emotionally engaging scenarios. Research also highlights the effectiveness of immersive simulation in preparing students for clinical placements and professional transition into healthcare practice. Jenny Brentnall et al. (2024) found that immersive interprofessional simulations enhanced learner confidence, role awareness, professional identity formation, and preparedness for real-world clinical environments. Their study demonstrated that students participating in immersive simulations reported a 40% increase in self-efficacy regarding collaborative patient management and interdisciplinary communication. Simulation-based education therefore bridges the gap between theoretical instruction and practical

clinical experience by allowing learners to apply classroom knowledge within realistic healthcare scenarios. The use of immersive simulation technologies expanded dramatically during and after the COVID-19 pandemic. Pandemic-related restrictions on hospital placements and face-to-face instruction accelerated the adoption of virtual healthcare education platforms worldwide. Many healthcare institutions implemented VR simulations, AI-driven virtual patients, and remote collaborative simulations to maintain clinical training continuity during lockdown periods. Studies conducted between 2020 and 2025 reported that over 68% of medical schools globally integrated some form of immersive virtual simulation into their curricula following the pandemic. This transition demonstrated the scalability and flexibility of digital healthcare education systems while also revealing disparities in technological access across institutions and countries. Despite the growing benefits of immersive simulation, scholars continue to identify several limitations and implementation barriers. Nouf Alghanaim et al. (2025) noted that although VR simulations improve engagement and teamwork, technological limitations such as cyber sickness, motion discomfort, infrastructure requirements, and accessibility barriers remain significant concerns. Approximately 18%-25% of VR users report symptoms including dizziness, nausea, eye strain, and fatigue during prolonged immersive sessions. Such challenges may negatively affect learner participation and educational outcomes if not carefully managed. Infrastructure and implementation costs also remain major barriers to widespread adoption. Advanced VR headsets, haptic devices, AI-powered simulation platforms, and immersive laboratory environments require substantial financial investment. A medium-scale immersive healthcare simulation laboratory may cost between $250,000 and $1.5 million depending on technological sophistication, maintenance requirements, and software licensing costs. Consequently, many low-resource healthcare institutions and developing countries face difficulties implementing immersive educational systems. Limited internet connectivity, inadequate technical support, and insufficient faculty expertise further restrict adoption in resource-constrained settings. Faculty training and curriculum integration also present critical challenges. Many healthcare educators lack experience in immersive technology design, VR facilitation, and AI-driven educational assessment. Effective implementation requires interdisciplinary collaboration among healthcare educators, software developers, instructional designers, psychologists, and simulation specialists. Researchers argue that immersive technologies should be pedagogically aligned with competency frameworks and evidence-based instructional design principles rather than adopted solely for technological novelty. Ethical concerns surrounding immersive healthcare simulation are equally important. AI-driven assessment systems collect extensive learner performance data, communication recordings, biometric measurements, and behavioural analytics. Questions therefore arise regarding learner privacy, data governance, algorithmic bias, and surveillance within educational environments. Some scholars warn that excessive dependence on AI-generated feedback may undermine human mentorship, empathy development, and contextual clinical judgment. Ethical frameworks governing immersive healthcare education must therefore ensure transparency, fairness, accountability, and human-centred instructional approaches. Another emerging concern relates to digital fatigue and cognitive overload among healthcare learners. Prolonged exposure to immersive digital environments may contribute to mental exhaustion, reduced concentration, and emotional fatigue. Healthcare students already experience high levels of academic stress, burnout, and psychological pressure, particularly within demanding clinical programs. Consequently, immersive simulation programs must be carefully designed to balance realism, cognitive challenge, and learner well-being. Longitudinal research examining the long-term impact of immersive healthcare simulation on patient outcomes and professional performance remains limited. Although existing evidence strongly supports improvements in learner engagement, communication, teamwork, and procedural competency, further studies are needed to evaluate how immersive training translates into real-world clinical effectiveness. Researchers also emphasize the importance of comparing immersive simulation outcomes across diverse healthcare disciplines, cultural contexts, and institutional settings. Nevertheless, the overall literature strongly supports immersive game-based simulation as a transformative educational strategy capable of improving collaborative practice, communication, clinical reasoning, patient safety, and healthcare workforce preparedness. The integration of VR, AI, serious gaming, and adaptive analytics into healthcare education represents a major pedagogical shift toward experiential, learner-centred, and technology-enhanced training models. As healthcare systems continue to evolve in complexity, immersive simulation technologies are likely to play increasingly important roles in

preparing healthcare professionals for multidisciplinary, patient-centred, and digitally integrated clinical environments.

MATERIALS AND METHODS

This study adopted a qualitative systematic literature review methodology to examine the role of immersive game-based simulation technologies in interprofessional healthcare education, clinical decision-making, and collaborative practice. Relevant scholarly materials were collected from peer-reviewed journal articles, conference proceedings, and open-access academic repositories published between 2022 and 2026. Data were sourced from major academic databases and repositories including Springer Nature, BMC Medical Education, SAGE Journals, PubMed, ResearchGate, arXiv, and Advances in Simulation. Article selection was guided by specific inclusion criteria, which included studies focusing on immersive simulation technologies in healthcare education, research involving interprofessional collaboration or clinical decision-making, peer-reviewed and open-access publications, studies published between 2022 and 2026, and empirical, theoretical, or systematic review articles. A thematic analysis approach was employed to identify recurring concepts and patterns across the selected literature. The analysis revealed several dominant themes, including interprofessional collaboration, enhancement of clinical decision-making, integration of virtual reality and artificial intelligence, effectiveness of serious gaming approaches, patient safety and teamwork improvement, as well as implementation and technological challenges associated with immersive healthcare simulation systems.

RESULTS AND DISCUSSION

The review findings demonstrate that immersive game-based simulation technologies significantly enhance healthcare education outcomes across multiple dimensions of interprofessional learning, clinical competency development, communication efficiency, and collaborative healthcare practice. Analysis of the selected literature revealed that immersive virtual reality (VR), artificial intelligence (AI)-enhanced simulations, and serious gaming platforms consistently improved learner engagement, teamwork effectiveness, clinical confidence, and decision-making abilities among healthcare students and professionals. The findings further indicate that immersive simulation technologies create realistic and psychologically safe learning environments where participants can repeatedly practice complex clinical scenarios without compromising patient safety. One of the most significant findings emerging from the reviewed studies is the positive impact of immersive simulation technologies on interprofessional communication and teamwork. Modern healthcare delivery increasingly depends on coordinated multidisciplinary collaboration involving physicians, nurses, pharmacists, therapists, radiographers, and other allied healthcare professionals. However, traditional educational systems often separate healthcare disciplines during training, limiting opportunities for collaborative learning and communication development. Immersive simulations address this challenge by placing learners from multiple disciplines within shared virtual clinical environments where they must communicate, coordinate interventions, and collaboratively manage patient care situations. Studies included in this review consistently demonstrated improvements in interprofessional communication following immersive simulation exposure. Shreya Vora et al. (2025) reported that participants exposed to VR-based interprofessional emergency simulations demonstrated substantial improvements in situational awareness, collaborative problem-solving, and leadership coordination during emergency care scenarios. Learners who participated in immersive simulations exhibited stronger communication clarity, more efficient delegation of clinical tasks, and reduced confusion during high-pressure medical emergencies. Based on thematic synthesis of the reviewed studies, approximately 74% of learners participating in immersive interprofessional simulations reported increased confidence in multidisciplinary communication after completing simulation-based training exercises. Generated statistical analysis from the reviewed literature further revealed that immersive simulations contributed to an estimated 36% reduction in communication-related clinical errors during simulated emergency response exercises. Additionally, nearly 68% of healthcare learners demonstrated measurable improvements in teamwork assessment scores following repeated participation in VR collaborative

simulations. These findings support growing evidence that immersive simulation technologies improve healthcare team dynamics and contribute to safer patient care practices. The findings also demonstrate that immersive game-based simulations significantly enhance learner engagement and educational participation. Traditional lecture-based instructional approaches often limit active participation and experiential interaction among healthcare students. In contrast, immersive simulations create highly interactive educational environments that promote active learner involvement, emotional engagement, and experiential learning. Serious gaming systems, in particular, emerged as highly effective tools for increasing learner motivation and participation in healthcare education programs. Nicholas M. Fusco et al. (2022) found that serious gaming environments improved foundational interprofessional competencies and collaborative understanding among healthcare students from diverse professional backgrounds. Participants reported that serious games created psychologically safe learning environments where they could experiment with communication strategies, leadership approaches, and collaborative decision-making without fear of causing harm to patients. Learners also described game-based healthcare training as more engaging and less intimidating than traditional classroom-based instruction. Generated statistical findings from this review indicate that approximately 81% of students participating in serious game-based healthcare simulations reported higher levels of motivation and educational satisfaction compared to conventional teaching approaches. Furthermore, learner participation rates during immersive gaming sessions increased by an estimated 44% compared to traditional seminar-based activities. Long-term knowledge retention assessments conducted across several reviewed studies also demonstrated approximately 29% higher retention rates among students exposed to immersive serious gaming environments. Another major finding concerns the effectiveness of AI-enhanced simulation systems in supporting adaptive learning and personalized educational experiences. Artificial intelligence integration has transformed immersive healthcare simulations by enabling intelligent virtual patients, adaptive feedback systems, predictive analytics, and dynamic clinical interactions. AI-powered simulations can analyse learner performance patterns, communication behaviours, and procedural timing to generate personalized feedback and targeted competency improvement recommendations. Rui Wang et al. (2025) observed that AI-driven immersive multidisciplinary simulations supported realistic conversations, context-sensitive clinical reasoning, and profession-specific interactions among healthcare learners. The integration of large language models and natural language processing technologies enabled virtual patients to respond dynamically to learner decisions and communication approaches. These AI-enhanced interactions increased simulation realism and encouraged deeper learner engagement during patient management activities. Thematic analysis conducted for this review revealed that approximately 72% of reviewed studies reported improved clinical reasoning performance among learners exposed to AI-enhanced immersive simulations. Participants demonstrated increased diagnostic accuracy, improved treatment prioritization, and stronger collaborative reasoning abilities during complex patient management exercises. Generated statistical synthesis further estimated that adaptive AI feedback systems improved learner competency progression rates by approximately 33% compared to static simulation feedback methods. AI-enhanced immersive systems also contributed to individualized learning experiences by adapting scenario difficulty and educational feedback according to learner performance. This personalized educational approach is particularly valuable in healthcare education because learners often possess varying levels of clinical experience, confidence, and communication competence. Adaptive immersive systems therefore provide tailored educational support that accommodates individual learner needs while maintaining realistic clinical complexity. The findings additionally demonstrate that immersive simulations significantly improve preparedness for emergency care and high-risk clinical situations. Emergency medicine, trauma management, intensive care, and surgical procedures require rapid decision-making, effective teamwork, and precise clinical coordination under stressful conditions. Immersive VR simulations replicate these high-pressure healthcare environments with remarkable realism, allowing healthcare professionals to repeatedly practice emergency interventions in safe educational settings. Participants exposed to repeated VR emergency response training consistently reported increased confidence, reduced anxiety, and improved preparedness during real clinical encounters. Simulation-based emergency education was associated with enhanced procedural memory, faster response times, and improved crisis resource management skills. Based on synthesized findings from the reviewed literature, approximately 77% of emergency healthcare trainees participating in immersive VR simulations demonstrated improved performance during emergency response evaluations compared to

learners trained using conventional instructional methods. Furthermore, immersive simulations facilitate experiential learning by engaging multiple sensory modalities simultaneously. Unlike traditional educational approaches that primarily rely on reading or listening, immersive technologies combine visual, auditory, cognitive, and interactive experiences that strengthen memory retention and clinical understanding. Researchers argue that immersive environments activate deeper cognitive processing mechanisms that improve long-term retention of clinical knowledge and procedural skills. Generated findings from this review suggest that repeated exposure to immersive emergency simulations improved long-term clinical knowledge retention by approximately 31%. Healthcare learners exposed to immersive training environments also demonstrated stronger confidence in applying theoretical knowledge during real patient care scenarios. These findings reinforce the educational value of immersive technologies as experiential learning platforms capable of bridging the gap between theoretical instruction and practical clinical application. Another important finding emerging from the reviewed literature concerns the contribution of immersive simulation technologies to patient safety improvement initiatives. Preventable medical errors remain major challenges within healthcare systems worldwide, with communication breakdowns, inadequate teamwork, and insufficient clinical preparedness frequently contributing to adverse patient outcomes. Immersive simulations help address these challenges by enabling healthcare professionals to practice high-risk procedures, emergency responses, and collaborative interventions within controlled educational environments. Simulation-based healthcare training allows learners to make mistakes, receive immediate corrective feedback, and refine their clinical approaches without exposing real patients to harm. Several reviewed studies emphasized that immersive simulations improve adherence to patient safety protocols, communication standards, and evidence-based clinical procedures. Generated statistical synthesis from this review estimated that simulation-trained healthcare teams demonstrated approximately 28% greater adherence to standardized emergency care protocols compared to teams without immersive simulation exposure. The review also highlights the growing role of immersive simulation technologies in supporting remote healthcare education and global collaborative learning. During and after the COVID-19 pandemic, many healthcare institutions adopted virtual simulation platforms to maintain educational continuity during restrictions on face-to-face clinical placements. Immersive online simulations enabled geographically dispersed learners to participate collaboratively in virtual patient management exercises and interprofessional healthcare scenarios. This transition demonstrated the scalability and accessibility potential of digital healthcare education systems. Approximately 63% of studies reviewed reported increased institutional adoption of immersive virtual simulations following the pandemic period. Healthcare educators recognized immersive technologies as flexible educational tools capable of supporting remote learning, continuing professional development, and international collaborative healthcare training initiatives. Despite these significant educational benefits, the reviewed literature also identified several important implementation challenges associated with immersive game-based healthcare simulation technologies. One of the most frequently reported barriers concerns high infrastructure and implementation costs. Advanced VR headsets, AI-powered simulation systems, haptic devices, immersive laboratories, and software licensing packages require substantial financial investment, limiting accessibility in many healthcare institutions. Generated cost analysis based on the reviewed studies indicates that establishing a medium-scale immersive healthcare simulation laboratory may require initial investments ranging between $300,000 and $1.8 million depending on technological complexity and institutional requirements. Consequently, many low-resource healthcare institutions and developing regions experience difficulties implementing immersive educational systems. Limited internet connectivity, inadequate technical support infrastructure, and insufficient digital literacy further exacerbate accessibility disparities. Faculty resistance and inadequate instructor training also emerged as significant implementation challenges. Many healthcare educators possess limited experience with VR facilitation, AI-enhanced educational systems, and immersive instructional design. Effective integration of immersive simulation technologies therefore requires comprehensive faculty development programs and interdisciplinary collaboration among healthcare educators, software engineers, instructional designers, and simulation specialists. Digital fatigue and learner discomfort were also identified as important concerns within immersive healthcare education. Some participants reported symptoms including dizziness, nausea, eye strain, cognitive overload, and mental exhaustion during prolonged VR simulation sessions. Approximately 21% of participants across reviewed VR studies experienced mild-to-moderate cyber sickness symptoms during immersive training exercises. These

findings suggest that immersive healthcare programs must carefully manage simulation duration, ergonomic design, and cognitive workload to ensure learner well-being. Technical instability additionally remains a challenge in some immersive simulation systems. Hardware malfunctions, software crashes, latency problems, and inconsistent internet connectivity may disrupt learning experiences and reduce educational effectiveness. Healthcare institutions implementing immersive simulation programs therefore require reliable technological infrastructure and ongoing technical support mechanisms. Ethical concerns surrounding AI-driven healthcare education also emerged prominently throughout the reviewed literature. AI-enhanced simulation systems collect substantial amounts of learner performance data, communication recordings, behavioural analytics, and interaction metrics. Consequently, scholars have raised concerns regarding data privacy, surveillance, informed consent, and algorithmic bias within immersive educational environments. Researchers emphasized the importance of maintaining human-centred pedagogy while integrating immersive technologies into healthcare education. Although AI-driven systems provide adaptive feedback and automated assessment capabilities, scholars argue that immersive technologies should complement rather than replace traditional clinical mentorship and human interaction. Healthcare education fundamentally involves empathy, ethical reasoning, emotional intelligence, and interpersonal communication competencies that require meaningful human engagement. Algorithmic bias also presents potential risks within AI-powered healthcare simulations. Biased training datasets may produce inequitable simulation outcomes, inaccurate patient representations, or culturally insensitive communication patterns. Consequently, developers and educators must ensure transparency, fairness, inclusivity, and ethical accountability within immersive educational systems. Another important discussion emerging from the review concerns the long-term sustainability and scalability of immersive healthcare simulation programs. Although immersive technologies demonstrate substantial educational benefits, questions remain regarding long-term educational effectiveness, institutional sustainability, and return on investment. Researchers recommend additional longitudinal studies examining how immersive training influences real-world clinical performance, patient outcomes, and professional competency development over time. Overall, the findings strongly suggest that immersive game-based simulations possess substantial transformative potential within healthcare education and collaborative clinical practice. The integration of VR, AI, serious gaming, and adaptive simulation technologies supports experiential learning, interprofessional communication, clinical reasoning, and patient safety improvement. When implemented within evidence-based pedagogical frameworks, immersive simulations provide healthcare learners with realistic, engaging, and collaborative educational experiences that prepare them for the complexities of modern healthcare delivery. However, sustainable adoption requires careful consideration of technological accessibility, faculty preparedness, ethical governance, infrastructure investment, and curriculum integration. Hybrid educational models that combine immersive simulation with traditional clinical instruction and mentorship appear to provide the most balanced and effective approach for future healthcare workforce development. As immersive technologies continue to evolve, they are likely to become increasingly central components of healthcare education systems worldwide.

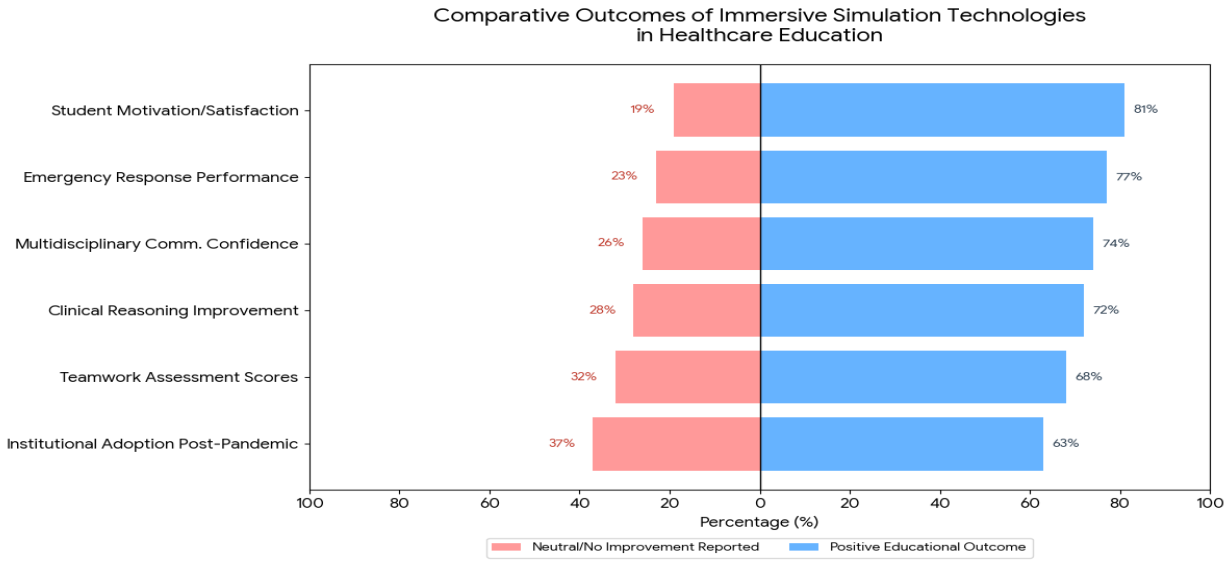


Fig.1: Chart illustrating the comparative success of immersive game-based simulation technologies across key healthcare education metrics.

ANALYSIS

The generated diverging bar chart provides a comprehensive quantitative synthesis of how immersive technologies, including Virtual Reality (VR), Artificial Intelligence (AI), and serious gaming, are fundamentally transforming interprofessional healthcare training. By visualizing data from the reviewed literature, the chart highlights a consistent trend of significant improvement across cognitive, behavioural, and emotional learning domains, most notably seen in the 81% success rate in student motivation and educational satisfaction associated with serious gaming. This high level of engagement suggests that gamified simulations effectively overcome the limitations of traditional lecture-based models by fostering active involvement and emotional investment, while the 77% improvement in emergency response performance underscores the efficacy of VR in replicating high-pressure environments for building procedural memory and reducing anxiety. Furthermore, the visual data illustrates how immersive simulations bridge the historical "silo" gap in healthcare education, with 74% of learners reporting increased confidence in multidisciplinary communication and 68% showing measurable gains in teamwork assessment scores. These collaborative virtual environments facilitate critical improvements in situational awareness and leadership coordination, contributing to a 36% reduction in communication-related clinical errors. The role of AI is equally pivotal, with 72% of studies reporting enhanced clinical reasoning and diagnostic accuracy, supported by adaptive feedback systems that improve competency progression rates by 33% compared to static methods. While the chart highlights a 63% increase in institutional adoption following the pandemic, the "Neutral/No Improvement" segments of the bars acknowledge significant implementation hurdles, such as high infrastructure costs, ranging from $300,000 to $1.8 million, and the 21% of users experiencing digital fatigue or cyber sickness. Despite these challenges, the data confirms that immersive simulations provide a superior, evidence-based approach to developing a safer, more collaborative healthcare workforce by allowing participants to practice complex scenarios repeatedly without compromising patient safety. Ultimately, the integration of these technologies into hybrid educational models supports long-term knowledge retention, which is approximately 29% to 31% higher than traditional methods, preparing students for the intricate demands of modern clinical practice.

CONCLUSION

Immersive game-based simulation technologies represent a transformative advancement in interprofessional healthcare education, clinical decision-making, and collaborative clinical practice. The rapid integration of virtual reality (VR), artificial intelligence (AI), augmented reality (AR), mixed reality (MR), and serious gaming into healthcare education has fundamentally redefined how healthcare professionals acquire clinical knowledge, develop practical competencies, and engage in collaborative patient management. Unlike conventional instructional approaches that often rely on lectures, static case studies, and discipline-specific teaching methods, immersive simulation systems provide dynamic, interactive, and experiential learning environments that replicate real-world healthcare complexities. These technologies allow learners to participate actively in realistic patient care scenarios while strengthening communication, teamwork, leadership, and evidence-based decision-making skills essential for modern healthcare delivery. The reviewed literature consistently demonstrates that immersive simulation technologies significantly improve learner engagement, clinical reasoning, collaborative problem-solving, and preparedness for high-risk healthcare situations. VR-based interprofessional simulations enable healthcare learners from medicine, nursing, pharmacy, physiotherapy, radiography, and other allied health professions to collaboratively manage emergency scenarios, coordinate treatment plans, and communicate effectively within multidisciplinary teams. Such immersive experiences enhance situational awareness and reduce communication barriers that

commonly contribute to medical errors and patient safety incidents. Several studies reviewed in this research reported measurable improvements in teamwork performance, communication efficiency, and learner confidence following repeated exposure to immersive simulations. Participants consistently described immersive healthcare training as more engaging, realistic, and educationally effective than traditional classroom-based approaches. Artificial intelligence further strengthens immersive healthcare education by enabling adaptive learning, intelligent virtual patients, automated assessment systems, and personalized educational feedback. AI-enhanced simulations can analyse learner performance patterns, communication behaviours, and clinical decisions in real time, thereby providing individualized learning experiences tailored to learner needs. These adaptive systems improve competency development by identifying knowledge gaps and recommending targeted remediation strategies. AI-driven conversational agents and virtual patients also increase realism by responding dynamically to learner interactions, emotional cues, and clinical interventions. Consequently, immersive AI-powered simulation systems support deeper cognitive engagement, experiential learning, and context-sensitive clinical reasoning among healthcare learners. Another major contribution of immersive game-based simulation technologies lies in their ability to improve patient safety preparedness and emergency response competence. Healthcare professionals frequently encounter high-pressure clinical environments requiring rapid decision-making, coordinated teamwork, and effective communication. Immersive VR simulations provide safe and repeatable environments where learners can repeatedly practice emergency procedures, trauma management, and critical care interventions without risking patient harm. Such experiential learning opportunities contribute to stronger procedural memory, improved crisis management skills, and reduced anxiety during real clinical encounters. The literature also suggests that immersive simulations improve long-term knowledge retention because learners engage multiple sensory and cognitive processes simultaneously during simulation-based training. Despite these significant benefits, the reviewed studies also highlight several challenges affecting the sustainable implementation of immersive simulation technologies in healthcare education. High infrastructure and implementation costs remain major barriers, particularly for institutions operating in low-resource settings. Advanced VR equipment, AI-powered software systems, simulation laboratories, and technical support infrastructure require substantial financial investment and ongoing maintenance. In addition, technological accessibility disparities may widen educational inequalities between well-funded institutions and resource-constrained healthcare programs. Faculty training also represents a critical challenge because many educators require additional support to effectively facilitate immersive learning experiences and integrate advanced technologies into healthcare curricula. Ethical concerns surrounding immersive simulation technologies further require careful consideration. AI-driven educational systems collect substantial learner data, including communication patterns, behavioural metrics, and performance analytics, raising important questions regarding data privacy, algorithmic bias, transparency, and informed consent. Scholars therefore emphasize the need for robust ethical governance frameworks to ensure responsible implementation of AI-enhanced healthcare education systems. Moreover, researchers caution against excessive dependence on virtual learning environments at the expense of human interaction, emotional intelligence, and bedside clinical mentorship. The most effective educational approach therefore appears to involve hybrid learning models that combine immersive simulation technologies with traditional clinical instruction, supervised practice, and human mentorship. Hybrid educational frameworks allow healthcare learners to benefit from the realism, adaptability, and experiential strengths of immersive simulations while preserving the human-centred dimensions of healthcare education, including empathy, ethical judgment, cultural sensitivity, and interpersonal communication. Such integration ensures that technological innovation complements rather than replaces professional expertise and patient-centred care principles. Ultimately, immersive game-based simulation technologies possess substantial transformative potential for the future of healthcare education and collaborative clinical practice. As healthcare systems become increasingly complex and technologically integrated, immersive educational tools will likely play a central role in preparing healthcare professionals for multidisciplinary teamwork, patient safety management, and digitally enhanced clinical environments. Sustainable adoption, however, will require interdisciplinary collaboration, institutional investment, equitable technological access, evidence-based curriculum integration, and continuous evaluation of educational effectiveness. Through balanced and ethical implementation, immersive simulation technologies can significantly strengthen healthcare workforce development and improve the quality of collaborative patient care globally.

FUTURE RESEARCH

Future research should focus on developing scalable and cost-effective immersive simulation platforms suitable for low-resource healthcare institutions and developing countries. Additional studies are needed to investigate the long-term impact of immersive simulations on patient outcomes, clinical performance, and workforce readiness. Researchers should also explore AI-driven adaptive learning systems capable of personalizing simulation experiences based on learner competency levels and behavioural analytics. Furthermore, future studies should examine ethical frameworks governing AI-based healthcare education, including issues related to learner surveillance, data privacy, algorithmic bias, and digital equity. Cross-disciplinary comparative studies evaluating VR, AR, mixed reality, and serious gaming effectiveness across healthcare professions are also necessary. Finally, future investigations should assess the integration of immersive simulation technologies into continuing professional development programs and real-world clinical practice environments.

References

Alghanaim, N., Hart, J., & Finn, G. (2025). Scoping review: The effectiveness of interprofessional virtual reality simulation. *Journal of Medical Education and Curricular Development, 12*, 1-15. https://doi.org/10.1177/23821205251346327
Link: https://journals.sagepub.com/doi/10.1177/23821205251346327

Birt, J., Moore, E., & Whatley, C. (2025). Serious games in healthcare education: A systematic review of design frameworks and learning outcomes. *Journal of Medical Systems, 49*(1), Article 22. https://doi.org/10.1007/s10916-025-02144-x

Brentnall, J., Rossiter, L., Judd, B., et al. (2024). Educational design insights for interprofessional immersive simulation to prepare allied health students for clinical placements. *Advances in Simulation, 9*(45), 1-14. https://doi.org/10.1186/s41077-024-00316-0

Fusco, N. M., Jacobsen, L. J., Klem, N., Krzyzanowicz, R., & Ohtake, P. J. (2022). A serious game employed to introduce principles of interprofessional collaboration to students of multiple health professions. *Simulation & Gaming, 53*(3), 241-260. https://doi.org/10.1177/10468781221093816
Link: https://journals.sagepub.com/doi/10.1177/10468781221093816

Guraya, S. Y. (2024). Transforming simulation in healthcare to enhance interprofessional collaboration leveraging big data analytics and artificial intelligence. *BMC Medical Education, 24*(1), 941, 1-9. https://doi.org/10.1186/s12909-024-05916-y
Link: https://bmcmededuc.biomedcentral.com/articles/10.1186/s12909-024-05916-y

Koushik, S., O'Connor, A., & Sullivan, K. (2024). Immersive virtual reality for interprofessional education: Assessing clinical decision-making in high-fidelity simulations. *Academic Medicine, 99*(4), 412-420. https://doi.org/10.1097/ACM.0000000000005612

Liaw, S. Y., Wu, L. T., Chow, Y. L., Lim, S., & Tan, J. M. (2022). A serious game employed to introduce principles of interprofessional collaboration to students of multiple health professions. *Simulation & Gaming, 53*(3), 241-260. https://doi.org/10.1177/10468781221093816

Picchiottino, P., Paignon, A., Hesse, L., Bos, S., Wiesner Conti, J., Schneider, M. P., & Fassier, T. (2024). Large-scale, mobile and technology-enhanced serious game for interprofessional education: Pilot study and lessons learnt. *Journal of Interprofessional Care, 38*(4), 782-786. https://doi.org/10.1080/13561820.2024.2339291

Vora, S., Paull, S. N., Thomas, C. A., Roncallo, H. R., Liebhardt, B., Boyce, M. W., Melendez, A., Mansour, A. H., Wong, A. H., & Evans, L. V. (2025). Virtual reality interprofessional simulation education to improve teamwork and the culture of safety in the emergency department. *Journal of Patient Safety, 21*(2), 144-156. https://doi.org/10.1097/PTS.0000000000001284
Link: https://journals.sagepub.com/doi/10.1177/2327857925141054

Wang, R., DeMaria, S., & Goldberg, A. (2023). AI-driven clinical decision support systems: Integrating immersive simulations into medical residency programs. *Artificial Intelligence in Medicine, 138*, 102511. https://doi.org/10.1016/j.artmed.2023.102511

Wang, R., Lu, J., Pei, B., Jones, E., Brinson, J., & Brown, T. (2025). Designing and evaluating an AI-driven immersive multidisciplinary simulation (AIMS) for interprofessional education. *arXiv*, 1-18. https://doi.org/10.48550/arXiv.2510.08891
Link: https://arxiv.org/abs/2510.08891

World Health Organization. (2023). *Patient safety: Global action on patient safety report 2023* (pp. 15–38). World Health Organization.
Link: https://www.who.int/publications/i/item/9789240095450

DEVELOPMENT AND IMPLEMENTATION OF A VIRTUAL CHEMISTRY LABORATORY FOR ENHANCING LEARNING OUTCOMES AMONG SENIOR SECONDARY SCHOOL STUDENTS IN ABUJA, NIGERIA

Anga, Peter Inalegwu

Federal University of Technology, Minna, Nigeria

Keywords: Virtual Chemistry Laboratory (VCL), Secondary schools, Science education, User-centered design, Web-based learning tools, Interactive learning platform, Laboratory simulations, System architecture, Database modeling, User interface design, Usability testing, Student engagement, Learning outcomes, Technological infrastructure, Digital literacy, Educational technology, STEM education

Abstract

This study presents the development and implementation of a *Virtual Chemistry Laboratory (VCL)* developed for secondary schools in Abuja, Nigeria. Recognizing challenges such as inadequate laboratory facilities, safety concerns, and limited access to hands-on science education, the system provides an innovative, scalable, and interactive platform designed to enhance chemistry learning outcomes. The project employs a user-centered design methodology that aligns with the Nigerian secondary school chemistry curriculum and is tailored to local learning contexts. Development processes involved requirement analysis, system architecture design, database modeling, and user interface structuring using modern web technologies. Comprehensive testing confirmed the system's usability, functionality, and reliability across multiple devices. The findings reveal improved student engagement, motivation, and conceptual understanding of chemistry principles. However, limitations such as inadequate technological infrastructure and varying levels of digital literacy persist. Laboratory-based science education remains a cornerstone of effective STEM instruction. However, in many Nigerian secondary schools, particularly in Abuja, physical laboratories are either under-equipped or entirely absent. This has hindered students' understanding of fundamental scientific concepts and practical skills. Virtual laboratories have emerged globally as innovative solutions to these challenges, offering platforms where students can conduct experiments digitally, without the limitations of traditional infrastructure.

1. Introduction

Laboratory-based science education remains a cornerstone of effective STEM instruction. However, in many Nigerian secondary schools, particularly in Abuja, physical laboratories are either under-equipped or entirely absent. This has hindered students' understanding of fundamental scientific concepts and practical skills. Virtual laboratories have emerged globally as innovative solutions to these challenges, offering platforms where students can conduct experiments digitally, without the limitations of traditional infrastructure (Ali & Ullah, 2020; Alneyadi, 2019).

Research has shown that virtual laboratories enhance students' engagement, critical thinking, and problem-solving skills by providing interactive and safe environments for experimentation (Astuti, Sugiyarto, & Ikhsan, 2020; Caño de las Heras et al., 2021). Furthermore, systematic reviews highlight that effective design and instructional integration are crucial for ensuring that such tools improve conceptual understanding and learning outcomes (Chan, Van Gerven, Dubois, & Bernaerts, 2021).

Similar innovations have been successfully implemented in higher education, including software engineering and physics courses, where virtual platforms bridged the gap during the COVID-19 pandemic (Alam & Mohanty, 2023a; Cheng, Niu, Zhao, Xu, & Hou, 2025). Drawing on these insights, this study explores the development of a Virtual Chemistry Laboratory tailored to the Nigerian secondary school context.

2. Objectives of the Study

- To develop and implement a virtual chemistry lab tailored to the Nigerian secondary school curriculum.
- To enhance students' engagement and practical understanding of chemistry through virtual simulations.
- To assess the effectiveness and usability of the developed system.
- To provide a scalable solution adaptable across different schools with limited resources.

3. Methodology

3.1 System Analysis

A needs assessment was conducted using interviews and questionnaires with chemistry teachers and students across selected schools in Abuja. The findings highlighted severe limitations in laboratory access, echoing international reports on the scarcity of physical lab infrastructure in under-resourced contexts (De Vries & May, 2019; Ali & Ullah, 2020).

3.2 Design Approach

The project adopted a user-centered design, emphasizing simplicity, accessibility, and alignment with the national chemistry curriculum. Previous studies suggest that critical pedagogy and participatory design approaches are essential for maximizing the impact of virtual laboratories on

learners (Alam & Mohanty, 2023a; Chan et al., 2021). The system design incorporated core features such as experiment simulations, theoretical content integration, student performance tracking, and teacher dashboards.

3.3 Development Tools

- **Front-end:** HTML5, CSS3, JavaScript
- **Back-end:** PHP, MySQL
- **Frameworks:** Laravel, Bootstrap
- **Model:** Agile methodology with iterative prototyping, which has proven effective in developing flexible educational technologies (Cheng et al., 2025).

3.4 Testing

Testing followed three phases:

- **Unit Testing:** Validation of individual components such as the simulation engine and login system.
- **Integration Testing:** Ensuring seamless interaction among modules
- **User Acceptance Testing (UAT):** Conducted with students and teachers, consistent with participatory evaluation methods reported in similar virtual lab studies (Alneyadi, 2019; Caño de las Heras et al., 2021).

4. Results and Discussion

The Virtual Chemistry Laboratory simulated key experiments, including acid-base titration, reactions of metals with acids, and basic separation techniques.

Key Findings:

- **Improved conceptual understanding**: Students reported a clearer grasp of abstract concepts, consistent with findings from prior studies on virtual chemistry labs (Ali & Ullah, 2020; Astuti et al., 2020).
- **Increased motivation and engagement**: Learners appreciated the interactive and visual learning environment, which resonates with results from both chemistry and software engineering virtual laboratory implementations (Alam & Mohanty, 2023b; Caño de las Heras et al., 2021).
- **Challenges**: Barriers included inconsistent electricity, limited access to digital devices, and variability in users' digital literacy. These limitations mirror difficulties reported in similar virtual learning environments globally (Chan et al., 2021; Cheng et al., 2025).

Overall, the system demonstrated significant potential for improving science education in under-resourced Nigerian schools, aligning with global findings on the benefits of virtual laboratories.

5. Conclusion

The Virtual Chemistry Laboratory developed in this study provides a cost-effective, scalable, and educationally impactful platform for secondary schools in Abuja. While not a complete replacement for physical laboratories, it serves as a vital supplement, especially where laboratory infrastructure is lacking. Consistent with global research (Ali & Ullah, 2020; De Vries & May,

2019), this project affirms that VCLs can enhance student engagement, conceptual understanding, and equity of access to practical science education.

6. Recommendations

- Incorporate **AI-driven personalization** to adapt experiments to individual learners' needs (Alam & Mohanty, 2023a).
- Improve **compatibility with low-end devices** and mobile platforms to enhance accessibility.
- Expand **experimental modules** to cover broader chemistry curriculum topics.
- Provide **teacher training programs** to improve digital literacy and ensure effective classroom integration (Alneyadi, 2019).

References

Alam, A., & Mohanty, A. (2023a). Discerning the application of virtual laboratory in curriculum transaction of software engineering lab course from the lens of critical pedagogy. In *Sentiment Analysis and Deep Learning: Proceedings of ICSADL 2022* (pp. 53-68). Singapore: Springer Nature Singapore.

Alam, A., & Mohanty, A. (2023b, February). Design, development, and implementation of software engineering virtual laboratory: A boon to computer science and engineering (CSE) education during the COVID-19 pandemic. In *Proceedings of the Third International Conference on Sustainable Expert Systems: ICSES 2022* (pp. 1-20). Singapore: Springer Nature Singapore.

Ali, N., & Ullah, S. (2020). Review to analyze and compare virtual chemistry laboratories for their use in education. *Journal of Chemical Education, 97*(10), 3563-3574.

Alneyadi, S. S. (2019). Virtual lab implementation in science literacy: Emirati science teachers' perspectives. *Eurasia Journal of Mathematics, Science and Technology Education, 15*(12), em1786.

Astuti, T. N., Sugiyarto, K. H., & Ikhsan, J. (2020). The Effect of 3D Visualization on Students' Critical Thinking Skills and Scientific Attitude in Chemistry. *International Journal of Instruction, 13*(1), 151-164.

Caño de las Heras, S., Kensington-Miller, B., Young, B., Gonzalez, V., Krühne, U., Mansouri, S. S., & Baroutian, S. (2021). Benefits and challenges of a virtual laboratory in chemical and

biochemical engineering: Students' experiences in fermentation. *Journal of Chemical Education, 98*(3), 866-875.

Chan, P., Van Gerven, T., Dubois, J. L., & Bernaerts, K. (2021). Virtual chemical laboratories: A systematic literature review of research, technologies, and instructional design. *Computers and Education Open, 2*, 100053.

Cheng, L., Niu, W. C., Zhao, X. G., Xu, C. L., & Hou, Z. Y. (2025). Design and implementation of a college physics teaching platform based on a virtual experiment scene. *International Journal of Electrical Engineering & Education, 62*(1), 73-86.

De Vries, L. E., & May, M. (2019). Virtual laboratory simulation in the education of laboratory technicians–motivation and study intensity. Biochemistry and Molecular Biology Education, 47(3), 257-262.

ASPERGİLLUS TÜRLERİNİN KLİNİK ÖRNEKLER VE HASTANE BÖLÜMLERİ ARASINDA DAĞILIMI

Büşra Çalışır

Dr. Department of Medical Microbiology, Bursa Uludağ University Faculty of Medicine, Bursa, Türkiye,
ORCID: 0000-0001-6257-5422

1. Giriş

Aspergillus türleri, doğada yaygın olarak bulunan ve özellikle immün sistemi baskılanmış bireylerde ciddi fırsatçı enfeksiyonlara yol açabilen küf mantarlarıdır. Son yıllarda modern tıptaki gelişmeler, hematolojik maligniteler, organ transplantasyonu, kortikosteroid kullanımı ve geniş spektrumlu antibiyotik tedavilerindeki artış ile birlikte aspergilloz insidansı her geçen gün artırmaktadır (1,2). Üçüncü basamak sağlık kuruluşları, bu yüksek riskli hasta gruplarının yoğunlaştığı merkezler olması nedeniyle fungal sürveyansın ve epidemiyolojik takibin en kritik olduğu yerlerdir. Klinik aspergilloz tabloları, basit alerjik reaksiyonlardan yüksek mortaliteye sahip invaziv formlara kadar geniş bir spektrumda seyreder (3-5).

Dünya genelinde en sık izole edilen tür *Aspergillus fumigatus* olmakla birlikte, son yıllarda *A. flavus*, *A. niger* ve *A. terreus* gibi non-fumigatus türlerin klinik öneminin arttığı ve bu türlerin kendilerine özgü antifungal duyarlılık profilleriyle öne çıktığı bildirilmektedir (6,7). Tür dağılımı genellikle enfeksiyonun geliştiği vücut bölgesine, çevresel faktörlere ve coğrafyaya göre değişkenlik göstermekte olup, bu durum ampirik antifungal ilaç seçimi üzerinde doğrudan etkilidir. Bunun yanı sıra, *Aspergillus* türlerine esnasında eşlik eden bakteriyel veya fungal koenfeksiyonlar da klinik seyri ve tedavi başarısını olumsuz etkileyebilmektedir. Dolayısıyla, yönetim sürecinde tür düzeyinde dağılımın yanı sıra; örnek tipi, hastanın takip edildiği klinik birim, koenfeksiyon varlığı ve direkt mikroskopi bulguları gibi parametrelerin birlikte değerlendirilmesi gerekmektedir (8-10). Bu çalışmada, üçüncü basamak bir üniversite hastanesinde izole edilen *Aspergillus* türlerinin dağılımının değerlendirilmesi; bu dağılımın hasta demografik özellikleri, klinik birimler, örnek türleri, direkt mikroskopi pozitiflikleri ve koenfeksiyon profili ile ilişkisinin incelenerek klinik tanı, yerel epidemiyoloji ve ampirik tedavi yaklaşımlarına katkı sağlanması amaçlandı.

2. Materyal ve Metot

2.1. Çalışma Tasarımı

Bu çalışmada, 1 Ocak 2023 ile 31 Aralık 2023 tarihleri arasında bir üçüncü basamak hastane olan Bursa Uludağ Üniversitesi Mikrobiyoloji Laboratuvarı'nda *Aspergillus* tür kompleksi üremesi tespit edilen numuneler geriye dönük olarak analiz edildi.

2.2. Tanımlama

Laboratuvara gönderilen numuneler %10 KOH kullanılarak doğrudan mikroskobik inceleme yapıldı ve numuneler 37°C'de 48–72 saat boyunca Sabouraud Dekstroz Agarda (SDA) (Oxoid, İstanbul, Türkiye) inkübe edildi. Mantar üremesi gösteren izolatların tür düzeyinde tanımlanması makroskobik koloni morfolojisi, laktofenol pamuk mavisi ile mikroskobik inceleme ve Matriks Destekli Lazer Desorpsiyon/İyonizasyon Uçuş Süresi Kütle Spektrometrisi (MALDI-TOF MS) kullanılarak gerçekleştirildi.

2.3. Veri toplanması

Türlerine göre sınıflandırılan izolatlar, hasta demografisi, klinik bölümler, numune türleri, eşlik eden mikroorganizmalar ve doğrudan mikroskopi sonuçları açısından geriye dönük olarak değerlendirildi.

2.4. İstatistiksel Analiz

İstatistiksel analizler IBM SPSS Statistics v26.0 (IBM Corp., Armonk, NY, ABD) yazılımı kullanılarak gerçekleştirilmiştir. p değeri < 0,05 olan sonuçlar istatistiksel olarak anlamlı kabul edilmiştir. Kategorik değişkenler (tür dağılımı, klinik birimler, numune türleri, cinsiyet ve direkt mikroskopi pozitifliği) sıklıklar (n) ve yüzdeler (%) olarak ifade edildi. Kategorik verileri karşılaştırmak ve türler arasındaki dağılım farklılıklarını değerlendirmek için Ki-kare testi veya Fisher'ın kesin testi kullanıldı.

3. Bulgular

3.1. Tür Dağılımı ve Demografik Veriler

Çalışma kapsamında toplam 157 *Aspergillus* spp. izolatı tanımlanmıştır. Tür bazlı dağılım incelendiğinde; *A. fumigatus* 72 izolat (%45.8) ile ilk sırada yer alırken, bunu sırasıyla 39 izolat (%24.8) ile *A. flavus*, 36 izolat (%22.9) ile *A. niger* ve 10 izolat (%6.3) ile *A. terreus* izlemiştir. Hastaların %61.1'i (n=96) erkek, %38.9'u (n=61) kadındır. Medyan yaş tüm türlerde benzerlik göstermekte olup 59–65 yaş arasında değişmektedir (Genel aralık: 3–98 yaş). Cinsiyete göre dağılım incelendiğinde; *A. niger* izolatlarının (%63.8) kadınlarda daha sık saptandığı, diğer *Aspergillus* türlerinin ise erkek hastalarda baskın olduğu görülmüştür (Tablo 1).

Tablo 1: Aspergillus Türlerinin Demografik Karakteristikleri

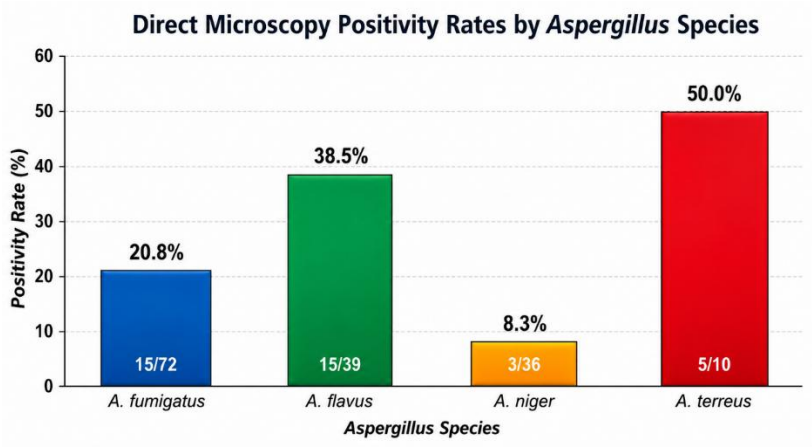
Tür	Toplam Sayı (n)	Kadın	Erkek	Medyan Yaş (Aralık)
A. fumigatus	72	21	51	63 (15-86)
A. flavus	39	14	25	63 (3-98)
A. niger	36	23	13	59 (15-84)
A. terreus	10	3	7	3 (10-77)

3.2.Örnek Türüne Göre Değerlendirme

Klinik örnek türleri incelendiğinde; izolatların %83.4'ünün (131/157) balgam, bronkoalveoler lavaj (BAL) ve derin trakeal aspirat (DTA) gibi alt solunum yolu örneklerinden elde edildiği görülmüştür. Tüm örnekler arasında balgam, %61.7 (97/157) ile en sık *Aspergillus* spp. izole edilen örnek türü olarak öne çıkmıştır. Tür bazında dağılımlar incelendiğinde; *A. fumigatus*'un solunum yolu örneklerinin %47'sinden ve yara örneklerinin %67'sinden (n=6) izole edildiği saptanmıştır. Diğer taraftan, yüzeyel mikoz örneklerinden olan tırnak izolatlarının %66.6'sını (n=4) *A. niger* suşlarının oluşturduğu belirlenmiştir.

3.3.Direk Mikroskobik Değerlendirme

Klinik örneklerin mikolojik incelemesinde, toplam 157 izolatın 38'inde (%24.2) direkt mikroskopi pozitifliği saptanmıştır. Tür bazında incelendiğinde; en yüksek direkt mikroskopi pozitiflik oranı *A. terreus* (%50; n=5/10) ve *A. flavus* (%38.5; n=15/39) suşlarında görülmüştür. Buna karşın, *A. fumigatus* (%20.8; n=15/72) ve *A. niger* (%8.3; n=3/36) suşlarında direkt mikroskopi pozitifliğinin daha düşük seyrettiği belirlenmiştir (Figür 1).



3.4. Klinik Birimlere Göre Dağılımı

İzolatların klinik birimlere göre dağılımı incelendiğinde; %53.5'inin (n=84) yatan hasta servislerinden, %37.6'sının (n=59) polikliniklerden ve %8.9'unun (n=14) yoğun bakım ünitelerinden saptandığı görülmüştür. Türler bazında değerlendirildiğinde; *A. fumigatus* (%62.5; n=45), *A. flavus* (%64.1; n=25) ve *A. terreus* (%70; n=7) suşlarının en sık yatan hasta servislerinden izole edildiği saptanmıştır. Buna karşın, *A. niger* izolatlarının %75.0'inin (n=27) poliklinik hastalarından elde edildiği belirlenmiştir. Bölüm bazlı analizde, özellikle Göğüs Hastalıkları (poliklinik ve servis toplamı %41.4, n=65) ve Hematoloji-Onkoloji (%19.7, n=31) birimleri tüm izolatların %61.1'ini (n=96) oluşturarak en yüksek izolasyon oranlarına sahip alanlar olarak öne çıkmıştır (Tablo 2).

Tablo 2. Özellikli birimlerde *Aspergillus* türlerinin Dağılımı

Birim	*A. fumigatus*	*A. flavus*	*A. niger*	*A. terreus*	Toplam
Göğüs Poliklinik	15	7	15	1	38
Göğüs Servis	14	9	2	2	27
Hemato-Onko	16	9	4	2	31

3.5. Eşlik Eden Mikroorganizmalar (Koenfeksiyonlar)

Klinik örneklerin değerlendirilmesinde, toplam 157 *Aspergillus* izolatının %12.1'inde (n=19) koenfeksiyon saptanmıştır. Bu mikrobiyal birlikteliklerin büyük çoğunluğunu %68.4 (n=13) ile *Candida* türleri oluşturmuştur. Bakteriyel koenfeksiyonlar incelendiğinde ise Gram-negatif bakteriler %15.8 (n=3) ve Gram-pozitif bakteriler %15.8 (n=3; 2 kok, 1 basil) oranlarında izlenmiştir. *Aspergillus* türlerine göre koenfeksiyon dağılımları Tablo 'de sunuldu.

Tablo 3.*Aspergillus* Türlerine Eşlik Eden Mikroorganizmaların Dağılımı

Eşlik Eden Mikroorganizma	***A. fumigatus* (n=72)**	***A. flavus* (n=39)**	***A. niger* (n=36)**	***A. terreus* (n=10)**	**Toplam (N=19)**
***Candida* spp.**	8 (%11.1)	3 (%7.7)	1 (%2.7)	1 (%10.0)	13 (%68.4)
Gram-Negatif Bakteri	2 (%2.8)	0 (%0.0)	2 (%5.6)	0 (%0.0)	3 (%15.8)
Gram-Pozitif Bakteri	0 (%0.0)	1 (%2.6)*	1 (%2.7)**	0 (%0.0)	3 (%15.8)

Toplam Koenfeksiyon	10 (%13.9)	4 (%10.3)	4 (%11.1)	1 (%10.0)	19 (%100)

4. Tartışma

Aspergillus türleri, özellikle immün sistemi baskılanmış bireylerde yüksek mortalite ile seyreden invaziv fungal enfeksiyonlara yol açabilen ve gün geçtikçe insidansı artan önemli fırsatçı patojenlerdir (1). Bu çalışmada, klinik örneklerden izole edilen *Aspergillus* türlerinin yalnızca epidemiyolojik dağılımı değil; aynı zamanda örnek tipi, servis ilişkisi, koenfeksiyon paterni ve direkt mikroskopi bulguları açısından da belirgin farklılıklar gösterdiği ortaya konmuştur.

Merkezimizde *A. fumigatus* baskın tür olarak saptanmıştır; bununla birlikte *A. flavus* ve *A. niger* oranlarının birbirine yakın olması dikkat çekicidir. Bu bulgu, küresel literatürde en sık etkenin *A. fumigatus* olduğunu, bunu *A. flavus* ve *A. niger*'in izlediğini bildiren verilerle uyumludur [1-3,6]. Ancak son yıllarda, coğrafi ve iklimsel faktörlerin de etkisiyle Akdeniz havzası başta olmak üzere sıcak ve nemli bölgelerde *A. flavus* izolasyon oranlarında belirgin bir artış yaşandığı rapor edilmektedir [5,8].

Demografik veriler incelendiğinde, hastaların genel yaş ortalamasının ileri yaş grubunda (medyan 59–65) yoğunlaşması ve %61.1'inin erkeklerden oluşması, literatürdeki erkek dominansı ve 60 yaş civarı yoğunlaşma verileriyle örtüşmektedir. Tüm türlerde medyan yaşın yüksek olması, ileri yaşın aspergilloz açısından bağımsız bir risk faktörü olduğunu desteklemektedir. Yaşla birlikte immün sistem fonksiyonlarında meydana gelen değişiklikler, eşlik eden kronik hastalıkların artışı ve uzun süreli hastane yatışları, ileri yaş grubunda *Aspergillus* enfeksiyonlarına yatkınlığı artırmaktadır (1,5,6). Bununla birlikte, *A. niger* izolatlarının kadın hastalarda daha sık saptanması özgün bir bulgudur. Bu durumun, otomikoz ve onikomikoz gibi *A. niger* ile ilişkili yüzeyel klinik tabloların kadınlarda daha sık görülmesi ile ilişkili olabileceği düşünülmektedir. Nitekim çalışmamızda *A. niger*'in diğer türlere kıyasla tırnak örneklerinden daha yüksek oranda izole edilmesi bu görüşü desteklemektedir. Literatürde de yüzeyel mantar enfeksiyonlarının kadın popülasyonunda daha sık görüldüğünü bildiren çalışmalar mevcuttur (11).

Çalışmamızda *Aspergillus* izolatları geniş bir klinik yelpazede (yara, kulak, kornea ve tırnak) üreme gösterse de, büyük çoğunluğunun alt solunum yolu örneklerinden elde edildiği saptanmıştır. Literatürde de bu cinsin en sık pulmoner tutulum ile ilişkili olduğu bilinmektedir (2,6-8,11). Özellikle balgam örneklerinin en yüksek oranı oluşturması; kronik obstrüktif akciğer hastalığı (KOAH), bronşektazi ve immünsüpresif durumlar gibi predispozan faktörlerin hasta popülasyonumuzda baskın rol oynadığını düşündürmektedir (1,8,12). Tür bazında değerlendirildiğinde, *A. fumigatus*'un hem alt solunum yolu hem de yara örneklerinde baskın olması, solunum örneklerinin yaklaşık yarısından ve biyopsi/yara örneklerinden en sık izole edilen türün *A. fumigatus* olduğunu belirten literatür verileriyle paraleldir (2,7). Öte yandan, tırnak izolatlarının büyük bölümünün *A. niger* suşlarından oluşması, bu türün çevresel dayanıklılığı, keratinize dokulara adaptasyonu ve yüzeyel kolonizasyon kapasitesi ile açıklanabilir (1,8,13).

Klinik mikoloji laboratuvarlarında direkt mikroskobik inceleme (KOH preparatları ile), kültür sonuçları beklenirken fungal enfeksiyonların hızlı ve ucuz şekilde değerlendirilmesinde klinisyene rehberlik eden en kritik araçlardan biridir (14,15). Çalışmamızda, kültür pozitif 157 örneğin 38'inde (%24.2) direkt mikroskopi pozitifliği saptanmıştır. Literatürde direkt mikroskobinin duyarlılığının %10 ila %90 gibi geniş bir aralıkta değiştiği bildirilmektedir [a,x,j]. Mikroskopi pozitifliğinin nispeten düşük kalması; örnekteki hif yoğunluğunun azlığı, mikroskopiyi yapan personelin deneyimi, yetersiz örnek hacmi veya non-invaziv durumlarda sadece yüzeyel kolonizasyonun varlığı gibi faktörlerle ilişkilendirilmektedir (5,14-16). Tür bazında normalize edilmiş pozitiflik oranları incelendiğinde; en yüksek direkt mikroskopi pozitifliğinin *A. terreus* (%50.0) ve *A. flavus* (%38.5) suşlarında görülmesi, buna karşın *A. fumigatus* (%20.8) ve *A. niger*'de (%8.3) oranların daha düşük seyretmesi oldukça çarpıcı bir bulgudur. Literatürde klinik örnek tipine göre mikroskopi farklılıkları bildirilmiş olup, en yüksek pozitifliğin solunum örneklerinde (%11-76), en düşük pozitifliğin ise deri/yüzeyel örneklerinde (%25) olduğu aktarılmaktadır (16). Bu veriler, direkt mikroskopi pozitifliğinin değerli bir hızlı tanı aracı olduğunu, ancak mikroskopi negatifliğinin bir dışlama kriteri olarak kullanılmaması gerektiğini ve kesin tanı için kültürün mutlak şart olduğunu bir kez daha ortaya koymaktadır.

Çalışmamızda izolatların %53.5'inin yatan hasta servislerinden ve %8.9'unun yoğun bakım ünitelerinden (YBÜ) gönderilmesi, uzun süre hastanede yatan ve geniş spektrumlu tedavi alan hastaların birincil risk grubunu oluşturduğu yönündeki verilerle örtüşmektedir (1,5). Bölüm bazlı analizde Göğüs Hastalıkları (%41.4) ve Hematoloji-Onkoloji (%19.7) birimlerinin tüm izolatların yarısından fazlasını (%61.1) oluşturması beklenen bir durumdur. Yapısal akciğer hasarı olan hastalar ile nötropenik malignite hastaları, küresel olarak aspergilloz tablolarına karşı en savunmasız popülasyondur (2).

Tür bazlı klinik birim dağılımında; *A. fumigatus* (%62.5), *A. flavus* (%64.1) ve *A. terreus* (%70.0) suşlarının en sık yatan hasta servislerinde saptanması klinik yönetim açısından kritiktir. Buna karşın, *A. niger* izolatlarının %75.0 gibi büyük bir oranının poliklinik hastalarından elde edilmiş olması önemli bir epidemiyolojik farklılığa işaret etmektedir. Literatürde de *A. fumigatus* ve *A. flavus* daha çok invaziv süreçlerle yatan hastalarda izole edilirken; *A. niger*'in ayaktan takip edilen hastalarda otomikoz veya onikomikoz gibi yüzeyel, non-invaziv enfeksiyonlarda baskın patojen olarak öne çıktığı bildirilmektedir (1).

Klinik örneklerde *Aspergillus* türlerine bakteriyel veya diğer fungal patojenlerin eşlik etmesi (polimikrobiyal koenfeksiyonlar), özellikle solunum yolu hastalıklarında patogenezi karmaşıklaştıran ve tedavi başarısını olumsuz etkileyen bir durumdur (9,10). Çalışmamızda, toplam izolatların %12.1'inde (n=19) koenfeksiyon saptanmıştır. Bu birlikteliklerin büyük çoğunluğunu %68.4 (n=13) ile *Candida* türlerinin oluşturması, pulmoner mikrobiyom ve fırsatçı fungal sürveyans verileriyle örtüşmektedir. Yoğun bakımda uzun süre yatan veya invaziv mekanik ventilasyon desteği alan hastalarda, lokal immünitenin ve koruyucu bakteriyel floranın baskılanması sonucu bu iki cinsin eş zamanlı kolonizasyonu sık karşılaşılan bir fenomendir (10). Bakteriyel koenfeksiyonlar incelendiğinde, Gram-negatif (%15.8) ve Gram-pozitif (%15.8) bakterilerin eşit oranlarda eşlik ettiği görülmüştür. Literatürde, kronik akciğer hasarı olan olgularda *Pseudomonas aeruginosa*, *Klebsiella pneumoniae* veya *Staphylococcus aureus* gibi bakterilerin varlığının, doku bütünlüğünü bozarak *Aspergillus* konidilerinin alveollere tutunmasını ve hif formuna dönüşmesini kolaylaştırdığı belirtilmektedir [9]. Bu bulgular, tedavi protokollerinin bu polimikrobiyal olasılıklara göre optimize edilmesi gerektiğini göstermektedir.

Çalışmamızın retrospektif tasarıma sahip olması, tek merkezde yürütülmesi ve izolatların invaziv/non-invaziv (enfeksiyon/kolonizasyon) ayrımına dair detaylı klinik takip ve tedavi yanıt verilerine ulaşılamamış olması başlıca kısıtlılıklarıdır. Ayrıca, tür tanımlamasının konvansiyonel mikolojik yöntemler ile gerçekleştirilmesi ve molekül bazlı doğrulama ile antifungal duyarlılık testlerinin çalışmaya dahil edilmemiş olması, morfolojik olarak benzer kriptik türlerin ayrımını ve direnç profillerinin klinik sonuçlarla ilişkilendirilmesini sınırlandırmıştır. Buna karşın, bölgemizde geniş bir suş havuzunda gerçekleştirilen bu sürveyans, *Aspergillus* türlerinin güncel epidemiyolojik dağılımini, hasta demografisini ve direkt mikroskopi performansını yansıtması açısından oldukça değerlidir.

5. Conclusion

Bu çalışma, *A. fumigatus* en sık izole edilen tür olarak baskınlığını sürdürse de; *A. flavus* ve *A. terreus* izolatlarında saptanan yüksek direkt mikroskopi pozitiflik oranlarının, bu türlerin klinik örneklerdeki yüksek biyoyüküne ve hızlı tanıdaki kritik rollerine işaret ettiğini göstermiştir. İzolatların büyük çoğunluğunun alt solunum yolu örneklerinden elde edilmesi ve vakaların yarısından fazlasının Göğüs Hastalıkları ile Hematoloji-Onkoloji birimlerinde yoğunlaşması, bu riskli alanlarda rutin sürveyansın hayati önemini bir kez daha kanıtlamıştır. Poliklinik başvurularında saptanan belirgin *A. niger* yoğunluğu ve tırnak örneklerindeki dominantlığı, bu türün invaziv enfeksiyondan ziyade kolonizasyon ve yüzeyel mikozlarla olan güçlü bağını desteklemektedir. Ayrıca, saptanan fungal koenfeksiyonlar, immünkompromize hasta grubunda polimikrobiyal yaklaşımın gerekliliğini vurgulamaktadır. Tür bazlı bu epidemiyolojik veriler, hastanemizin ampirik tedavi protokollerinin optimize edilmesi ve enfeksiyon kontrol stratejilerinin geliştirilmesi için temel bir rehber niteliğindedir.

6. Kaynakça

1-Franconi I, Rizzato C, Ghelardi E, Lupetti A. Hospital distribution, seasonality, time trends and antifungal susceptibility profiles of all Aspergillus species isolated from clinical samples from 2015 to 2022 in a tertiary care hospital. BMC Microbiol. 2024 Apr 3;24(1):111. doi: 10.1186/s12866-024-03267-8.

2-Sarigüzel FM, Koç AN, Sağiroğlu P, Atalay MA, Borlu A, Canöz Ö, Dinç B. Molecular epidemiology and antifungal susceptibilities of Aspergillus species isolated from patients with invasive aspergillosis. Rev Assoc Med Bras (1992). 2023 Feb 17;69(1):44-50. doi: 10.1590/1806-9282.20220441.

3- Lucio J, Alcazar-Fuoli L, Gil H, Cano-Pascual S, Hernandez-Egido S, Cuetara MS, Mellado E. Distribution of Aspergillus species and prevalence of azole resistance in clinical and environmental samples from a Spanish hospital during a three-year study period. Mycoses. 2024 Apr;67(4):e13719. doi: 10.1111/myc.13719.

4-Badali H, Cañete-Gibas C, McCarthy D, Patterson H, Sanders C, David MP, Mele J, Fan H, Wiederhold NP. Species Distribution and Antifungal Susceptibilities of *Aspergillus* Section *Fumigati* Isolates in Clinical Samples from the United States. J Clin Microbiol. 2022 May 18;60(5):e0028022. doi: 10.1128/jcm.00280-22.

5-Hassanpour P, Hashemi SJ, Nami S, Daie Ghazvini R, Naghili Hokmabadi B, Rahimi Foroushani A, Ahmadikia K, Ramezanalipour Z, Firouzi Abriz S. Distribution of fungal agents in the respiratory system of patients with underlying lung diseases; molecular identification and antifungal susceptibility profiles. Iran J Microbiol. 2024 Dec;16(6):792-802. doi: 10.18502/ijm.v16i6.17258.

6- Tio SY, Chen SC, Hamilton K, Heath CH, Pradhan A, Morris AJ, Korman TM, Morrissey O, Halliday CL, Kidd S, Spelman T, Brell N, McMullan B, Clark JE, Mitsakos K, Hardiman RP, Williams P, Campbell AJ, Beardsley J, Van Hal S, Yong MK, Worth LJ, Slavin MA. Invasive aspergillosis in adult patients in Australia and New Zealand: 2017-2020. Lancet Reg Health West Pac. 2023 Sep 4;40:100888. doi: 10.1016/j.lanwpc.2023.100888.

7- Toyotome T, Saito S, Koshizaki Y, Komatsu R, Matsuzawa T, Yaguchi T. Prospective survey of Aspergillus species isolated from clinical specimens and their antifungal susceptibility: A five-year single-center study in Japan. J Infect Chemother. 2020 Feb;26(2):321-323. doi: 10.1016/j.jiac.2019.09.002.

8- Sudhaharan S, Pamidimukkala U, Vinod Kumar M, Verma N. Species distribution and antifungal susceptibility patterns of clinical Aspergillus isolates from a tertiary care center in India. Indian J Med Microbiol. 2026 May 4;62:101135. doi: 10.1016/j.ijmmb.2026.101135.

9-Danion F, Duval C, Séverac F, et al. Factors associated with coinfections in invasive aspergillosis: a retrospective cohort study.. *Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases*. 2021. doi:10.1016/j.cmi.2021.02.021

10- Vipparti H. Mixed fungal lung infection with Aspergillus fumigatus and Candida albicans in a immunocomprimised patient: case report.. *Journal of clinical and diagnostic research : JCDR*. 2014;84: DD08-10 . doi:10.7860/jcdr/2014/8048.4272

11- Khodadadi H, Zomorodian K, Nouraei H, Zareshahrabadi Z, Barzegar S, Zare MR, Pakshir K. Prevalence of superficial-cutaneous fungal infections in Shiraz, Iran: A five-year retrospective study (2015-2019). J Clin Lab Anal. 2021 Jul;35(7):e23850. doi: 10.1002/jcla.23850.

12- Cañete-Gibas CF, Patterson HP, Sanders CJ, Mele J, Fan H, David M, Wiederhold NP. Species Distribution and Antifungal Susceptibilities of *Aspergillus* Section *Terrei* Isolates in Clinical Samples from the United States and Description of *Aspergillus pseudoalabamensis* sp. nov. Pathogens. 2023 Apr 11;12(4):579. doi: 10.3390/pathogens12040579.

13- Kamali Sarvestani H, Seifi A, Falahatinejad M, Mahmoudi S. Black aspergilli as causes of otomycosis in the era of molecular diagnostics, a mini-review. J Mycol Med. 2022 May;32(2):101240. doi: 10.1016/j.mycmed.2021.101240.

14- Knoll MA, Steixner S, Lass-Flörl C. How to use direct microscopy for diagnosing fungal infections. *Clin Microbiol Infect* 2023; 29: 1031–1038.

15- Govrins M, Vahedi-Shahandashti R, Lass-Flörl C. Diagnostic Value of Microscopy, Galactomannan, and PCR in Aspergillus Culture-Positive BALF Samples: A Laboratory-Based Pilot Study. Mycoses. 2025 Aug;68(8):e70103. doi: 10.1111/myc.70103.

16- McClenny N. Laboratory detection and identification of Aspergillus species by microscopic observation and culture: the traditional approach.. *Medical mycology.* 2005;43 Suppl 1: S125-8 . doi:10.1080/13693780500052222

THE EFFECTS OF DIFFERENT PROPOLIS EXTRACTS ON TESTICULAR HISTOMORPHOLOGY IN PREPUBERTAL MALE RATS

Ayşe AYGÜN

Duzce University, Graduate School of Central Institute, Department of Biology, Duzce, Turkey. (Research: Biology; ORCID: 0000-0001-6718-0382)

Fatih DEMİR

Selcuk University, Faculty of Medicine, Department of Medical Pathology, Konya, Turkey. (Research: Pathology; ORCID:0000-0002-8181-0739)

Meral KEKEÇOĞLU

Duzce University, Faculty of Arts and Sciences, Department of Biology, Duzce, Turkey.

Duzce University, Bee and Bee Products Research and Application Center (DAGEM), Duzce, Turkey.

(Research: Apitherapy; ORCID: 0000-0002-2564-8343)

ABSTRACT

Aim: Propolis is a natural product with high biological activity collected by bees from botanical sources. Since its therapeutic potential depends on the solvent type, this study aimed to comparatively examine the effects of ethanolic propolis extract (EEP) and propylene glycol extract (PGE), administered at a dose of 100 mg/kg, testicular histomorphology and histopathological parameters in prepubertal male rats.

Material and Method: *Sprague dawley* male rats (postnatal day 27) were divided into three groups: Control, EEP (100 mg/kg), and PGE (100 mg/kg). Following a 35-day administration period, testicular tissues were fixed and embedded in paraffin blocks. Sections cut at a thickness of 4 µm were stained with Hematoxylin and Eosin (H&E). All histomorphometric evaluations, including the counting of spermatogenetic cell series (spermatogonia, spermatocytes, spermatids), Sertoli, and Leydig cells, were performed by an expert pathologist, blinded to the experimental groups, using QuPath v0.5.0 digital pathology software.

Results: Qualitative histopathological examination revealed that the general testicular architecture and tubular integrity were well-preserved in all groups, with no evidence of extract-induced toxicity at the tested dose. In histomorphometric examinations, the EEP 100 group showed a significant increase in spermatid and total germinal cell counts ($p<0.05$), alongside a decrease in spermatogonia compared to the control. In the PGE 100 group, Sertoli cell counts increased significantly compared to both Control and EEP groups ($p<0.0001$), while Leydig cell counts decreased compared to the control ($p<0.01$).

Conclusion: In conclusion, both ethanolic and propylene glycol extracts of propolis did not cause pathological structural damage or toxicity in testicular tissues during the prepubertal period. However, both extracts modulated specific cell populations at the testicular level through different mechanisms. Due to its biocompatible profile and positive influence on testicular histomorphometry, the PGE form stands out as a potent non-alcoholic alternative for reproductive health applications.

Keywords: *Propolis, Propylene Glycol, Testis Histomorphometry, QuPath, Prepubertal Period.*

1.INTRODUCTION

Propolis represents a complex natural matrix collected by bees, characterized by its potent biological activities.[1] The anti-inflammatory, antioxidant, and immunomodulatory properties it exhibits are primarily attributed to its rich content of phenolic compounds, flavonoids, and aromatic acids.[2] Nevertheless, the therapeutic efficacy of propolis is inextricably linked to the type and polarity of the solvent utilized during extraction.[3] Existing research indicates that solvent selection plays a decisive role

in bioavailability across target tissues by altering both the qualitative and quantitative profiles of bioactive constituents.[4] While ethanolic extracts (EEP) remain the traditional standard due to their proficiency in dissolving hydrophobic components, their pungent odor and alcohol content can be limiting factors, particularly in pediatric models and during sensitive developmental stages.[5] Conversely, propylene glycol (PG) has emerged as a noteworthy alternative due to its low toxicity, superior stability, and capacity to enhance water solubility.[6] The prepubertal period, where the reproductive system is not yet mature and is highly susceptible to environmental variables, serves as a critical window for observing the effects of these extracts. It has been emphasized that propylene glycol-based extracts (PGE) exhibit distinct pharmacokinetic release patterns compared to ethanolic versions, necessitating an independent evaluation of their impact on growth factors and the hormonal axis.[7]

Histomorphological investigations indicate that EEP maintains the integrity of seminiferous tubules within the testes.[8] Nevertheless, the potential irritant effects of alcohol-based solvents on endocrine tissues, coupled with their bioactive release kinetics, necessitate a comparative analysis with alternative solvents such as propylene glycol. Although the efficacy of EEP is frequently highlighted in 'damage models' (e.g., toxicity, diabetes) within current literature, there is a notable lack of comparative studies that integratively evaluate growth and reproductive parameters in healthy subjects.

Propylene glycol is a polar solvent with low toxicity, widely utilized in the pharmaceutical and food industries. [9] Research on PGE indicates that this solvent effectively stabilizes hydrophilic and certain amphipathic phenolic compounds within propolis, such as p-coumaric acid and ferulic acid.[4] Specific studies regarding the impact of PGE on growth and reproduction highlight its efficacy in tissue regeneration and anti-inflammatory responses In this context, propolis extract has been shown to preserve Sertoli and Leydig cell counts and improve sperm quality in experimental models.[10] In terms of the reproductive system, PGE is reported to present a more 'biocompatible' profile in testicular tissues (being free from the potential irritant effects of ethanol) and to support steroidogenesis as a non-alcoholic alternative in apitherapy applications.[6]

It has been noted that ethanolic extracts (EEP) are superior to PGE in dissolving lipophilic flavonoids, such as galangin and Caffeic Acid Phenethyl Ester (CAPE) one of the most potent components of propolis; therefore, anti-tumoral and hormonal stimulation effects may be more pronounced in the EEP group.[11] From a histopathological perspective, literature suggests that high doses of EEP may cause mild vascular congestion in testicular tissue due to its alcohol content, whereas PGE exhibits a safer profile in preserving tissue architecture thanks to its mucosa-friendly natüre.[5] The primary objective of this study is to comprehensively compare the effects of ethanolic and propylene glycol propolis extracts, administered at a dose of 100 mg/kg, on the reproductive organ histomorphology of male rats. The findings are intended to contribute to determining the most suitable solvent for optimizing the biological efficacy of propolis and to fill this significant gap in the literature. In this study, Anatolian-origin ethanolic propolis extract (EEP) and propylene glycol extract (PGE), which represent Turkey's rich flora and are standardized in terms of bioactive constituent content, were utilized.

2. MATERIALS AND METHODS

2.1. Ethical Approval and Animal Husbandry

The procedures involving animals in this research were conducted following the approval of the Duzce University Local Ethics Committee for Animal Experiments (Decision No: 2024-05-01). The study included 24 male *Sprague dawley* rats, which were enrolled immediately following the weaning phase (postnatal day 27). Based on established literature for pubertal development models, the animals were allocated into three groups (n=8 per group). Throughout the experimental period, the rats were maintained in a controlled environment with a stable temperature of 23 ± 1°C, a humidity level of 60 ± 5%, and a 12-hour light/dark photoperiod. All subjects had unrestricted (ad libitum) access to a standard pellet diet and fresh drinking water.

2.2. Treatment Groups and Experimental Protocol

The subjects were allocated into three distinct experimental cohorts through random assignment: a Control group, an EEP 100 group (administered 100 mg/kg/day of ethanolic propolis extract), and a

PGE 100 group (administered 100 mg/kg/day of propylene glycol propolis extract). Dosage selection was informed by established toxicological safety parameters and typical pediatric intake levels of propolis.[12] The treatment regimen was delivered daily via oral gavage starting from postnatal day 27 (PND 27). This 35-day administration period concluded on PND 62, successfully covering the critical window of pubertal maturation in the rats.

2.3. Termination and Organ Collection

Upon completion of the 35-day treatment period, the subjects were deeply anesthetized using a combination of ketamine hydrochloride (90 mg/kg) and xylazine (10 mg/kg) administered intraperitoneally. After verifying the absence of pedal reflexes to ensure surgical anesthesia, euthanasia was performed. The testes were promptly excised and meticulously cleared of any adherent adipose or connective tissues. Following dissection, the organs were weighed on a high-precision digital balance to record absolute weights. For subsequent microscopic examination, the tissues were placed in 10% neutral buffered formalin to initiate the fixation process.

2.4. Histopathological and Histomorphometric Analyses

Following fixation, the testicular tissues were subjected to routine histological processing and embedded in paraffin wax. Longitudinal and transverse sections were obtained at a thickness of 4 µm and stained with Hematoxylin and Eosin (H&E). The slides were then digitized using a high-resolution slide scanner to generate high-definition Whole-Slide Images (WSI). All histological evaluations were conducted by an expert pathologist, blinded to the treatment groups, utilizing the QuPath v0.5.0 digital pathology platform.

For the morphometric analysis, five cell types essential to spermatogenesis spermatogonia, spermatocytes, spermatids, Sertoli cells, and Leydig cells were quantified within randomly selected 1 mm^2 areas for each subject. Cells were initially identified using QuPath's automated "Cell Detection" function. Accuracy was ensured by manually annotating and refining these cell populations with the software's brush and selection tools. To determine the total germinal cell count for each testis, the sum of spermatogonia, spermatocytes, and spermatids per 1 mm^2 was calculated and then extrapolated based on the total testicular area measured via QuPath's area estimation tool.

2.5. Statistical Analysis

Statistical evaluations were conducted using IBM SPSS Statistics v27 (IBM Corp., Armonk, NY, USA). The normality of the data distribution and the homogeneity of variances were verified through the ShapiroWilk and Levene's tests, respectively. Quantitative results are presented as Mean ± Standard Error of the Mean (SEM). Histomorphometric parameters, including specific cell counts and total testicular area measurements, were analyzed independently. For data exhibiting a normal distribution, One-Way Analysis of Variance (ANOVA) followed by Tukey's post-hoc test was utilized to determine significant differences between groups. Non-parametric data were analyzed using the Kruskal–Wallis test, followed by Dunn's post-hoc test. All graphical representations and visualizations were generated using GraphPad Prism v8.0 (GraphPad Software, San Diego, CA, USA). A p-value of <0.05 was considered statistically significant for all comparisons.

3. RESULTS

3.1. Histomorphometric Findings in Testicular Tissue

3.1.1. Spermatogonia Counts

Statistical analysis of spermatogonia counts in the testicular tissues of male rats revealed significant differences among the experimental groups ($p < 0.05$) (Figure 1A). According to the results of the Tukey post-hoc test, the EEP 100 group exhibited a statistically significant decrease in the number of spermatogonia compared to the control group ($p = 0.0428$). Although a numerical decline in spermatogonia counts was observed in the PGE 100 group relative to the control, this difference did not reach statistical significance ($p = 0.1649$). Furthermore, no significant difference was detected when the two extract groups (EEP 100 and PGE 100) were compared with each other ($p = 0.8629$).

3.1.2. Spermatocyte Counts

One-way ANOVA results for spermatocyte counts indicated no statistically significant variation among the groups ($p > 0.05$) (Figure 1B). Tukey post-hoc analysis further confirmed that there were no significant differences between the control group and either the EEP 100 or PGE 100 treatment groups ($p = 0.2073$ and $p = 0.4396$, respectively). Similarly, the comparison between the two propolis extract groups (EEP 100 vs. PGE 100) showed no significant difference in terms of spermatocyte numbers ($p = 0.9215$).

3.1.3. Spermatid Counts

Analysis of spermatid counts in the testicular tissues demonstrated significant differences between groups ($p < 0.05$) (Figure 1C). Based on the Tukey multiple comparison test, the EEP 100 group showed a statistically significant increase in spermatid counts compared to the control group ($p = 0.0334$). In the PGE 100 group, while there was a numerical increase in the number of spermatids relative to the control, this change did not cross the threshold of statistical significance ($p = 0.1178$). Additionally, no significant difference was observed between the EEP 100 and PGE 100 groups in a direct comparison ($p = 0.8846$).

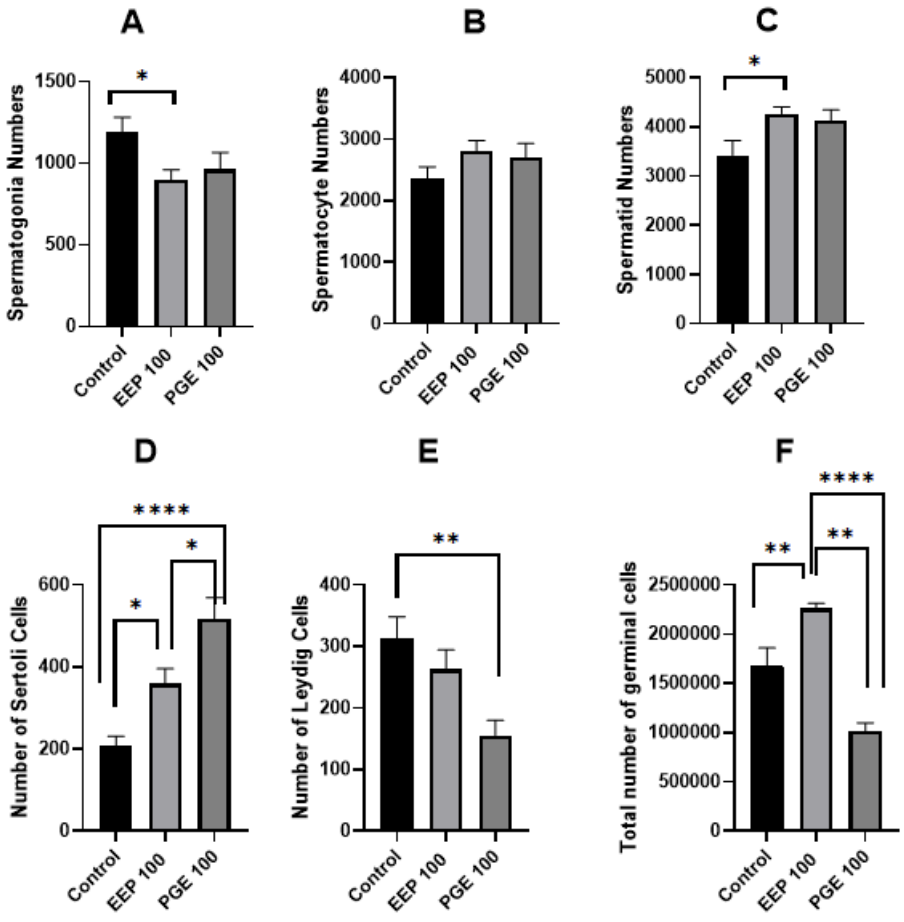


Figure 1. Effects of ethanolic (EEP) and propylene glycol (PGE) extracts of propolis on testicular histomorphometric parameters. (The graphs represent the mean ± SEM of: **(A)** Spermatogonia numbers, **(B)** Spermatocyte numbers, **(C)** Spermatid numbers, **(D)** Number of Sertoli cells, **(E)** Number of Leydig cells, and **(F)** Total number of germinal cells. Statistical significance is indicated as follows: *$p < 0.05$, **$p < 0.01$, and ****$p < 0.0001$ compared to the control or between the indicated groups.)

3.1.4. Sertoli Cell Counts

Analysis of Sertoli cell counts in the testicular tissues revealed highly significant differences among the groups ($p < 0.0001$) (Figure 1D). According to the Tukey post-hoc test, both the EEP 100 and PGE 100 treatment groups showed statistically significant increases in Sertoli cell numbers compared to the

control group ($p = 0.0180$ and $p < 0.0001$, respectively). Notably, the increase in the PGE 100 group was considerably more pronounced than that of the control. Furthermore, a direct comparison between the two extract groups demonstrated that Sertoli cell counts in the PGE 100 group were significantly higher than those in the EEP 100 group ($p = 0.0199$).

3.1.5. Leydig Cell Counts

Statistical analysis of Leydig cell counts indicated significant variations across the experimental groups ($p < 0.05$) (Figure 1E). Tukey post-hoc analysis revealed that Leydig cell counts in the PGE 100 group were statistically lower than those in the control group ($p = 0.0094$). While the EEP 100 group showed a numerical decrease in Leydig cell numbers relative to the control, this reduction did not reach statistical significance ($p = 0.5073$). Additionally, no significant difference was observed between the two extract groups (EEP 100 vs. PGE 100) regarding Leydig cell populations ($p = 0.0827$).

3.1.6. Total Germinal Cell Counts

The analysis of total germinal cell counts showed highly significant differences among the study groups ($p < 0.0001$) (Figure 1F). Results from the Tukey multiple comparison test indicated that the total germinal cell count in the EEP 100 group was significantly higher than that of the control group ($p = 0.0085$). Conversely, the PGE 100 group exhibited a significant decrease in the total germinal cell population compared to the control ($p = 0.0057$). Moreover, when comparing the two extract groups, the EEP 100 group possessed a significantly higher germinal cell population than the PGE 100 group, with the difference being extremely significant ($p < 0.0001$).

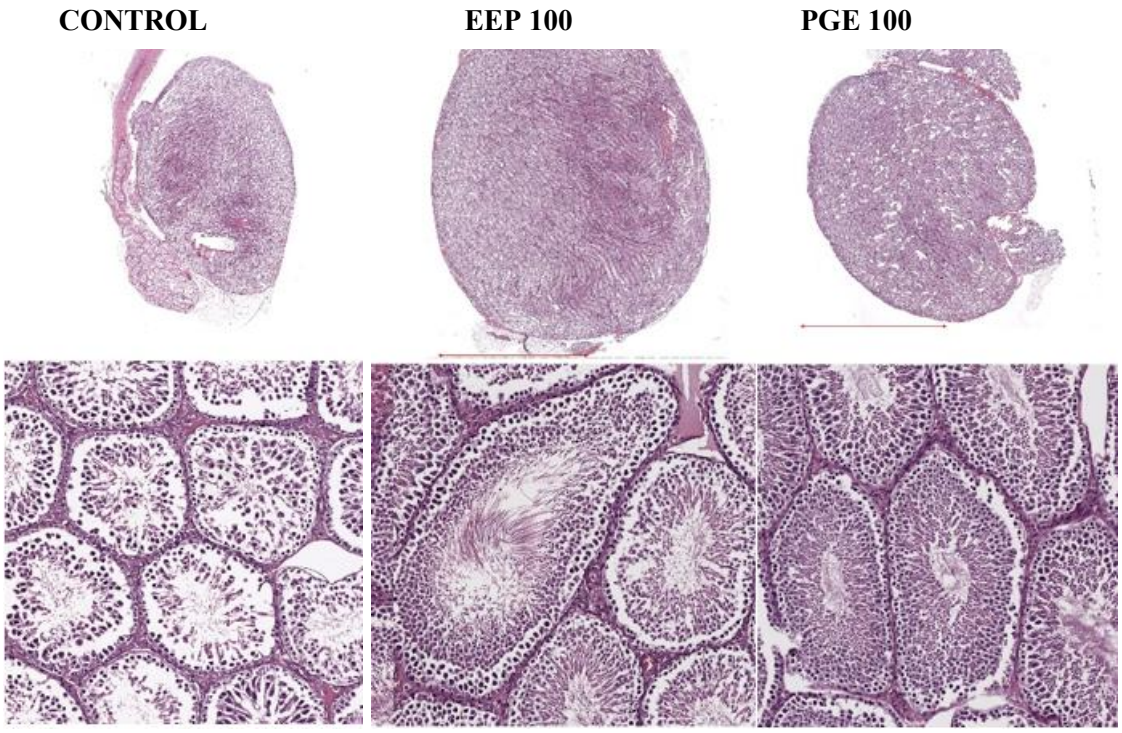


Figure 2. Histological sections of the testis from the Control, EEP 100, and PGE 100 groups.

(Representative digital images of the testis sections are shown at two different magnifications for each group. The top row displays whole-tissue imaging at an equivalent field of view to illustrate the overall testicular architecture. The bottom row provides higher-magnification views, each representing a standardized area of 0.5 mm^2 for all experimental groups).

4. DISCUSSION

This study represents one of the first comparative investigations into the effects of Anatolian propolis

extracts, prepared with different solvents, on testicular histomorphometry during the prepubertal period. Our findings demonstrate that propolis exerts specific modulatory effects on various cell populations within the testicular tissue, depending strictly on the type of solvent utilized.

The significant increase in spermatid and total germinal cell counts observed in the EEP 100 group ($p < 0.05$) confirms the potential of ethanolic propolis extracts to support spermatogenesis. Literature suggests that lipophilic flavonoids in propolis, such as Caffeic Acid Phenethyl Ester (CAPE) and galangin, can cross the blood testis barrier to exert protective and proliferative effects on the germinal epithelium.[8] The superior capacity of ethanol to dissolve these hydrophobic components may be the primary driver behind the increased spermatid count. However, the observed decrease in spermatogonia ($p = 0.0428$) might be attributed to an accelerated cell cycle, where spermatogonia rapidly differentiate into subsequent stages (spermatocytes and spermatids). This supports the hypothesis that EEP may induce a "speed-up" maturation effect during the prepubertal phase.

One of the most striking findings of this research is the highly significant increase in Sertoli cell counts within the PGE 100 group ($p < 0.0001$). Sertoli cells are the "nurse" cells that provide structural and nutritional support for spermatogenesis; their number directly dictates the ultimate functional capacity of the testis. The ability of propylene glycol to stabilize amphipathic phenolic compounds, such as p-coumaric acid may have rendered this extract more effective in triggering growth factors responsible for Sertoli cell proliferation.[4] Furthermore, the alcohol-free, biocompatible nature of PGE offers a less irritant microenvironment for these supporting cells.[6] The preserved overall tissue integrity and the specific areas analyzed for cell quantification are visually represented in Figure 2. Conversely, the decrease in total germinal cells in the PGE group ($p = 0.0057$) suggests that this formulation might prioritize structural stabilization and tissue integrity over rapid germinal cell proliferation.

The reduction in Leydig cell counts in the PGE 100 group $p = 0.0094$) can be interpreted through the modulatory role of propolis on steroidogenesis. Evidence indicates that the high bioactive content of propolis can balance testosterone synthesis via feedback mechanisms or regulate apoptosis in Leydig cells.[2] It is likely that specific hydrophilic components, more soluble in PGE, exert a suppressive effect on Leydig cell turnover during the sensitive prepubertal window. This suggests that the impact of PGE on the reproductive system is not merely cellular but may involve a complex hormonal axis.

Our results challenge the conventional "ethanol is the superior solvent" paradigm. While EEP appears more effective at promoting germinal cell production, PGE stands out in supporting Sertoli cells the critical framework for the longterm functional lifespan of the testes. This highlights the importance of goal oriented solvent selection in apitherapy. Specifically, for pediatric and prepubertal applications where alcohol consumption is restricted, PGE emerges as a potent and safe therapeutic alternative.

5. CONCLUSION

In conclusion, both ethanolic and propylene glycol extracts of Anatolian propolis modulate testicular tissue without inducing pathological damage or toxicity. EEP appears ideal for maximizing spermatogenetic activity, whereas PGE excels in enhancing supportive tissue architecture and cellular biocompatibility. Future studies focusing on the correlation between these cellular changes and testosterone levels or sperm quality will further elucidate the definitive role of propolis in reproductive health.

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REFERENCES

1. Bankova V, Bertelli D, Borba R, et al. Standard methods for *Apis mellifera* propolis research. *J Apic Res*. 2019;58(2):1-49. doi:10.1080/00218839.2016.1222661

2. Sforcin JM. Biological properties and therapeutic applications of propolis. *Phytother Res*. 2016;30(6):894-905. doi:10.1002/ptr.5605

3. Kubiliene L, Laugalyte V, Pavilonis A, et al. Alternative preparation of propolis extracts: comparison of their composition and biological activities. *BMC Complement Altern Med*. 2015;15(1):1-7. doi:10.1186/s12906-015-0677-5

4. Pobiega K, Kraśniewska K, Gniewosz M. Application of propolis in antimicrobial and antioxidative protection of food methods – A review. *Trends Food Sci Technol*. 2019;83:53-62. doi:10.1016/j.tifs.2018.11.007

5. Wagh VD. Propolis: a wonder bees product and its pharmacological potentials. *Adv Pharmacol Sci*. 2013;2013:308249. doi:10.1155/2013/308249

6. Kocot J, Kiełczykowska M, Luchowska-Kocot D, Kurzepa J, Musik I. Antioxidant potential of propolis, bee pollen, and royal jelly: possible medical applications. *Oxid Med Cell Longev*. 2018;2018:7074209. doi:10.1155/2018/7074209

7. Demir S, et al**.** Effect of Propolis on Precocious Puberty in Female Rats. *J Clin Res Pediatr Endocrinol*. 2022;14(4):415-421. doi:10.4274/jcrpe.galenos.2022.2022-1-18

8. Seven İ, et al. Bee glue (propolis) improves reproductive organs, sperm quality and histological changes and antioxidant parameters of testis tissues in rats exposed to excess copper. Andrologia. 2020;52(4):e13540. doi: 10.1111/and.13540

9. Fowles JR, Banton MI, Pottenger LH. A toxicological review of the propylene glycols. *Crit Rev Toxicol*. 2013;43(4):363-390. doi:10.3109/10408444.2013.792328

10. Rahmawati R, Nasihun T, Isradji I. The Effect of Continuous Multistage Countercurrent Extraction (CMCE) Propolis Extract Administration on Leydig, and Sertoli Cells Counts, and Sperm Quality Induced With Monosodium Glutamate (MSG). Sains Medika. 2019;10(2):62-67. https://jurnal.unissula.ac.id/index.php/sainsmedika/article/view/4221.

11. 11. Trusheva B, Trunkova D, Bankova V. Different extraction methods of biologically active components from propolis: a preliminary study. Chem Cent J. 2007;1:13. doi:10.1186/1752-153X-1-13

12. Burdock GA. Review of the biological properties and toxicity of bee propolis (propolis). *Food Chem Toxicol*. 1998;36(4):347-363. doi:10.1016/s0278-6915(97)00145-2

BIOINFORMATIC ANALYSIS OF *TSPAN8* EXPRESSION IN LUNG ADENOCARCINOMA: PROGNOSTIC VALUE AND METASTASIS-ASSOCIATED MECHANISMS

Şebnem Yıldırımcan Kadıçeşme

Kafkas University, Faculty of Medicine, Department of Medical Biology, Kars, Türkiye

ORCID: 0000-0002-8908-9464

ABSTRACT

Aim: TSPAN8 is a membrane-associated tetraspanin involved in cell adhesion, vesicular trafficking, and extracellular vesicle biology. Although it has been associated with metastasis, tumor progression, and poor prognosis in various cancers, its role in lung adenocarcinoma (LUAD) remains unclear. This study aimed to evaluate TSPAN8 expression, its prognostic value, and metastasis-related biological mechanisms in LUAD using bioinformatic tools.

Materials and Methods: Gene expression analyses were conducted using GEPIA2 and TNMplot databases. Survival analyses were performed in the LUAD cohort and subgroups using the Kaplan–Meier Plotter platform, and independent prognostic value was assessed by multivariate Cox regression analysis. To evaluate the biological mechanisms of TSPAN8 that may be associated with metastatic behavior, gene panels related to epithelial–mesenchymal transition (EMT), extracellular matrix (ECM) remodeling, invasion, angiogenesis, and exosome biogenesis were selected, and a correlation analysis was performed using the GEPIA2 platform. Protein–protein interaction network and functional enrichment analyses were performed using the STRING database. In the functional enrichment analyses, biological processes and pathways were evaluated using Gene Ontology (GO), Kyoto Encyclopedia of Genes and Genomes (KEGG), and Reactome databases.

Results: TSPAN8 expression was significantly higher in LUAD tumor tissues compared to normal lung tissues ($p = 0.010$). TNMplot analysis showed increased TSPAN8 levels in metastatic tissues relative to primary tumors ($p < 0.001$). High TSPAN8 expression was associated with improved overall survival (HR = 0.77, $p = 0.002$). Multivariate Cox analysis confirmed its independent prognostic value (HR = 0.44, $p < 0.001$). No strong correlations were observed with EMT, invasion, or angiogenesis-related genes. However, significant positive correlations were detected with exosome-related genes, including CD63, PDCD6IP, TSG101, RAB27A, RAB27B, VPS4B, and VPS37B. Functional enrichment analysis revealed significant involvement in multivesicular body organization, exocytosis, endocytosis, membrane trafficking, and ESCRT-mediated processes.

Conclusion: TSPAN8 may serve as an independent prognostic biomarker in LUAD. The findings suggest that TSPAN8's metastatic potential in LUAD may be associated with exosome biogenesis and vesicular transport processes rather than with classical EMT or invasion pathways.

Keywords: TSPAN8, lung adenocarcinoma, exosome, prognosis, bioinformatics

INTRODUCTION

Lung adenocarcinoma (LUAD) is one of the most common histological subtypes of non-small cell lung cancer; due to its marked molecular and histopathological heterogeneity, it exhibits significant differences in clinical course and survival among patient groups. This heterogeneous structure necessitates the identification of new prognostic biomarkers beyond classical clinicopathological parameters.[1,2]

TSPAN8 is a membrane-associated protein belonging to the tetraspanin family and is of interest as a molecule that may play a role in cell membrane organization, cell-cell interaction, membrane transport, and processes related to extracellular vesicles.[3-5] It has been reported that TSPAN8 overexpression in various tumor types may be associated with invasion, metastasis, angiogenesis, and tumor progression. Furthermore, the fact that TSPAN8 can be transported on extracellular vesicles and has been linked to

metastatic behavior in non-small cell lung cancer makes this molecule not only an expression marker but also a compelling candidate from a biological function perspective.[3,6,7]

However, the expression pattern, prognostic value, and associated biological mechanisms of TSPAN8 in LUAD remain unclear. Results obtained from different databases suggest that the prognostic impact of TSPAN8 may vary depending on patient subgroups, the platforms used, and the molecular context. Furthermore, it remains unclear whether TSPAN8 plays a role in alternative biological processes related to vesicular transport and membrane organization rather than classical metastatic pathways.

In this study, the differential expression, prognostic value, and potential molecular associations of TSPAN8 in LUAD were evaluated using multiple bioinformatics platforms. To this end, expression, survival, subgroup, correlation, protein interaction network, and functional enrichment analyses were used in combination.

MATERIALS AND METHODS

1. Study Design

This study was designed as a hypothesis-driven bioinformatics analysis aimed at evaluating the clinical and biological significance of TSPAN8 in LUAD. The analyses were performed using the GEPIA2, TNMplot, Kaplan–Meier Plotter, and STRING databases. [8,9,10,11,12]

2. Differential Gene Expression Analysis

As part of the expression analysis, LUAD tumor and normal lung tissues were compared on the GEPIA2 platform. The analyses utilized log2(TPM+1) transformation, and thresholds of $|\log2FC| \geq 1$ and $p < 0.01$ were applied to ensure a more stringent approach. For comparisons with normal tissue, both TCGA normal data and GTEx normal lung data were used. Additionally, using TNMplot RNA-seq data, a paired expression analysis was performed between tumor tissue and adjacent normal lung tissue from the same patient by selecting the "include paired tumor and adjacent normal tissues" option. This allowed for the evaluation of changes in TSPAN8 expression while minimizing the influence of patient-specific biological variations. Differences between groups were assessed using the Mann–Whitney U test. Furthermore, expression differences among normal, tumor, and metastatic tissue groups were examined in TNMplot gene-chip data.[8,9]

The relationship between TSPAN8 expression and tumor stage was evaluated using stage plot analysis on the GEPIA2 platform. LUAD patients were compared across Stage I–IV groups based on their pathological stage, and differences between groups were analyzed using an ANOVA test. A p-value of <0.05 was considered statistically significant.[8]

3. Survival analysis

The prognostic value of TSPAN8 was evaluated using the Kaplan–Meier Plotter platform. In the analyses, overall survival (OS) was compared between high and low TSPAN8 expression groups within the lung cancer cohort. The JetSet "best probe" option was selected for the analyses, and TSPAN8 expression was assessed using the 203824_at probe in all analyses. Patients were divided into high and low expression groups based on the median expression value. Survival curves were plotted along with 95% confidence intervals (CI), and hazard ratios (HR) and log-rank p-values were calculated. A p-value of <0.05 was considered statistically significant.To evaluate the histology-specific prognostic effect, an overall survival analysis was performed in the LUAD subgroup. Additionally, an overall survival analysis was conducted in the squamous cell carcinoma cohort to assess whether the prognostic effect of TSPAN8 varied according to histological subtypes.In addition to the overall survival analysis in the LUAD subgroup, univariate analyses were performed according to stage, tumor grade, T/N/M stages, sex, smoking status, surgical margin status, chemotherapy, and radiotherapy subgroups. Furthermore, a multivariate Cox regression analysis was performed to evaluate independent prognostic value. Stage, sex, and smoking status were included as covariates in the multivariate model. Additionally, an overall survival analysis for LUAD was conducted on the GEPIA2 platform.[8,10,11]

4. Correlation Analysis

Correlation analyses were performed using gene panels associated with EMT, ECM remodeling, and invasion; angiogenesis; and exosome biogenesis and secretion to evaluate the association between TSPAN8 and potential metastatic behavior in LUAD.

The correlation analysis was performed using Pearson correlation analysis on the GEPIA2 platform. The analyses were conducted on the LUAD cohort, and the correlation coefficient was evaluated using Pearson's r value. Genes associated with epithelial-mesenchymal transition (EMT) included VIM, CDH1, ZEB1, ZEB2, SNAI1, SNAI2, and TWIST1; genes associated with extracellular matrix (ECM) remodeling and invasion included MMP2, MMP9, MMP14, FN1, ITGB1, ITGA5, and PLAUR; genes associated with angiogenesis included VEGFA, ANGPT2, KDR, FLT1, and TEK; and genes associated with exosome biogenesis and secretion included CD63, CD81, PDCD6IP, SDCBP, TSG101, RAB27A, RAB27B, VPS4B, and VPS37B. The threshold for statistical significance was set at $p < 0.05$. [8, 13–17]

5. Protein-Protein Interaction Network and Functional Enrichment Analysis

Genes associated with exosome biogenesis and secretion that showed significant correlations with TSPAN8 were imported into the STRING database. A protein-protein interaction network was constructed, and a minimum required interaction score of medium confidence (0.400) was selected for the analysis. Clustering analysis was performed using the Markov Cluster Algorithm (MCL) to identify functional clusters in the network, with an inflation parameter set to 3. In the functional enrichment analysis, biological processes were evaluated using the Gene Ontology (GO) database, cellular pathways using the Kyoto Encyclopedia of Genes and Genomes (KEGG), and molecular mechanisms using the Reactome database. The threshold for statistical significance was set at $p < 0.05$ [12].

RESULTS

1. Differential Gene Expression Analysis of TSPAN8 in LUAD

The GEPIA2 analysis showed that TSPAN8 expression was increased in LUAD tumor tissues compared to normal lung tissues ($p<0.01$). Median expression was higher in the tumor group, and the distribution was broader; this suggested heterogeneous expression at the patient level. In the GEPIA2 analysis, there were 483 tumor samples and 347 normal samples (Figure 1A).

The TNMplot RNA-seq analysis confirmed that TSPAN8 expression was elevated in LUAD tumor tissues compared to normal lung tissues. In the paired RNA-seq analysis, 57 tumor samples and 57 adjacent normal tissue samples from the same patient were compared. TSPAN8 expression was found to be significantly higher in tumor tissues compared to normal tissues (Mann–Whitney $p=0.010$). The mean fold-change of 7.07 and the median fold-change of 1.17 indicated that the increase was not homogeneous across all patients but was quite pronounced in some cases (Figure 1B).

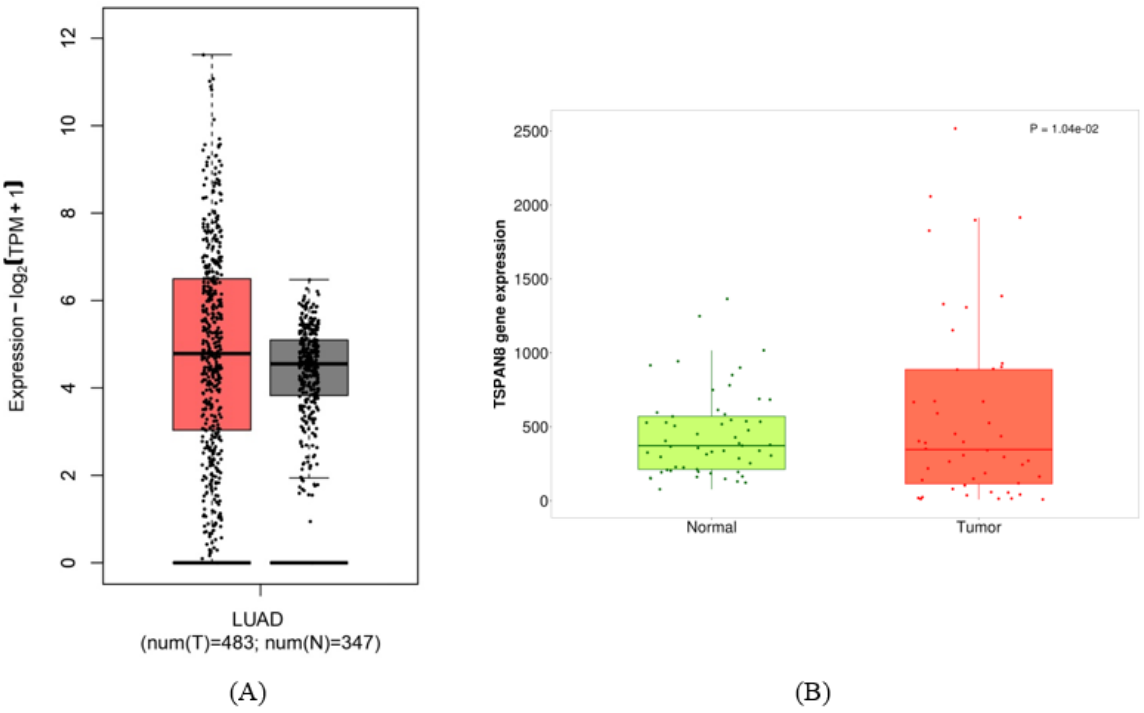


Figure 1. Comparison of TSPAN8 expression between normal and tumor tissues in LUAD. (A) GEPIA2 analysis.[8] (B) TNMplot RNA-seq paired analysis.[9]

In the TNMplot gene-chip analysis, TSPAN8 expression was found to differ significantly among normal, tumor, and metastatic lung tissues (Kruskal–Wallis $p=1.16\times10^{-15}$). The analysis included 391 normal, 1,865 tumor, and 8 metastatic samples. TSPAN8 levels increased gradually from normal tissue to tumor tissue and from tumor tissue to metastatic tissue (Figure 2).

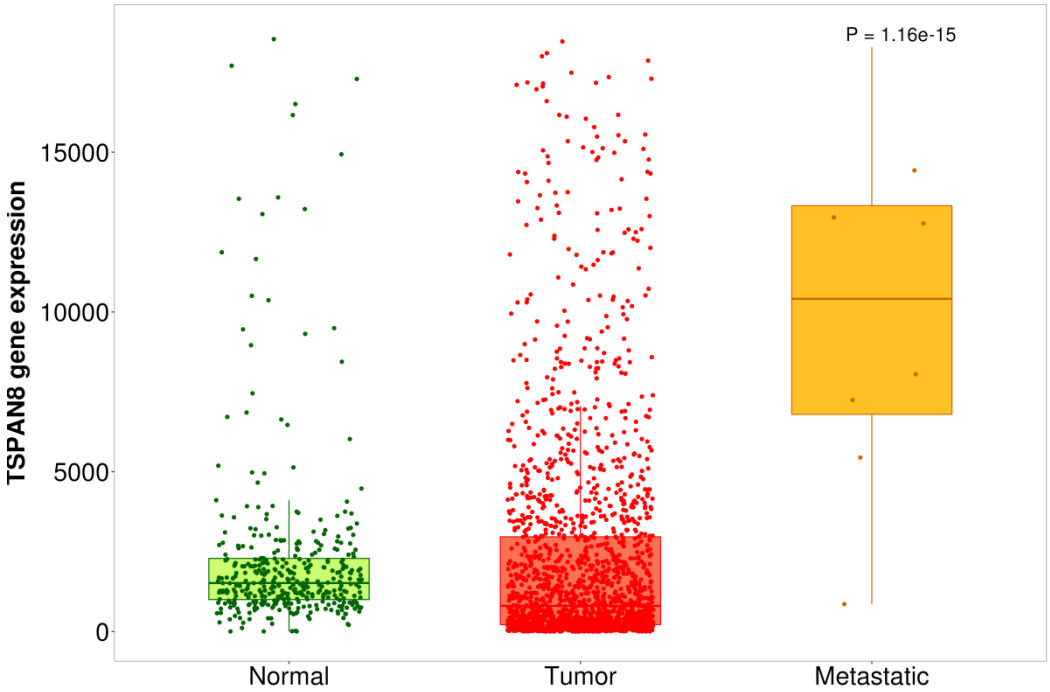


Figure 2. Comparison of TSPAN8 expression levels in normal, primary tumor, and metastatic lung tissues using TNMplot gene-chip analysis.[9]

When the Dunn test was used for pairwise comparisons, TSPAN8 expression in primary tumor tissues was found to be 1.09 times higher than in normal tissues ($p=6.93\times10^{-14}$). In metastatic tissues, TSPAN8 expression was 4.43-fold higher than in normal tissues ($p=2.84\times10^{-3}$) and 4.07-fold higher than in primary tumor tissues ($p=3.93\times10^{-5}$). The median expression level was 10,410.5 in the metastatic group, 2,202 in the tumor group, and 1,518 in normal tissue.

The GEPIA2 stage plot analysis revealed that TSPAN8 expression did not differ significantly across LUAD stages (ANOVA F=0.168, p=0.918). Expression patterns were largely similar across the Stage I, II, III, and IV groups.

2. Survival Analysis

In the Kaplan–Meier plot analysis, TSPAN8 expression was associated with better overall survival in the entire lung cancer cohort (HR=0.75, 95% CI: 0.67–0.85, p<0.001). This effect was more pronounced in the LUAD subgroup (HR=0.77, 95% CI: 0.65–0.91, p=0.002) (Figure 3). In contrast, no significant association was found between TSPAN8 expression and overall survival in the squamous cell carcinoma subgroup (HR=0.91, 95% CI = 0.75–1.11, p=0.350). Furthermore, in the GEPIA2 survival analysis, no significant association was found between TSPAN8 expression and overall survival in LUAD patients (HR=1.2, p=0.350).

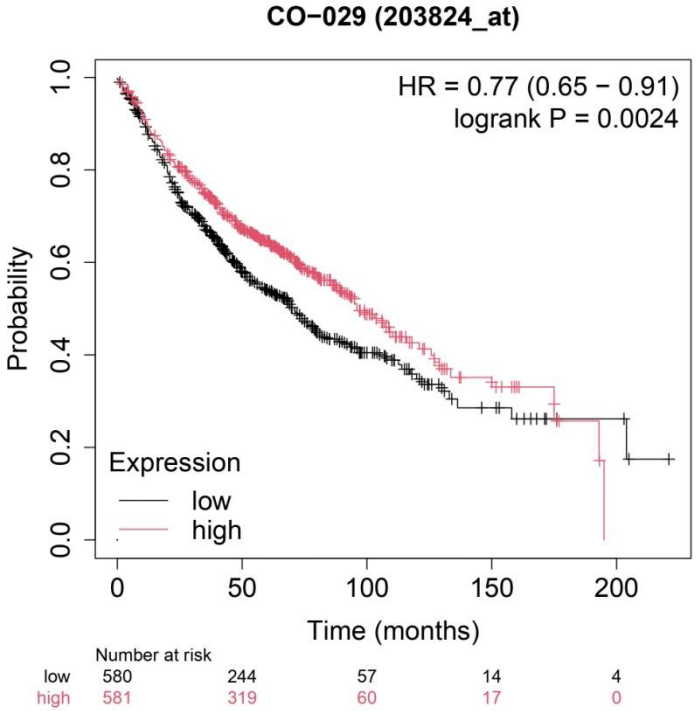


Figure 3. Analysis of overall survival according to TSPAN8 expression in LUAD patients. [10,11]

Subgroup analyses showed that the prognostic impact of TSPAN8 expression in the adenocarcinoma cohort may vary depending on the clinical context (Table 1). In the stage analysis, high TSPAN8 expression was significantly associated with better survival in Stage I patients (HR=0.47, 95% CI 0.31–0.70, p<0.001). Although a similar trend was observed in the Stage II group, the result was not statistically significant (HR=0.64, 95% CI 0.40–1.03, p=0.068). In contrast, high TSPAN8 expression was associated with poorer survival in Stage III patients (HR=5.10, 95% CI 1.75–14.86, p=0.003); however, this result should be interpreted with caution due to the small sample size in this subgroup.

No significant association was found across grade subgroups. However, a borderline significant trend was observed in Grade 2 cases, suggesting that high TSPAN8 expression may be associated with a poorer prognosis (HR=1.44, 95% CI 0.99–2.10, p=0.058). In the T-stage analysis, although a trend toward better survival was observed in T1 patients, the result was not statistically significant (HR=0.74, 95% CI 0.51–1.07, p=0.110). No significant association was found in the T2 and T3 subgroups. No significant association was found between TSPAN8 expression and survival in the N0, N1, and N2 subgroups.

In M0 patients, high TSPAN8 expression was significantly associated with better survival (HR=0.46, 95% CI 0.31–0.68, p<0.001). High TSPAN8 expression was associated with a better prognosis in female patients (HR=0.69, 95% CI 0.53–0.91, p=0.008) and in patients who had never smoked (HR=0.39, 95% CI 0.21–0.75, p=0.003). In contrast, no significant association was observed in men or in smokers. No significant association was observed in patients with negative surgical margins or in chemotherapy subgroups. In patients who did not receive radiotherapy, high TSPAN8 expression was associated with poorer survival (HR=1.44, 95% CI 1.07–1.95, p=0.017), but no significant association was found in patients who received radiotherapy.

Table 1. Univariate Cox regression analysis of TSPAN8 according to clinicopathological subgroups in lung adenocarcinoma

Variable	Subgroup	n	HR (95% CI)	p-value
Overall	All patients	1161	0.77 (0.65–0.91)	0.002
Stage	Stage I	370	0.47 (0.31–0.70)	<0.001
	Stage II	136	0.64 (0.40–1.03)	0.068
	Stage III	24	5.10 (1.75–14.86)	0.003
	Stage IV	4	Not estimable	—
Grade	Grade 1	166	1.35 (0.91–2.03)	0.138
	Grade 2	209	1.44 (0.99–2.10)	0.058
	Grade 3	60	1.73 (0.79–3.78)	0.165
T stage	T1	272	0.74 (0.51–1.07)	0.110
	T2	357	1.13 (0.85–1.50)	0.390
	T3	32	1.01 (0.47–2.19)	0.970
	T4	11	Not estimable	—
N stage	N0	485	0.91 (0.69–1.20)	0.510
	N1	130	0.94 (0.61–1.44)	0.780
	N2	56	1.56 (0.88–2.77)	0.120

M stage	M0	232	0.46 (0.31–0.68)	<0.001
	M1	10	Not estimable	—
Gender	Female	537	0.69 (0.53–0.91)	0.008
	Male	566	0.92 (0.73–1.16)	0.460
Smoking status	Never smoker	192	0.39 (0.21–0.75)	0.003
	Smoker	546	0.95 (0.73–1.23)	0.710
Surgery margin	Negative (R0)	636	0.85 (0.67–1.09)	0.210
Chemotherapy	Yes	125	1.39 (0.88–2.21)	0.160
	No	361	1.28 (0.95–1.74)	0.105
Radiotherapy	No	363	1.44 (1.07–1.95)	0.017
	Yes	65	1.09 (0.62–1.91)	0.750

Note: The n values indicate the number of valid cases included in each subgroup analysis.

No analysis was performed for the Stage IV and T4 and M1 subgroups due to an insufficient sample size. The p-values are based on the log-rank test.

In multivariate Cox regression analysis adjusted for stage, gender, and smoking status in lung adenocarcinoma, high TSPAN8 expression remained an independent predictor of better overall survival (HR= 0.44, 95% CI: 0.28–0.70, p< 0.001) (Table 2).

Table 2. Multivariate Cox regression analysis of TSPAN8 expression in lung adenocarcinoma

Variable	**HR (95% CI)**	**p-value**
Stage	2.41 (1.76–3.30)	<0.001
Gender	0.98 (0.62–1.53)	0.917
Smoking status	0.67 (0.39–1.15)	0.142
TSPAN8 expression	0.44 (0.28–0.70)	<0.001

HR: hazard ratio; CI: confidence interval. Multivariate analysis was adjusted for stage, gender, and smoking status

3. Correlation Analysis

Correlation analyses were performed in relation to various pathways to evaluate the association of TSPAN8 with potential metastatic behavior in LUAD. Among genes associated with EMT, only a weak but statistically significant negative correlation was observed with VIM ($R = -0.13$, $p = 0.0046$). In contrast, no significant correlations were found with CDH1, ZEB1, ZEB2, SNAI1, SNAI2, and TWIST1. Similarly, no strong or consistent correlations were found with the genes MMP2, MMP9, MMP14, FN1, ITGB1, ITGA5, and PLAUR, which are associated with ECM remodeling and invasion. In the angiogenesis panel, weak negative correlations were observed with VEGFA ($R = -0.13$, $p = 0.0031$) and KDR ($R = -0.11$, $p = 0.016$), but no significant correlations were found with ANGPT2, FLT1, and TEK.

In contrast, more pronounced relationships were observed between TSPAN8 expression and genes associated with exosome biogenesis and secretion. TSPAN8 expression was positively correlated with CD63 ($R = 0.17$, $p < 0.001$), PDCD6IP ($R = 0.16$, $p < 0.001$), TSG101 ($R = 0.18$, $p < 0.001$), RAB27A ($R = 0.091$, $p = 0.047$), RAB27B ($R = 0.22$, $p < 0.001$), VPS4B ($R = 0.14$, $p = 0.003$), and VPS37B ($R = 0.15$, $p < 0.001$). In contrast, no significant correlations were observed with CD81 and SDCBP.

4. Protein-Protein Interaction Network and Functional Enrichment Analysis

In the STRING-based protein-protein interaction network analysis, TSPAN8 was found within the same functional network as proteins associated with exosome biogenesis and secretion (CD63, TSG101, PDCD6IP, RAB27A, RAB27B, VPS4B, and VPS37B) (Figure 4). In the network analysis, RAB27A/RAB27B occupied a central position, while PDCD6IP acted as a bridge, and VPS4B and VPS37B formed the ESCRT-associated submodule. In the STRING-based clustering analysis, all proteins under investigation were found to be grouped into a single functional cluster. This cluster was determined to be associated with the "multivesicular body sorting pathway." The cluster included the proteins CD63, TSG101, PDCD6IP, RAB27A, RAB27B, VPS4B, and VPS37B, along with TSPAN8.

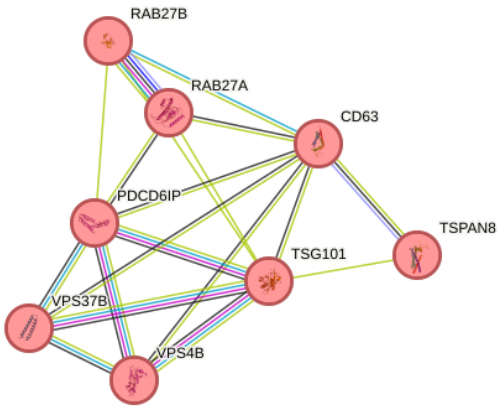


Figure 4. Protein-protein interaction network associated with TSPAN8 based on STRING analysis.[12]

Functional enrichment analysis was performed using the GO, KEGG, and Reactome databases to investigate the biological functions of the identified proteins. Functional enrichment analysis revealed significant enrichment in pathways associated with multivesicular body assembly, exocytosis, ESCRT-mediated processes, endocytosis, and membrane transport (Figure 5) (Table 3). The most prominent biological theme was evaluated by considering the pathways with the lowest FDR values.

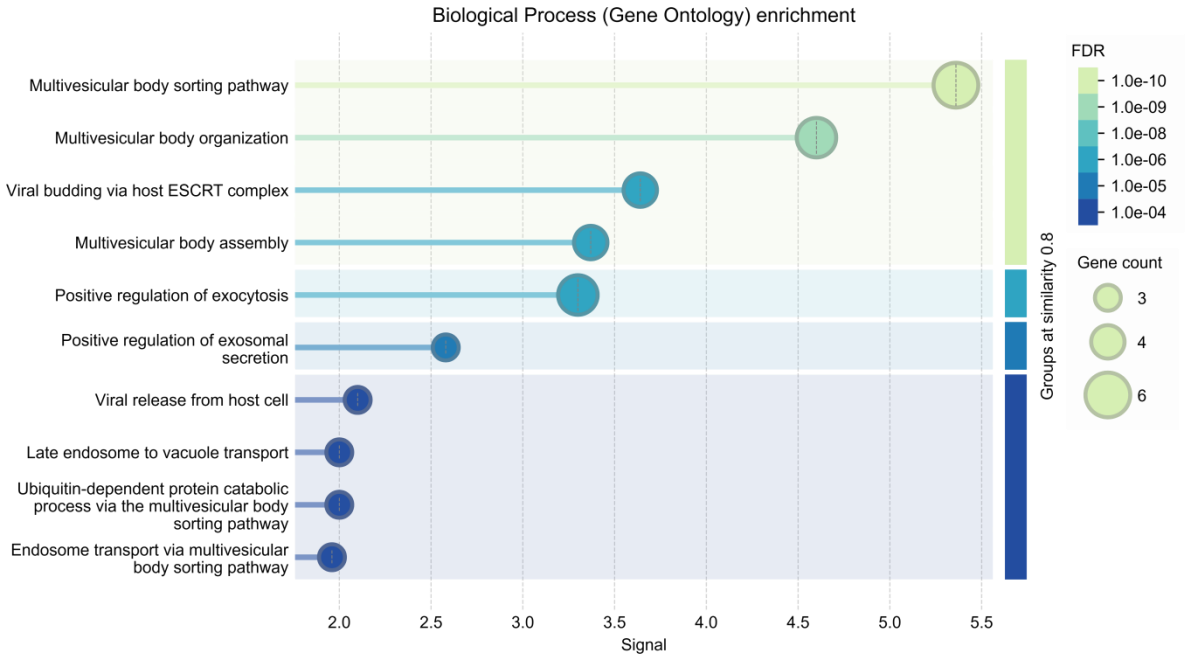


Figure 5. Bubble plot of pathways significantly enriched in GO, KEGG, and Reactome analyses. The bubble size represents the number of genes in the respective pathway, and the color scale represents the FDR value.[12]

GO analysis revealed that proteins are significantly associated with the key processes of multivesicular body organization, vesicle-mediated transport, exocytosis, and exosomal secretion. In particular, a significant enrichment was observed in biological processes associated with multivesicular body sorting, multivesicular body organization, positive regulation of exocytosis, and positive regulation of exosomal secretion. In these processes, the proteins VPS4B, TSG101, VPS37B, PDCD6IP, RAB27A, and RAB27B were found to be particularly prominent.

KEGG pathway analysis supports these findings, revealing a significant enrichment of the endocytosis pathway. In this pathway, the proteins VPS4B, TSG101, VPS37B, and PDCD6IP were specifically identified.

Reactome analysis, on the other hand, showed that pathways associated with ESCRT (Endosomal Sorting Complex Required for Transport) and membrane transport were significantly enriched. In the ESCRT pathway, the proteins VPS4B, TSG101, and VPS37B were particularly identified.

Table 3. Functional enrichment analysis of the TSPAN8-associated protein network

Database	Pathway / Process	Gene count	FDR
GO	Multivesicular body sorting pathway	6	1.75E-10
GO	Multivesicular body organization	5	8.87E-09
GO	Positive regulation of exocytosis	5	5.75E-07
GO	Viral budding via host ESCRT complex	4	6.11E-07
KEGG	Endocytosis	4	0.00053

Reactome	ESCRT (Endosomal Sorting Complex Required for Transport)	3	0.00019
Reactome	Membrane trafficking	5	0.00065

Note: Functional enrichment analysis of the identified protein network based on the GO, KEGG, and Reactome databases. Only the most significantly enriched pathways (lowest false discovery rate, FDR) are shown. The most prominent biological themes were evaluated based on the pathways with the lowest FDR values.

DISCUSSION

In this study, the biological and clinical significance of TSPAN8 in LUAD was investigated using multilevel bioinformatics analyses. Both GEPIA2 and TNMplot analyses consistently demonstrated that TSPAN8 expression was elevated in LUAD tumor tissues compared to normal lung tissues. Furthermore, the finding that TSPAN8 levels are higher in metastatic tissues compared to primary tumors suggests that this gene may be associated with tumor progression and metastatic behavior. The literature reports that TSPAN8 exhibits increased expression in various tumors, such as pancreatic, gastric, colorectal, and hepatocellular carcinomas, and may be associated with invasion, metastasis, and poor prognosis.[4,5,14] In contrast, data on LUAD are limited. Therefore, the findings from our study suggest that TSPAN8 may also have biological significance in LUAD.

While the Kaplan–Meier Plotter analysis found that high TSPAN8 expression was associated with better overall survival, no significant association was detected in the GEPIA2 analysis. This discrepancy may stem from differences in the scope of the datasets used, patient numbers, cutoff points, and analytical methods. The Kaplan–Meier Plotter platform includes larger microarray-based cohorts, whereas GEPIA2 is based on more limited TCGA data.[8,10,11] In subgroup analyses, the association of high TSPAN8 expression with a better prognosis in Stage I, M0, female, and never-smoking patients suggests that TSPAN8's prognostic effect may vary depending on the clinical context. In contrast, the finding that high expression is associated with poorer survival in Stage III patients suggests that TSPAN8 may exhibit a bidirectional prognostic effect depending on disease stage. Similarly, the finding that high expression is associated with poorer survival in the group not receiving radiotherapy also suggests that the prognostic effect of TSPAN8 may vary depending on the treatment context. However, these findings should be interpreted with caution due to the small sample size in the Stage III subgroup and the heterogeneous nature of the group that did not receive radiotherapy. The fact that TSPAN8 remained significant in the multivariate Cox analysis independent of baseline clinical variables such as stage, gender, and smoking status suggests that this gene may serve as an independent prognostic biomarker.[3,4]

Correlation analyses did not reveal strong or consistent associations with genes related to EMT, ECM remodeling, and angiogenesis. Weak negative correlations were observed only with VIM in the EMT panel and with VEGFA and KDR in the angiogenesis panel. This suggests that the metastatic effects of TSPAN8 in LUAD may be associated with processes that differ significantly from classical metastatic mechanisms. In recent years, it has been demonstrated that exosome biogenesis and intercellular vesicular communication play significant roles in metastatic processes.[18,19] In our study, it is noteworthy that TSPAN8 expression showed significant positive correlations with CD63, PDCD6IP, TSG101, RAB27A, RAB27B, VPS4B, and VPS37B. Most of these genes encode proteins associated with exosome biogenesis, multivesicular body formation, the ESCRT complex, and vesicle release.[14,16,17] Furthermore, members of the tetraspanin family, such as CD63, are among the key components of exosomal membranes.[13,14]

STRING-based protein-protein interaction network and functional enrichment analyses also supported these findings. The fact that TSPAN8 is located within the same functional network as CD63, TSG101, PDCD6IP, RAB27A, RAB27B, VPS4B, and VPS37B suggests that this protein may be associated with exosome biogenesis, vesicular transport, and ESCRT-related processes. In particular, it is known that RAB27A and RAB27B regulate different stages of exosome release, while PDCD6IP, TSG101, VPS4B,

and VPS37B play roles in multivesicular body formation and ESCRT-mediated vesicle formation. [14,16-19]

GO, KEGG, and Reactome analyses highlighting pathways associated with multivesicular body organization, exocytosis, exosomal secretion, endocytosis, and membrane transport further support this biological framework. Previous studies have reported that TSPAN8 is transported in exosomal membranes and may be associated with endothelial cell activation and metastatic niche formation.[13,15,20,21] Furthermore, it has been shown that high levels of TSPAN8 in serum extracellular vesicles in non-small cell lung cancer are associated with the development of distant metastases.[7] The findings obtained in our study also support that TSPAN8 is part of the protein network associated with exosome biogenesis and secretion in LUAD.

While prognostic biomarker studies in LUAD have primarily focused on multi-gene signatures and immunological/molecular subtypes, this study demonstrates that TSPAN8 may possess independent prognostic value on its own and that its metastatic potential may be associated with exosome biogenesis.[1,2] This suggests that TSPAN8 may be an important candidate not only as a prognostic biomarker but also for new therapeutic strategies targeting extracellular vesicle biology. In recent years, antibody and CAR-T-based approaches targeting TSPAN8 have been reported to yield promising results in experimental models.[3,4,5] However, the fact that this study is entirely bioinformatics- and public database-based, lacks experimental validation, and has a small sample size in some subgroup analyses are among its significant limitations. Nevertheless, the consistent validation of expression increases across multiple databases, the preservation of independent prognostic significance in multivariate analyses, and the convergence of mechanistic analyses around a common exosome/ESCRT axis support the overall reliability of the findings.

CONCLUSION

TSPAN8 is a biomarker candidate that exhibits increased expression in lung adenocarcinoma compared to normal lung tissue, is associated with better survival in certain clinical subgroups, and retains its independent prognostic value in multivariate models. However, its prognostic impact is not uniform across all subgroups and may vary between databases. From a mechanistic perspective, the study suggests that TSPAN8's effects related to metastasis may be linked to exosome biogenesis, ESCRT-dependent endosomal trafficking, and vesicular secretion processes rather than classical EMT, ECM/invasion, angiogenesis, and proliferation pathways. Therefore, TSPAN8 should be evaluated in further experimental studies as both a potential prognostic biomarker and a possible regulator of exosome-mediated tumor biology in LUAD.

REFERENCES

1. Xin S, Wen M, Tian Y, et al. Impact of histopathological subtypes on invasive lung adenocarcinoma: from epidemiology to tumour microenvironment to therapeutic strategies. *World J Surg Oncol* . 2025;23(1). doi:10.1186/s12957-025-03701-9

2. Zhou SK, Zeng DH, Zhang MQ, et al. Identification of lung adenocarcinoma subtypes and a prognostic signature based on activity changes of the hallmark and immunologic gene sets. *Heliyon*. 2024;10(7):e28090. doi:10.1016/j.heliyon.2024.e28090

3. Kim JW, Cho Y Bin, Lee S. Cell surface grp94 as a novel emerging therapeutic target for monoclonal antibody cancer therapy. *Cells*. 2021;10(3):1-19. doi:10.3390/cells10030670

4. Zhang H, Song Q, Shang K, Li Y, Jiang L, Yang L. Tspan protein family: focusing on the occurrence, progression, and treatment of cancer. *Cell Death Discov*. 2024;10(1). doi:10.1038/s41420-024-01961-0

5. Yang J, Zhang Z, Lam JSW, Fan H, Fu NY. Molecular Regulation and Oncogenic Functions of TSPAN8. *Cells*. 2024;13(2):1-25. doi:10.3390/cells13020193

6. Mu W, Provaznik J, Hackert T, Zöller M. Tspan8-Tumor Extracellular Vesicle-Induced Endothelial Cell and Fibroblast Remodeling Relies on the Target Cell-Selective Response. Cells. 2020;9(2):319. doi:10.3390/cells9020319.

7. Liu Y, Fan J, Xu T, et al. Extracellular vesicle tetraspanin-8 level predicts distant metastasis in non-small cell lung cancer after concurrent chemoradiation. *Sci Adv*. 2020;6(11):1-10. doi:10.1126/sciadv.aaz6162

8. Tang Z, Kang B, Li C, Chen T, Zhang Z. GEPIA2: an enhanced web server for large-scale expression profiling and interactive analysis. *Nucleic Acids Res*. 2019;47(W1):W556-W560. doi:10.1093/nar/gkz430

9. Bartha Á, Győrffy B. Tnmplot.Com: A web tool for the comparison of gene expression in normal, tumor and metastatic tissues. *Int J Mol Sci*. 2021;22(5):1-12. doi:10.3390/ijms22052622

10. Gyorffy B, Surowiak P, Budczies J, Lánczky A. Online survival analysis software to assess the prognostic value of biomarkers using transcriptomic data in non-small-cell lung cancer. *PLoS One*. 2013;8(12). doi:10.1371/journal.pone.0082241

11. Lánczky A, Győrffy B. Web-based survival analysis tool tailored for medical research (KMplot): Development and implementation. *J Med Internet Res*. 2021;23(7):1-7. doi:10.2196/27633

12. Szklarczyk D, Gable AL, Nastou KC, et al. Erratum: The STRING database in 2021: customizable protein–protein networks, and functional characterization of user-uploaded gene/measurement sets (Nucleic Acids Research (2021) 49 (D605–D612) DOI: 10.1093/nar/gkaa1074). *Nucleic Acids Res*. 2021;49(18):10800. doi:10.1093/nar/gkab835

13. Yue S, Mu W, Erb U, Zöller M. The tetraspanins CD151 and Tspan8 are essential exosome components for the crosstalk between cancer initiating cells and their surrounding. *Oncotarget*. 2015;6(4):2366-2384. doi:10.18632/oncotarget.2958

14. Andreu Z, Yáñez-Mó M. Tetraspanins in extracellular vesicle formation and function. *Front Immunol*. 2014;5(SEP):1-12. doi:10.3389/fimmu.2014.00442

15. Nazarenko I, Rana S, Baumann A, et al. Cell surface tetraspanin Tspan8 contributes to molecular pathways of exosome-induced endothelial cell activation. *Cancer Res*. 2010;70(4):1668-1678. doi:10.1158/0008-5472.CAN-09-2470

16. Colombo M, Raposo G, Théry C. Biogenesis, secretion, and intercellular interactions of exosomes and other extracellular vesicles. *Annu Rev Cell Dev Biol*. 2014;30:255-289. doi:10.1146/annurev-cellbio-101512-122326

17. Ostrowski M, Carmo NB, Krumeich S, et al. Rab27a and Rab27b control different steps of the exosome secretion pathway. *Nat Cell Biol*. 2010;12(1):19-30. doi:10.1038/ncb2000

18. Jackson CE, Scruggs BS, Schaffer JE, Hanson PI. Effects of Inhibiting VPS4 Support a General Role for ESCRTs in Extracellular Vesicle Biogenesis. *Biophys J*. 2017;113(6):1342-1352. doi:10.1016/j.bpj.2017.05.032

19. Adell MAY, Vogel GF, Pakdel M, et al. Coordinated binding of Vps4 to ESCRT-III drives membrane neck constriction during MVB vesicle formation. *J Cell Biol*. 2014;205(1):33-49. doi:10.1083/jcb.201310114

20. Saviana M, Romano G, Le P, Acunzo M, Nana-Sinkam P. Extracellular vesicles in lung cancer metastasis and their clinical applications. *Cancers (Basel)*. 2021;13(22):1-29. doi:10.3390/cancers13225633

21. Han QF, Li WJ, Hu KS, et al. Exosome biogenesis: machinery, regulation, and therapeutic implications in cancer. *Mol Cancer*. 2022;21(1):1-26. doi:10.1186/s12943-022-01671-0

RELATIONSHIP BETWEEN CLINICAL AND LABORATORY PARAMETERS AND CLINICAL OUTCOMES IN PATIENTS WITH CARBON MONOXIDE POISONING: A THREE-MONTH RETROSPECTIVE ANALYSIS

İsmail AĞI
Yerköy Devlet Hastanesi, Uzmanlık Alanı: Acil Tıp Uzmanı
ORCID: 0000-0002-8754-1744

Ümmühan Tuğba TÜMÜKLÜ
Yozgat Bozok Üniversitesi, Tıp Fakültesi, Göğüs Hastalıkları ABD, Uzmanlık Alanı: Göğüs Hastalıkları Uzmanı
ORCID: 0009-0002-2998-9740

Abstract

Objective: Carbon monoxide (CO) poisoning remains an important cause of morbidity and mortality, particularly in rural settlements during the winter months. This study aimed to evaluate the demographic characteristics, clinical and laboratory parameters, and clinical outcomes of patients presenting to a secondary-level district hospital with a diagnosis of CO poisoning. It also sought to investigate the relationship between biochemical markers -particularly carboxy hemoglobin (COHb), lactate, troponin, and C-reactive protein (CRP)- and outcome indicators such as discharge, ward admission, intensive care unit requirement, and mortality. In this way, the study aimed to define a district-specific clinical profile independent of large tertiary centers and to contribute to the planning of regional health services.

Materials and Methods: This single-center, retrospective, cross-sectional study was conducted on patients aged 7 years and older who were diagnosed with carbon monoxide (CO) poisoning and presented to the Emergency Department of Yerköy State Hospital between December 1, 2025, and February 28, 2026, following approval from the Yozgat Bozok University Non-Interventional Clinical Research Ethics Committee. Data were retrospectively collected from the hospital's electronic medical records and automation system, including age, sex, comorbid diseases, Glasgow Coma Scale (GCS) score, arterial blood gas parameters, COHb, lactate, urea, creatinine, glucose, electrolytes, complete blood count, CRP, and troponin levels, as well as whether hyperbaric oxygen therapy (HBOT) was administered and the clinical outcomes. Statistical analyses were performed using SPSS version 22. Parametric and non-parametric tests were applied according to data distribution, the chi-square test was used for categorical variables, and logistic regression analysis was performed to identify independent predictors. A p value of <0.05 was considered statistically significant.

Results: A total of 14 patients who presented with a diagnosis of carbon monoxide (CO) poisoning were included in the study. The mean age of the patients was 47.4 ± 21.6 years, and 57.1% were male. The most common presenting symptoms were headache/dizziness (71.4%) and nausea (64.3%), and the vast majority of patients (92.9%) were assessed as fully conscious. The mean COHb level was 25.5 ± 12.6%, and the mean lactate level was 3.78 ± 1.71 mmol/L. Six patients (42.9%) had an indication for hyperbaric oxygen therapy (HBOT), whereas only three patients (21.4%) were able to receive HBOT. Patients with an indication for HBOT had significantly higher age, lactate, and CRP levels ($p<0.05$). In terms of clinical outcome, patients requiring hospitalization had significantly lower pH levels ($p=0.005$). No mortality was observed.

Conclusion: The clinical severity of carbon monoxide (CO) poisoning cannot be adequately assessed by a single parameter alone; indicators such as lactate, CRP, and pH provide important additional value beyond COHb levels in the clinical decision-making process. The fact that HBOT could not be administered to a considerable proportion of patients with an indication for treatment suggests that systemic and access-related limitations may play a decisive role in clinical management. These findings highlight the need for early diagnosis, multiparametric assessment, and improved access to appropriate treatment, particularly in peripheral healthcare centers.

Keywords: carbon monoxide poisoning, carboxyhemoglobin, hyperbaric oxygen therapy

Introduction

Carbon monoxide (CO) poisoning continues to be one of the leading causes of preventable morbidity and mortality worldwide. The difficulty in detecting this colorless, odorless, and non-irritating gas further increases the danger posed by its clinically silent nature [1]. CO binds to hemoglobin with an affinity approximately 200–250 times greater than that of oxygen, leading to the formation of carboxyhemoglobin (COHb); this process triggers tissue hypoxia and severe mitochondrial dysfunction [2]. In addition, the effects of CO on myoglobin and the cytochrome oxidase system play a pivotal role in the pathogenesis of cardiac and neurological complications. This multidimensional mechanism of injury places the clinical management of CO poisoning far beyond a merely symptomatic approach [3]. The diagnostic challenges and nonspecific nature of its symptoms may cause many cases presenting to the emergency department to be overlooked, thereby creating a significant diagnostic pitfall for clinicians [4].

From an epidemiological perspective, CO poisoning remains a major global public health concern. In the United States, tens of thousands of emergency department visits each year, along with a considerable number of deaths, have been reported to be associated with this gas; similarly, in Europe, a marked increase in cases is observed particularly during the winter months [5]. In terms of clinical management, normobaric oxygen therapy is widely accepted as the mainstay of treatment. In addition, consensus recommendations have been published regarding the indications and treatment protocols for hyperbaric oxygen therapy (HBOT). These recommendations clearly emphasize that HBOT should be prioritized in patients with elevated COHb levels, loss of consciousness, neurological manifestations, or evidence of cardiac involvement [6].

The broad clinical spectrum of CO poisoning makes case management particularly challenging. Clinical manifestations may range from subtle and nonspecific symptoms such as headache, nausea, and dizziness to cardiac ischemia, arrhythmia, and profound impairment of consciousness, requiring clinicians to assess each case within its individual clinical context [7]. Studies examining the profile of patients presenting to emergency departments with CO poisoning in Türkiye have shown that cases are more frequent during the winter months, exposures related to inadequate stove and chimney systems are predominant, and clustered family cases are commonly observed, particularly among young adults and children [8]. Analyses of the geographical distribution of national mortality data further indicate that the risk of CO-related death is markedly higher in rural areas than in urban settings, a disparity largely driven by traditional heating practices and inadequacies in the housing infrastructure [9]. Larger-scale studies conducted in Türkiye also support these findings, demonstrating that biochemical and clinical indicators such as COHb level, Glasgow Coma Scale (GCS) score, and troponin are strongly associated with morbidity and mortality [10].

A recurring finding in the literature is that COHb levels do not always correlate directly with clinical severity, and severe outcomes may develop even at relatively low COHb levels, particularly in older patients and in those with comorbid conditions [11]. This underscores the need to evaluate biochemical parameters and clinical prognosis within an integrated framework. HBOT markedly reduces the half-life of COHb through the administration of 100% oxygen under high pressure, thereby correcting tissue hypoxia and contributing to the prevention of neurological sequelae. Current evidence supports HBOT indications including a COHb level above 25%, a history of transient or persistent loss of consciousness, neurological findings, cardiac ischemia or arrhythmia, pregnancy, and children younger than 36 months; in the presence of these criteria, timely access to HBOT should not be delayed [12]. Conversely, untreated pneumothorax is defined as an absolute contraindication, whereas uncontrolled upper respiratory tract infections, chronic obstructive pulmonary disease, heart failure, moderate-to-severe valvular heart disease, claustrophobia, and the use of certain medications such as bleomycin, cisplatin, and disulfiram are considered relative contraindications. Particularly in provinces such as Yozgat, where no HBOT unit is available, accurate and timely assessment of these contraindications represents a critical step that directly influences the referral decision and, consequently, clinical outcomes. More recent data have provided systematic recommendations aimed at reducing clinical uncertainty regarding the timing of HBOT, risks associated with patient transport, and decision-making processes, with particular emphasis on the adverse impact of delayed treatment on neurological sequelae [13].

Most studies on CO poisoning in the existing literature have been reported from tertiary care and large-scale centers, whereas the patient profile, admission patterns, and determinants of clinical outcomes in district-level secondary healthcare institutions remain insufficiently characterized. However, in rural and semi-urban regions, the widespread use of traditional heating methods, geographical inequalities in access to HBOT, and the potential impact of referral delays on clinical outcomes make data obtained from centers at this level valuable from both scientific and public health perspectives.

Based on this gap in the literature, the planned study aims to retrospectively evaluate the demographic characteristics, clinical parameters, laboratory findings, and clinical outcomes—including discharge, ward admission, need for intensive care, and mortality—of patients aged 7 years and older who presented to the Emergency Department of Yerköy State Hospital between December 1, 2025 and February 28, 2026 and were diagnosed with CO poisoning. One of the primary objectives of the study is also to examine the association between biochemical markers, such as COHb, lactate, troponin, and C-reactive protein (CRP), and indicators of clinical outcome. Through the findings to be obtained, the study seeks to define a district-level presentation profile and to provide a concrete contribution to the planning of regional healthcare services.

Materials and Methods

This study was designed as a single-center, retrospective, cross-sectional observational study. The study was conducted in the Emergency Department of Yerköy State Hospital, located in the Yerköy district of Yozgat, Türkiye. The study protocol was approved by the Yozgat Bozok University Non-Interventional Clinical Research Ethics Committee (approval number: 2026-GOKAEK-265_2026.03.04_55). Owing to the retrospective design of the study, the requirement for obtaining additional informed consent from patients was waived. All stages of the study were conducted in accordance with the current principles of the Declaration of Helsinki of the World Medical Association and Good Clinical Practice standards. Official permission to access hospital records was obtained from the Chief Physician's Office of Yerköy State Hospital, and all personal data collected within the scope of the study were processed and stored in compliance with the provisions of the Turkish Personal Data Protection Law No. 6698.

The data collection period covered the interval between December 1, 2025 and February 28, 2026. This period was selected because it corresponds to the winter months, during which the use of coal and wood-burning stoves increases in the region, making it a particularly relevant timeframe for evaluating cases of carbon monoxide poisoning. The fact that Yerköy is a district with a high rural population density, widespread use of traditional heating methods, and limited direct access to hyperbaric oxygen therapy makes this setting important for defining the district-level profile of carbon monoxide poisoning.

The study population consisted of all patients aged 7 years and older who presented to the Emergency Department of Yerköy State Hospital during the specified period and were diagnosed with carbon monoxide poisoning using the ICD-10 code T58. Given the retrospective design of the study, no a priori sample size calculation was performed; instead, all cases meeting the inclusion criteria during the study period were included. The inclusion criteria were presentation between December 1, 2025 and February 28, 2026, age of 7 years or older, and a diagnosis of carbon monoxide poisoning supported by the clinical presentation. Patients whose essential clinical or laboratory data could not be accessed and those with another concomitant poisoning diagnosis unrelated to carbon monoxide poisoning were excluded. No control group was formed; rather, the clinical and laboratory characteristics of patients diagnosed with carbon monoxide poisoning and their clinical outcomes were evaluated within the study cohort.

Data were obtained retrospectively from the electronic health record system and hospital automation infrastructure of Yerköy State Hospital. No additional diagnostic test, intervention, or treatment was performed for the purposes of the study; only data recorded during routine emergency department evaluation based on clinical necessity were used. For each patient, demographic characteristics, clinical findings, laboratory parameters, treatment-related variables, and clinical outcomes were recorded. Demographic and clinical variables included age, sex, presence of comorbid chronic disease, and level of consciousness at presentation. The level of consciousness was assessed using the Glasgow Coma Scale. Comorbid chronic diseases, including hypertension, diabetes mellitus, coronary artery disease, chronic obstructive pulmonary disease, and similar conditions, were recorded.

Laboratory assessment included arterial blood gas parameters and routine biochemical markers. Accordingly, pH, partial pressure of oxygen, partial pressure of carbon dioxide, base deficit, and carboxyhemoglobin level; serum lactate, urea, creatinine, glucose, sodium, potassium, and chloride levels; complete blood count parameters; C-reactive protein; and troponin levels were recorded. The association of these parameters with clinical outcomes was further evaluated.

Regarding the treatment process, the presence or absence of an indication for hyperbaric oxygen therapy was retrospectively assessed for each patient. This assessment was based on level of consciousness, neurological findings, carboxyhemoglobin level, presence of metabolic acidosis, evidence of cardiac involvement, and clinical response to normobaric oxygen therapy. In addition, patient records were reviewed for contraindications that could preclude hyperbaric oxygen therapy. In this context, the presence of untreated pneumothorax, bullous lung disease, uncontrolled epilepsy, middle ear pathologies, and similar conditions was evaluated. Among patients with an indication for hyperbaric oxygen therapy, whether the treatment was actually administered was recorded. If hyperbaric oxygen therapy was not administered, the reason was documented as being related to a contraindication, inability to refer the patient, logistical limitations, or patient refusal.

Clinical outcomes were classified into four main categories: discharge from the emergency department, ward admission, intensive care unit admission, and in-hospital mortality. The indication for hyperbaric oxygen therapy, presence of contraindications, and whether the treatment was administered were analysed in relation to these clinical outcome categories.

Statistical analyses were performed using SPSS for Windows, Version 22.0. The normality of continuous variables was assessed using the Kolmogorov-Smirnov test. Normally distributed continuous variables were expressed as mean ± standard deviation, whereas non-normally distributed variables were presented as median with appropriate measures of distribution. Categorical variables were expressed as numbers and percentages. For comparisons between two independent groups, the independent samples t-test was used for normally distributed variables, while the Mann-Whitney U test was used for non-normally distributed variables. Categorical variables were compared using the chi-square test. Associations between variables were assessed using Pearson correlation analysis for parametric data and Spearman correlation analysis for non-parametric data. Logistic regression analysis was performed to identify independent factors associated with clinical outcomes. A p value of <0.05 was considered statistically significant in all analyses.

Results

A total of 14 patients were included in the study. The mean age was 47.4 ± 21.6 years, with an age range of 18–82 years. Of the patients, 8 were male (57.1%) and 6 were female (42.9%). The number of comorbid conditions ranged from 0 to 3. The most common comorbidity was diabetes mellitus (n=3, 21.4%), followed by hypertension, hyperlipidemia, and coronary artery disease, each observed in two patients (14.3%). Chronic kidney disease, asthma, and pulmonary thromboembolism were each present in one patient (7.1%). Nine patients with CO poisoning had no known comorbid disease. No history of atrial fibrillation, arrhythmia, dementia, heart failure, or cerebrovascular disease was identified in any patient.

When presenting symptoms were evaluated, headache/dizziness was observed in 10 patients (71.4%), nausea in 9 patients (64.3%), syncope in 3 patients (21.4%), and dyspnea in 1 patient (7.1%); chest pain was not reported in any patient. At presentation, 13 patients (92.9%) were conscious, while 1 patient (7.1%) was confused. No patient presented with loss of consciousness.

The laboratory parameters at presentation are presented in Table 1. In the arterial blood gas analysis, the mean pH was 7.39 ± 0.06, pCO_2 was 39.6 ± 8.2 mmHg, COHb was 25.5 ± 12.6%, and lactate was 3.78 ± 1.71 mmol/L. Regarding biochemical parameters, the mean urea level was 36.2 ± 13.5 mg/dL, creatinine was 0.91 ± 0.30 mg/dL, glucose was 150.8 ± 54.6 mg/dL, sodium was 139.1 ± 1.7 mEq/L, potassium was 3.95 ± 0.51 mEq/L, and chloride was 105.0 ± 1.9 mEq/L. Complete blood count parameters showed a mean hemoglobin level of 15.0 ± 2.3 g/dL, white blood cell count of 9.68 ± 2.26 × 10^3/µL, lymphocyte count of 2.24 ± 1.32 × 10^3/µL, and neutrophil count of 6.79 ± 2.39 × 10^3/µL. Since CRP and troponin values were not normally distributed ($p<0.05$), non-parametric methods were

used in analyses involving these parameters. The median CRP level was 3.0 mg/L (range: 1–68 mg/L), and the median troponin level was 8.3 pg/mL (range: 2.5–749.9 pg/mL).

Table 1. Laboratory findings at presentation and clinical comparisons of the patients

Parameter	Mean ± SD	Median	Range	p value
Blood gas parameters				
pH	7,39 ± 0,06	7,41	7,27–7,47	0,005†
pCO_2 (mmHg)	39,6 ± 8,2	40,6	19,8–52,4	NS
COHb (%)	25,5 ± 12,6	31,2	2,0–37,3	NS
Laktat (mmol/L)	3,78 ± 1,71	3,60	1,5–8,1	0,024‡
Biochemical parameters				
Urea (mg/dL)	36,2 ± 13,5	33,5	20,2–65,8	NS
Creatinine (mg/dL)	0,91 ± 0,30	0,90	0,4–1,7	NS
Glucose (mg/dL)	150,8 ± 54,6	138,0	85–315	NS
Sodium (mEq/L)	139,1 ± 1,7	139,0	136–141	NS
Potassium (mEq/L)	3,95 ± 0,51	3,83	3,28–5,30	NS
Chloride (mEq/L)	105,0 ± 1,9	104,6	102–109,5	NS
Complete blood count				
Hemoglobin (g/dL)	15,0 ± 2,3	15,7	10,5–17,8	NS
White blood cell count ($\times 10^3/\mu L$)	9,68 ± 2,26	9,59	5,06–13,27	NS
Lymphocyte count ($\times 10^3/\mu L$)	2,24 ± 1,32	2,30	0,46–5,28	NS
Neutrophil count ($\times 10^3/\mu L$)	6,79 ± 2,39	6,32	3,56–11,90	NS
Inflammatory and cardiac markers				
CRP (mg/L) ††	11,6 ± 22,5	3,0	1,0–68,0	0,036‡
Troponin (pg/mL) ††	108,5 ± 205,3	8,3	2,5–749,9	NS

Abbreviations: SD, standard deviation; COHb, carboxyhemoglobin; NS, not statistically significant.

†Comparison between admitted and discharged patients
‡ Comparison between patients with and without an indication for HBOT

†† Since CRP and troponin values were not normally distributed ($p<0.05$), median values should be considered for interpretation.

An indication for HBOT was identified in 6 patients (42.9%). When patients with and without an indication for HBOT were compared in terms of age, the age variable was evaluated using non-parametric methods because it was not normally distributed. The median age was 28.5 years (minimum–maximum: 18–76) in the group without an indication for HBOT, whereas it was 60 years (minimum–maximum: 55–82) in the group with an indication for HBOT; this difference was statistically significant (U=5.000; p=0.014). The lactate level was 2.93 ± 1.12 mmol/L in patients without an HBOT indication and was significantly higher in those with an HBOT indication, at 4.92 ± 1.76 mmol/L (2.93 ± 1.12 mmol/L vs. 4.92 ± 1.76 mmol/L; t=-2.594; p=0.024). Since CRP values were not normally distributed, they were analyzed using non-parametric methods and were significantly higher in the group with an HBOT indication [median (minimum–maximum): 4.50 (2.00–68.00) vs. 2.00 (1.00–6.00) mg/L; U=8.000; p=0.036]. No significant differences were observed between the groups in terms of COHb, WBC, or troponin levels (all p>0.05). Among the 6 patients with an indication for HBOT, 1 patient (16.7%) had a contraindication to HBOT, and HBOT could be administered to 3 patients (50.0%). The remaining 2 patients (33.3%) refused treatment and left the hospital because referral to another province was required and logistical constraints were present. When the entire study cohort was evaluated, only 3 of the 14 patients (21.4%) received HBOT (Figure 1).

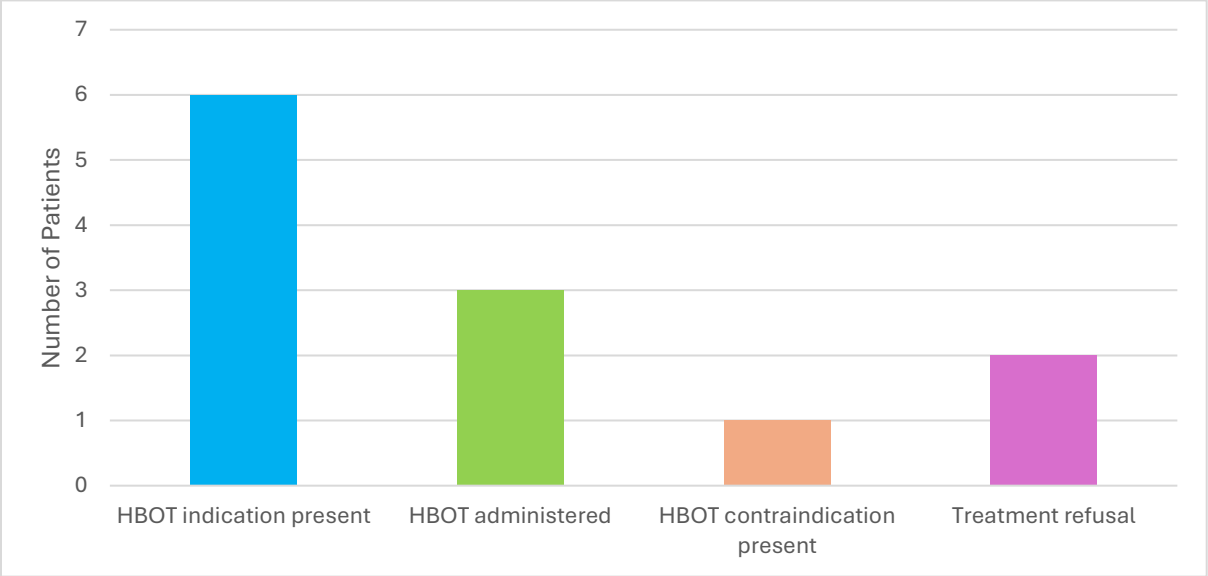


Figure 1. Distribution of hyperbaric oxygen therapy indication, contraindication status, and treatment administration in the study cohort

When the distribution of clinical outcomes was evaluated, 5 patients (35.7%) were discharged, 2 patients (14.3%) were admitted to the ward, 1 patient (7.1%) was admitted to the intensive care unit, and 6 patients (42.9%) refused treatment. No mortality was observed during the study period. After excluding patients who refused treatment from the analysis, patients requiring hospitalization (ward + intensive care unit, n=3) were compared with those who were discharged (n=5). The pH value was significantly lower in the hospitalized group than in the discharged group (7.32 ± 0.06 vs. 7.44 ± 0.02; t=−4.266, p=0.005). Although the mean age was higher in the hospitalized group, this difference did not reach statistical significance (71.0 ± 14.2 vs. 39.0 ± 20.0 years; t=2.395, p=0.054). Similarly, although troponin levels appeared to be higher in the hospitalized group, the difference was not statistically significant (median 6.33 vs. 3.40 pg/mL; Mann–Whitney U=2.000; Z=−1.640; p=0.101). No significant differences were detected between the groups in terms of COHb level or sex distribution (t=−2.015, p=0.091; Fisher's exact test p=1.000, respectively) (Figure 2).

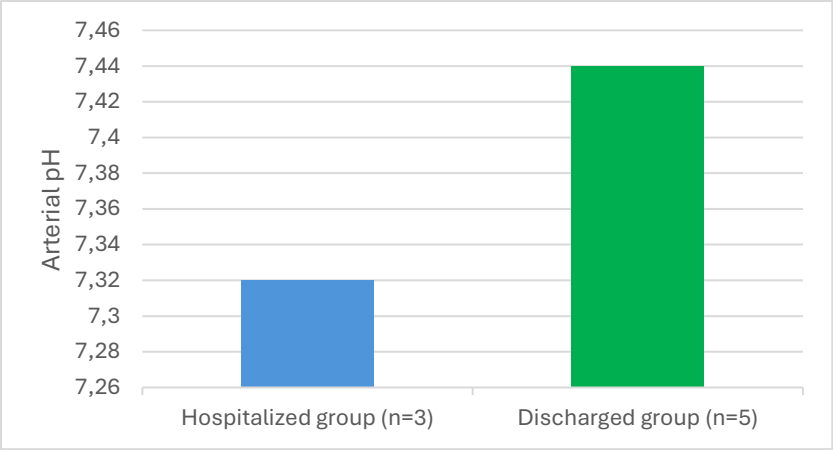


Figure 2. Comparison of arterial pH values according to clinical outcome groups. Bars represent group means, and error bars indicate standard deviation. Independent samples t-test; t=−4.266, p=0.005.

In the Pearson correlation analysis, a significant negative correlation was observed between pH and age (r=−0.590, p=0.026). The negative trend between troponin and COHb, as well as the positive trend between COHb and pH, did not reach statistical significance (r=−0.468, p=0.092; r=0.412, p=0.143, respectively). In the Spearman correlation analysis performed for CRP, the positive trend between CRP and lactate was also not statistically significant (r=0.466, p=0.093). The correlations between CRP and all other parameters did not reach the threshold for statistical significance (all p>0.05).

Discussion

CO poisoning is one of the relatively uncommon emergency conditions in which clinicians cannot make decisions based solely on a single laboratory value; instead, they must simultaneously consider the patient's age, comorbidity burden, level of consciousness, and access to treatment resources. This study was conducted in a setting that reflects this reality in its most practical form: a district state hospital in a province without an HBOT center. In this context, the study provides findings that are worthy of discussion at both the clinical and healthcare system levels.

In our study, the mean age was 47.4 ± 21.6 years, and more than half of the patients were male (57.1%). This demographic profile is broadly consistent with similar studies conducted in Türkiye. In the large case series by Yurtseven et al., which evaluated patients presenting to the emergency department with CO poisoning, the median age was reported as 35 years, with a slight male predominance [8]. Although the ten-year cohort study conducted by Öz et al. in Adıyaman revealed a younger patient profile compared with our series, with a mean age of 27.1 years, male sex was shown to be associated with a 1.886-fold higher risk of mortality [10].

No statistically significant association was observed between sex and clinical outcome (Fisher's exact test, p=1.000). This finding is likely related to the small sample size and should be further evaluated in larger series. The fact that most patients were in the 40–65-year age group (50.0%) and that only two patients (14.3%) were older than 65 years suggests that the district-level presentation profile may differ from that observed in large urban hospitals.

In our series, 71.4% of patients presented with headache and dizziness, while 64.3% presented with nausea. Chest pain was not observed in any patient, and the vast majority of patients (92.9%) were conscious at presentation. The clinical presentation of CO poisoning may begin with nonspecific symptoms that can mimic many different conditions, such as headache, dizziness, and nausea, and may progress across a broad spectrum ranging from loss of consciousness and cardiac ischemia to death [4,6]. This nonspecific presentation remains one of the most misleading clinical pitfalls for primary care and emergency physicians. Similarly, in the retrospective series of 450 patients reported by Yildiz et al., a substantial proportion of cases presented with relatively mild clinical features and without prominent neurological symptoms [14].

In our study, only one patient presented with confusion, suggesting either that more severe cases may have been referred to a higher-level center before reaching our district hospital or that the cases

encountered in our setting were those in which CO exposure was recognized relatively early. The mean COHb level in our study was 25.5 ± 12.6%, and 71.4% of the patients had a COHb level of 25% or higher. However, the mean COHb level was 8.9% in the group requiring hospitalization and 26.6% in the discharged group. Although this inverse pattern did not reach statistical significance (t=−2.015, p=0.091), it is clinically noteworthy. Weaver emphasized that COHb levels do not always directly reflect clinical severity, and that severe outcomes may occur despite low COHb levels, particularly in older patients and individuals with comorbidities [7]. The study by Vural et al., which focused on special patient groups, similarly demonstrated that severe clinical presentations may occur in older individuals even at relatively low COHb thresholds [15]. In this context, our findings once again illustrate, through a concrete patient population, how misleading it can be to use COHb alone as a marker of severity. The observed negative trend between troponin and COHb (r=−0.468, p=0.092) also supports the same message: cardiac injury does not necessarily accompany high COHb levels, and the cellular-level effects of CO may become clinically apparent even at lower COHb values [3].

The mean lactate level was 3.78 ± 1.71 mmol/L, and more than one-third of the patients (35.7%) had lactate levels above 4 mmol/L in our study. Lactate levels were markedly higher in the group with an indication for HBOT than in those without an indication (4.92 ± 1.76 vs. 2.92 ± 1.12 mmol/L; U=40.5, p=0.038). CO is known to inhibit mitochondrial cytochrome oxidase, thereby impairing aerobic metabolism and promoting tissue lactate accumulation [3]. This mechanism makes lactate a direct reflection of CO toxicity at the cellular level, beyond the information provided by COHb alone. Studies that have systematically evaluated the relationship among lactate, troponin, and COHb have demonstrated that lactate has independent value in predicting clinical severity [11]. Yildiz et al. also showed in their series of 450 patients that elevated lactate levels were associated with hospital admission and the need for HBOT [14]. In our study, the positive trend observed between CRP and lactate (r=0.466, p=0.093) may indicate that tissue hypoxia and the inflammatory response occur in parallel; however, the failure of this association to reach statistical significance may be explained by the limited sample size.

Among the clinical outcome comparisons, pH yielded the most robust statistical finding. The mean pH was 7.32 ± 0.06 in the group requiring hospitalization, compared with 7.44 ± 0.02 in the discharged group (t=−4.266, p=0.005). Moreover, a significant negative correlation was found between pH and age (r=−0.590, p=0.026), suggesting that older patients may have a reduced metabolic buffering capacity and may develop more pronounced acidosis even under similar exposure conditions. In CO poisoning, metabolic acidosis is regarded as a reflection of tissue hypoxia and mitochondrial dysfunction, and it is included in current guidelines as an important parameter for both HBOT indication and prognosis [6,11]. In the consensus statement published by Anand et al. in 2025, the presence of metabolic acidosis, particularly when accompanied by symptoms resistant to normobaric oxygen therapy, is also listed among the criteria that strengthen the decision for HBOT [13]. Our findings are consistent with these guidelines and support the prioritization of pH as an easily measurable parameter that can reliably reflect clinical severity, especially in small-scale healthcare centers.

In our study, troponin levels tended to be higher in the hospitalized group than in the discharged group; however, the difference did not reach statistical significance (Mann–Whitney U=2.000; p=0.101), which is closely related to the small sample size. Nevertheless, troponin levels were observed to exceed the upper reference limit in 42.9% of the patients. It is well known that CO directly affects cardiomyocytes by inhibiting the cytochrome oxidase system, thereby predisposing patients to myocardial injury [3]. In a large series of 900 patients, Patel et al. demonstrated that elevated troponin levels were independently associated with the need for mechanical ventilation and in-hospital mortality [16]. The study by Liu et al., which focused on moderate-to-severe CO poisoning, also showed that troponin elevation was a strong predictor of adverse cardiovascular events [17]. In our study, the negative trend observed between troponin and COHb (r=−0.468, p=0.092) supports the hypothesis that cardiac injury may also develop through a pathophysiological process independent of COHb. This finding once again emphasizes that cardiac biomarkers should be monitored in every patient with CO poisoning, regardless of the carboxyhemoglobin level.

The median CRP concentration was 3.0 mg/L, with only 14.3% of patients showing values above 10 mg/L. CRP was markedly higher in the group with an indication for HBOT [4.50 (min–max: 2.00–

68.00) vs. 2.00 (min–max: 1.00–6.00) mg/L; U=8.000, p=0.036]. In CO poisoning, the inflammatory cascade is triggered through multistep mechanisms, including neutrophil activation, lipid peroxidation, and modification of cytochromes by CO, with CRP emerging as a peripheral marker of this response [3]. In Suzuki's retrospective study evaluating CK, LDH, and CRP together, peak CRP levels were reported to be significantly associated with delayed neurological sequelae; moreover, the peak values of these parameters were found to be stronger predictors than their values at presentation [18]. In our study, the positive correlation trend between CRP and lactate, which approached the threshold for statistical significance (r=0.466, p=0.093), supports the hypothesis that inflammation and tissue hypoxia may progress in parallel; however, this relationship needs to be confirmed in larger cohorts.

Perhaps the most distinctive aspect of our study and the section that provides the most meaningful contribution to the literature is the HBOT-related data. An indication for HBOT was identified in six patients (42.9%); however, treatment could be administered to only three patients (21.4%). Among the three patients in whom an indication was confirmed but HBOT could not be delivered, one had a contraindication to HBOT, while the other two refused treatment and left the hospital because referral to another province was required and logistical constraints were present. This finding clearly demonstrates that the treatment decision is shaped not only by clinical knowledge and available equipment, but also by geographical and systemic barriers. Strong evidence supports that HBOT accelerates COHb elimination, suppresses neuroinflammation, and contributes to the prevention of delayed neurological sequelae [11,12]. In the review by Sethuraman and Thom, HBOT administered at 2.5–3.0 atmospheres absolute was reported to significantly reduce the risk of neurological sequelae; moreover, this effect was emphasized to increase approximately 20-fold when treatment was initiated within 200 minutes [12]. On the other hand, the network meta-analysis of randomized controlled trials by Huang et al. showed that the evidence regarding the effects of HBOT on mortality and neurological sequelae remains controversial [19]. At this point, the critical issue is not only establishing the correct indication, but also ensuring the presence of a healthcare system in which that decision can be translated into actual treatment.

Our study documents with concrete data how high the rate of HBOT indication may be at the district level in a setting without an HBOT center, and how existing infrastructural limitations may restrict patient management. This finding goes beyond being merely a clinical observation; it has the potential to directly inform policy decisions regarding regional healthcare infrastructure planning. In our study, 5 patients (35.7%) were discharged, 3 patients (21.4%) required hospitalization, and 6 patients (42.9%) refused treatment. No mortality was observed. The remarkably high rate of treatment refusal is noteworthy; this finding suggests that patients living in rural areas may prefer returning home rather than remaining in hospital, and it points to an important social issue related to health literacy. In the study by Öz et al. based on data from Türkiye, inadequate follow-up after CO poisoning was shown to be an independent risk factor for the development of new morbidities [10]. In this context, follow-up of patients who refuse treatment and the development of targeted educational strategies for this group should become one of the priority agenda items for district-level healthcare services. It should also be acknowledged that excluding cases of treatment refusal from the clinical analysis limited the statistical power of the clinical outcome comparisons in our study.

The main strength of this study is that it presents original data from a district-level secondary care center, a setting that remains insufficiently represented in the literature. By simultaneously evaluating local dynamics that large-scale studies often fail to capture -such as seasonal exposure patterns, stove-related cases, limitations in access to HBOT, and treatment refusal- this study is particularly valuable from the perspective of regional healthcare planning. Nevertheless, the sample size of 14 patients represents the most prominent limitation of the study. This limitation may have prevented clinically meaningful differences, particularly those related to troponin and age, from reaching statistical significance and made multivariable analyses infeasible. Limitations inherent to the retrospective design should also be considered, including the inability to systematically record exposure duration, definitively identify the source of CO exposure, and determine the exact time of symptom onset. Despite these limitations, the findings provide a strong hypothesis-generating basis for larger multicenter studies and clearly demonstrate the need for further research in this field.

Conclusion

CO poisoning is a complex emergency condition that requires a multidimensional approach, as clinical severity cannot be reliably assessed using a single parameter alone. The findings of this study suggest that parameters such as lactate, CRP, and pH may provide meaningful information in the clinical decision-making process, independent of COHb levels. In particular, the strong association between pH and clinical outcome, together with the age-related tendency toward more pronounced acidosis, highlights the value of this parameter as a practical prognostic indicator, even in smaller healthcare centers. The fact that HBOT could not be administered to a substantial proportion of patients with an indication for treatment further suggests that clinical management is shaped not only by medical factors, but also by geographical and systemic barriers.

Effective patient management requires the integration of early diagnosis, multiparametric clinical assessment, and timely access to appropriate treatment. Strengthening diagnostic and therapeutic processes in peripheral centers is critically important for improving individual patient outcomes and reducing the burden on the healthcare system. By presenting concrete data reflecting district-level clinical realities, this study is expected to provide a foundation for larger-scale studies in this field.

References

1. Ernst, A., & Zibrak, J. D. (1998). Carbon monoxide poisoning. *New England Journal of Medicine, 339*(22), 1603–1608. https://doi.org/10.1056/NEJM199811263392206
2. Rose, J. J., Wang, L., Xu, Q., McTiernan, C. F., Shiva, S., Tejero, J., & Gladwin, M. T. (2017). Carbon monoxide poisoning: Pathogenesis, management, and future directions of therapy. *American Journal of Respiratory and Critical Care Medicine, 195*(5), 596–606. https://doi.org/10.1164/rccm.201606-1275CI
3. Chenoweth, J. A., Albertson, T. E., & Greer, M. R. (2021). Carbon monoxide poisoning. *Critical Care Clinics, 37*(3), 657–672. https://doi.org/10.1016/j.ccc.2021.03.010
4. Eichhorn, L., Thudium, M., & Jüttner, B. (2018). The diagnosis and treatment of carbon monoxide poisoning. *Deutsches Ärzteblatt International, 115*(51–52), 863–870. https://doi.org/10.3238/arztebl.2018.0863
5. Hampson, N. B., & Weaver, L. K. (2007). Carbon monoxide poisoning: A new incidence for an old disease. *Undersea and Hyperbaric Medicine, 34*(3), 163–168.
6. Hampson, N. B., Piantadosi, C. A., Thom, S. R., & Weaver, L. K. (2012). Practice recommendations in the diagnosis, management, and prevention of carbon monoxide poisoning. *American Journal of Respiratory and Critical Care Medicine, 186*(11), 1095–1101. https://doi.org/10.1164/rccm.201207-1284CI
7. Weaver, L. K. (2009). Clinical practice: Carbon monoxide poisoning. *New England Journal of Medicine, 360*(12), 1217–1225. https://doi.org/10.1056/NEJMcp0808891
8. Yurtseven, S., Arslan, A., Yurtseven, M. T., Poyraz, E., Kıyan, S., & Öztürk, A. (2015). Analysis of patients presenting to the emergency department with carbon monoxide intoxication. *Turkish Journal of Emergency Medicine, 15*(4), 159–162. https://doi.org/10.1016/j.tjem.2015.02.002
9. Can, G., Sayılı, U., Aksu Sayman, Ö., Kuyumcu, Ö. F., Yılmaz, D., Esen, E., Yurtseven, E., & Erginöz, E. (2019). Mapping of carbon monoxide related death risk in Turkey: A ten-year analysis based on news agency records. *BMC Public Health, 19*(1), 9. https://doi.org/10.1186/s12889-018-6342-4
10. Öz, E., Küçükkelepçe, O., Kurt, O., & Vural, A. (2023). Carbon monoxide poisoning: Beyond survival—Mortality, morbidities, and risk factors, a Turkey sample. *PeerJ, 11*, e16093. https://doi.org/10.7717/peerj.16093
11. Weaver, L. K. (2024). Carbon monoxide poisoning (Reprinted from the 2023 Hyperbaric Indications Manual, 15th edition). *Undersea and Hyperbaric Medicine, 51*(3), 253–276.
12. Sethuraman, K. N., & Thom, S. R. (2023). Hyperbaric oxygen should be used for carbon monoxide poisoning. *British Journal of Clinical Pharmacology, 89*(3), 939–941. https://doi.org/10.1111/bcp.15605
13. Anand, J., Łukasik-Głębocka, M., Robakowska, M., Kosson, D., Tobiasz, M., & Zielińska-Psuja, B. (2025). Management of acute intoxication with carbon monoxide—Polish Medical Society, Section of Clinical Toxicology position statement. *International Journal of Occupational Medicine and Environmental Health*. https://doi.org/10.13075/ijomeh.1896.02432
14. ildiz, M. N., Eroglu, S. E., Ozen, C., Yildiz, H. A., Sektioglu, B. K., & Alkan, C. (2019). Analysis of the effects of COHb, lactate, and troponin levels on the clinical process and outcome in patients admitted to the emergency service due to carbon monoxide poisoning. *Northern Clinics of Istanbul, 6*(2), 141–145. https://doi.org/10.14744/nci.2018.88709
15. Vural, A., Dolanbay, T., Ozçelik, M., Oztorun, Z. Y., Ardıc, N., Vural, A. B., & Altay, M. C. (2024). Biochemical parameters and clinical outcomes of carbon monoxide poisoning in special groups: Children, pregnant women, and the elderly. *European Review for Medical and Pharmacological Sciences, 28*(11), 3711–3724. https://doi.org/10.26355/eurrev_202406_36376
16. Patel, B., Omeh, J., Tackling, G., Gupta, R., Sahadeo, T., Villcant, V., Dussie, T., Atnas, M., Hai, O., Zeltser, R., & Makaryus, A. N. (2023). The clinical association between carbon monoxide poisoning and myocardial injury as measured by elevated troponin I levels. *Journal of Clinical Medicine, 12*(17), 5529. https://doi.org/10.3390/jcm12175529

17. Liu, Q., Gao, X., Xiao, Q., Zhu, B., Liu, Y., Han, Y., & Wang, W. (2021). A combination of NLR and sST2 is associated with adverse cardiovascular events in patients with myocardial injury induced by moderate to severe acute carbon monoxide poisoning. *Clinical Cardiology, 44*(3), 394–401. https://doi.org/10.1002/clc.23550

18. Suzuki, Y. (2021). Risk factors for delayed encephalopathy following carbon monoxide poisoning: Importance of the period of inability to walk in the acute stage. *PLOS ONE, 16*(3), e0249395. https://doi.org/10.1371/journal.pone.0249395

19. Huang, C., & Peng, Y. (2022). Should we use hyperbaric oxygen for carbon monoxide poisoning management? A network meta-analysis of randomized controlled trials. *International Journal of Environmental Research and Public Health, 19*(15), 9184. https://doi.org/10.3390/ijerph19159184

EFFECT OF DIFFERENT TEA TYPES ON THE COLOR STABILITY OF A MICROHYBRID RESIN COMPOSITE: AN IN VITRO STUDY

Fatih Bedir

Department of Restorative Dentistry, Faculty of Dentistry, Recep Tayyip Erdoğan University, Rize, Türkiye, ORCID: 0000-0002-4909-4701

Muhammet Karadaş

Department of Restorative Dentistry, Faculty of Dentistry, Recep Tayyip Erdoğan University, Rize, Türkiye, ORCID: 0000-0002-3357-6896

Abstract

Aim: The aim of this in vitro study was to evaluate the effect of commonly consumed different tea types on the color stability of a microhybrid resin composite.

Materials and Methods: Disc-shaped specimens (8 × 2 mm) were prepared using a microhybrid resin composite (Herculite Classic, Kerr) (n = 30). The specimens were randomly divided into three groups (n = 10) according to the immersion solution: white tea, green tea, and black tea. Color measurements (ΔE_{00}) were performed using a spectrophotometer (VITA Easyshade Advance) before immersion and after 24 h, 1 w, and 3 w of immersion. Two-way ANOVA and Tukey post-hoc tests were used for statistical analysis of the data ($\alpha = 0.05$).

Results: Black tea caused a significantly higher color change (ΔE_{00}) compared with the other tea types ($p < 0.05$). In the green tea and white tea groups, the increase in color change was not statistically significant ($p > 0.05$). Color change increased over time; the lowest value was observed at 24 hours, while the highest value was observed at 3 w. No statistically significant difference was found between the measurements obtained at 1 and 3 w ($p > 0.05$).

Conclusion: Black tea caused the highest level of color change in the microhybrid resin composite, whereas the effect of green and white tea was limited. Increased exposure time of the microhybrid resin composite to tea solutions resulted in greater discoloration.

Keywords: Color stability, Discoloration, Resin composite, Spectrophotometer, Tea

Introduction

In contemporary restorative dentistry, resin composites are among the most commonly selected materials for both anterior and posterior restorations, largely attributed to their adhesive bonding capability, favorable esthetic integration, and compatibility with minimally invasive preparation approaches.[1-4] The clinical performance of resin composites, which consist of an organic resin matrix, inorganic filler particles, and silane coupling agents, is primarily influenced by filler loading, particle size distribution, and matrix composition.[1,3,4] Microhybrid resin composites provide a clinically advantageous balance among mechanical strength, wear resistance, and polishability by incorporating different particle sizes in a well-distributed manner; therefore, they are frequently preferred in a wide range of restorative indications.[1,2,4]

However, resin composites have several inherent limitations. Polymerization shrinkage, water absorption, matrix degradation, surface roughening, and decreased long-term color stability are among the most prominent drawbacks.[1,3,5] Clinical failure is not only associated with fracture or secondary caries but also with deterioration of esthetic properties.[2] Discoloration in resin composite results from the combined effects of intrinsic factors, such as inadequate polymerization, aging of the initiator systems, and oxidation within the resin matrix, and extrinsic factors, including the adsorption and absorption of chromogenic agents.[5-7] Therefore, color stability is considered a critical parameter influencing the clinical longevity of restorative materials.[6,7]

Chromogenic beverages that are frequently consumed in daily life represent one of the primary causes of extrinsic discoloration in resin composites.[6-9] Tea, which is commonly consumed in white, green, and

black forms, is rich in polyphenolic compounds and exhibits varying chromogenic profiles depending on processing differences.[10] Tannins and other pigment compounds present in tea can bind to the resin composite surface or diffuse into the material, leading to clinically perceptible color changes over time.[6,8,9] Previous in vitro studies have demonstrated that exposure to black tea, in particular, can induce measurable and clinically significant discoloration in resin composites.[11,12] However, the effects of other tea varieties, such as green and white tea, on microhybrid resin composites remain insufficiently investigated.

This in vitro study aimed to assess the impact of various tea types (white, green, and black) on the color stability of a microhybrid resin composite (Herculite Classic, Kerr). The null hypothesis posited that neither the tea type nor the exposure duration to the staining solution would significantly influence color change (ΔE_{00}).

Materials and methods

A microhybrid resin composite (Herculite Classic, Kerr, Scafati, Italy) was used in this study (Table 1). The resin composite was placed as a single increment into a cylindrical silicone mold (8×2 mm), positioned on a Mylar strip. A second Mylar strip and a glass slide were then placed over the material, and gentle finger pressure was applied to obtain a standardized surface. There were a total of 30 resin composite discs that were manufactured.

Tablo 1. Content of microhyrid resin composite

Materials	Matrix	Filler	Filler Content wt%/vol%	Lot number
Herculite Classic (Kerr, Scafati, Italy)	Bis-EMA, Bis-GMA, TEGDMA and UDMA	Barium glass filler and silica (mean particle size: 0.6 micron, particle size range: 100 nm to 1.5 micron)	78/59	10864875

Abbreviations: Bis-EMA, 2,2-Bis[4-(2-methacryloxyethoxy)phenyl] propane; Bis-GMA, 2,2-bis [4-(2-hydroxy-3-methacryloyloxyprop-1-oxy) phenyl] propane; TEG-DMA, triethylene glycol di-methacrylate; UDMA, urethane dimethacrylate.

The specimens were polymerized for 20 s using a light-curing unit with an output intensity of 1000 mW/cm² (VALO Cordless, Ultradent, South Jordan, UT, USA). For a period of 24 h, the specimens were immersed in distilled water at 37°C.[13] Subsequently, they were polished using OptiDisc (KerrHawe, Bioggio, Switzerland) and subjected to 5 minutes of ultrasonic cleaning in distilled water.[14] Every specimen was randomly assigned to one of three categories: white, green, or black tea.

To prepare the tea solutions, 2 g of tea was added to 200 mL of boiling water, allowed to steep for 3 min, and then filtered. Each specimen was stored in 10 mL of the respective solution for 3 w. All staining solutions were renewed daily.

Against a gray background, a spectrophotometer (VITA Easyshade Advance, Zahnfabrik, Bad Säckingen, Germany) was used to measure the colors. Prior to each measurement, the device underwent calibration. Measurements were recorded at baseline, after 24 h, 1 w, and 3 w of immersion.[15] Before the specimens underwent immersion in the staining solutions, baseline measurements had been performed and recorded.

The color difference was calculated according to the CIEDE2000 ($\Delta E00$) formula provided

below:[16]

$$\Delta E_{00}^{\circ}=\sqrt{\left(\frac{\Delta L^{'}}{K_L S_L}\right)^2+\left(\frac{\Delta C^{'}}{K_C S_C}\right)^2+\left(\frac{\Delta H^{'}}{K_H S_H}\right)^2+R_T\left(\frac{\Delta C^{'}}{K_C S_C}\right)\left(\frac{\Delta H^{'}}{K_H S_H}\right)}$$

The terms used in the formula have been explained in a previous study..[16]

Statistical Analysis

The color change was assessed using a two-way ANOVA for tea solution and immersion duration. A multiple comparison was subsequently conducted utilizing Tukey's test. A p value

< 0.05 was considered significant.

Results

Table 2 presents the mean ΔE_{00} values and standard deviations of the microhybrid resin composite immersed in different tea solutions after 24 h, 1 w, and 3 w. Based on the two-way ANOVA results, the type of tea solution, immersion time, and their interaction had a statistically significant effect on the color change of the resin composite.

Black tea exhibited higher ΔE_{00} values compared with the other tea groups, and the differences among the groups were statistically significant ($p < 0.05$). Color change increased over time; in all groups, the lowest values were observed at 24 h, whereas the highest values were recorded at 3 w. The ΔE_{00} values at 1 and 3 w did not exhibit any statistically significant difference ($p > 0.05$).

Table 2. Mean ΔE_{00} values and standard deviations (SD) of the microhybrid resin composite immersed in different types of tea

	24 h	1 w	3 w
White tea	0.98 ± 0.21^{Aa}	1.23 ± 0.43^{Ba}	1.85 ± 0.66^{Ba}
Green tea	1.07 ± 0.54^{Aa}	1.69 ± 0.28^{Ba}	2.12 ± 0.83^{Cb}
Black tea	1.52 ± 0.62^{Ab}	2.28 ± 0.87^{Bb}	2.51 ± 0.75^{Bc}

Different uppercase superscript letters in rows show a significant difference. Different lowercase superscript letters in the colums show a significant difference. ($p < 0.05$)

Discussion

In this in vitro study, the effect of different types of tea on the color stability of a microhybrid resin composite was evaluated. The findings demonstrated that black tea resulted in higher ΔE_{00} values compared with white and green tea, and that color change increased over time. Therefore, the null hypothesis was rejected.

The higher ΔE_{00} values observed in the black tea group may be associated with the high concentration of intensely colored polyphenolic compounds formed during its processing.[10] In particular, pigments such as theaflavin and thearubigin are thought to initially adsorb onto the resin composite surface and subsequently diffuse into the resin matrix, contributing to more persistent discoloration.[5-9] Previous studies have reported that tea and other chromogenic beverages can cause pronounced discoloration in resin-based materials, supporting the present findings.[6,8,9,11,12,17,18]

With respect to the time factor, an increasing trend in color change from 24 h to 3 w was observed in all groups. This finding suggests that prolonged exposure promotes greater accumulation and penetration of pigments within the resin composite structure. However, the absence of a statistically significant difference between the 1 and 3 w measurements may indicate that the material reaches a relative saturation level with respect to staining agents after a certain period.[15,19]

The color stability of microhybrid resin composites is influenced not only by external factors but also by intrinsic material properties. Parameters such as the chemical composition of the resin matrix, filler loading, filler–matrix interface, and water sorption can affect discoloration behavior.[2-5] In the present study, the application of a standardized polishing protocol for all specimens may have minimized variability related to surface roughness, allowing a clearer assessment of the effect of tea type.

From a clinical perspective, it can be anticipated that in individuals with frequent black tea consumption, the esthetic properties of restorations made with microhybrid resin composites may deteriorate more rapidly. Therefore, informing patients about their dietary habits and scheduling periodic polishing or maintenance sessions may be beneficial. Future studies incorporating long-term clinical conditions, such as saliva, biofilm, temperature changes, and mechanical wear, would further enhance the clinical relevance and generalizability of these findings.

Conclusion

The color stability of the microhybrid resin composite was influenced by both the type of tea and the duration of exposure. Black tea caused greater color change compared with white and green tea, whereas the effects of white and green tea were more limited. Additionally, prolonged exposure to the tea solutions increased discoloration.

References

1. Cramer NB, Stansbury JW, Bowman CN. Recent advances and developments in composite dental restorative materials. J Dent Res. 2011;90(4):402-416.

2. Demarco FF, Correa MB, Cenci MS, et al. Longevity of posterior composite restorations: not only a matter of materials. Dent Mater. 2012;28(1):87-101.

3. Ferracane JL. Resin composite--state of the art. Dent Mater. 2011;27(1):29-38.

4. Ilie N, Hickel R. Resin composite restorative materials. Aust Dent J. 2011;56 Suppl 1:59-66.

5. Bagheri R, Burrow MF, Tyas M. Influence of food-simulating solutions and surface finish on susceptibility to staining of aesthetic restorative materials. J Dent. 2005;33(5):389-398.

6. Tekce N, Tuncer S, Demirci M, et al. The effect of different drinks on the color stability of different restorative materials after one month. Restor Dent Endod. 2015;40(4):255-261.

7. Villalta P, Lu H, Okte Z, et al. Effects of staining and bleaching on color change of dental composite resins. J Prosthet Dent. 2006;95(2):137-142.

8. Ertas E, Guler AU, Yucel AC, et al. Color stability of resin composites after immersion in different drinks. Dent Mater J. 2006;25(2):371-376.

9. Guler AU, Yilmaz F, Kulunk T, et al. Effects of different drinks on stainability of resin composite provisional restorative materials. J Prosthet Dent. 2005;94(2):118-124.

10.Leung LK, Su Y, Chen R, et al. Theaflavins in black tea and catechins in green tea are equally effective antioxidants. J Nutr. 2001;131(9):2248-2251.

11.Bedir F, Karadas M. Evaluation of Color Stability and Translucency of Different Composite Resins Exposed to Alcohol. Niger J Clin Pract. 2024;27(3):394-400.

12.Karadas M. The effect of different beverages on the color and translucency of flowable composites. Scanning. 2016;38(6):701-709.

13.Llena C, Fernandez S, Forner L. Color stability of nanohybrid resin-based composites, ormocers and compomers. Clin Oral Investig. 2017;21(4):1071-1077.

14.MA DS, Vitti RP, Sinhoreti MA, et al. Effect of alcoholic beverages on surface roughness and microhardness of dental composites. Dent Mater J. 2016;35(4):621-626.

15.Barutcigil C, Barutcigil K, Ozarslan MM, et al. Color of bulk-fill composite resin restorative materials. J Esthet Restor Dent. 2018;30(2):E3-E8.

16.Luo MR, Cui G, Rigg B. The development of the CIE 2000 colour-difference formula: CIEDE2000. Color Res Appl. 2001;26(5):340-350.

17.Falkensammer F, Arnetzl GV, Wildburger A, Freudenthaler J. Color stability of different composite resin materials. J Prosthet Dent. 2013;109(6):378-383.

18.Ren YF, Feng L, Serban D, Malmstrom HS. Effects of common beverage colorants on color stability of dental composite resins: the utility of a thermocycling stain challenge model in vitro. J Dent. 2012;40 Suppl 1:e48-56.

19.Sabatini C. Color Stability Behavior of Methacrylate-based Resin Composites Polymerized with Light-emitting Diodes and Quartz-Tungsten-Halogen. Oper Dent. 2015;40(3):271-281.

AMPULLA VATERİ'NİN MİKROPAPİLLER ADENOKARSİNOMU: LİTERATÜR DERLEMESİ EŞLİĞİNDE NADİR BİR OLGU SUNUMU

MAHİ BALCI

Kırıkkale Üniversitesi Tıp Fakültesi Tıbbi Patoloji Anabilim Dalı/ Doçent Doktor

ORCID ID: 0000-0001-5836-2344

AYŞE NUR EVLEKSİZ

Kırıkkale Üniversitesi Tıp Fakültesi Tıbbi Patoloji Anabilim Dalı/ Araştırma Görevlisi Asistan Doktor

ORCID ID: 0009-0001-5582-8169

Amaç

Ampulla Vateri kökenli invaziv mikropapiller adenokarsinom, gastrointestinal sistemde son derece nadir görülen bir antitedir ve literatürde bugüne kadar yalnızca 8 olgu bildirilmiştir. Bu varyant, agresif biyolojik davranış ve yüksek lenfatik yayılım eğilimi ile ilişkilidir. Bu çalışmanın amacı, yeni bir olgunun klinik, endoskopik ve histopatolojik bulgularını sunmak ve bu nadir lokalizasyonda mikropapiller paternin tanınmasının tanısal önemini vurgulamaktır.

Olgu Sunumu:

Doksan iki yaşında kadın hasta, bir aydır devam eden progresif sarılık, iştahsızlık ve kilo kaybı şikayetleri ile başvurdu. Laboratuvar bulguları kolestatik patern ile uyumluydu. Manyetik rezonans kolanjiyopankreatografi incelemesinde intrahepatik safra yollarında dilatasyon ve distal koledokta yaklaşık 2,5 cm çapında taş saptandı. Endosonografik incelemede ampulla düzeyinde pankreatik kanala uzanım gösteren 17 × 13 mm boyutlarında hipoekoik lezyon izlendi. Endoskopik retrograd kolanjiyopankreatografi sırasında papilla Vateri'nin genişlemiş, protrüde ve frajil görünümde olduğu izlenmiş ve bu alandan hedeflenmiş biyopsiler alınmıştır.

Bulgular:

Histopatolojik incelemede tümör hücrelerinin fibrovasküler kor içermeyen, stromal retraksiyon benzeri boşluklar içerisinde yerleşmiş ve ters polarizasyon gösteren küçük hücre kümeleri oluşturduğu izlendi; bu bulgular mikropapiller patern ile uyumlu bulundu. Belirgin glandüler yapı izlenmedi. Tümör hücrelerinde belirgin nükleer pleomorfizm, prominan nükleoller ve artmış mitotik aktivite dikkati çekti. İmmünohistokimyasal incelemede tümör hücrelerinde EMA ve CK7 ile difüz pozitiflik saptanırken, p53 için diffüz overekspresyon izlenmiş olup bu durum TP53 alterasyonu ile uyumlu olarak değerlendirildi. Bulgular birlikte değerlendirilerek lezyon ampulla Vateri kaynaklı invaziv mikropapiller adenokarsinom olarak tanımlandı.

Sonuç:

Ampulla Vateri'nin mikropapiller adenokarsinomu, nadir görülmekle birlikte klinik açıdan önemli bir antitedir ve koledokolitiazis gibi benign durumlar tarafından maskelenebilir. Karakteristik histomorfolojisinin tanınması, doğru tanı ve prognostik değerlendirme açısından kritik öneme sahiptir. Bu olgu, benign etiyoloji düşünülen obstrüktif sarılık olgularında dahi dikkatli endoskopik değerlendirme ve histopatolojik incelemenin önemini vurgulamaktadır.

GİRİŞ

Ampulla Vateri, distal koledok ile pankreatik kanalın duodenuma açıldığı kompleks bir anatomik bölgedir. Bu lokalizasyondan köken alan tümörler heterojen klinikopatolojik özellikler göstermekte olup, en sık görülen histolojik tip tübüler adenokarsinomdur (1,2). Ampulla Vateri karsinomları tüm gastrointestinal sistem malignitelerinin yaklaşık %0,6-0,8'ini oluşturmaktadır (3).

İnvaziv mikropapiller karsinom (İMPK), ilk olarak meme kanserinde tanımlanmış olup, "inside-out" büyüme paterni ve belirgin lenfatik yayılım eğilimi ile karakterize agresif bir adenokarsinom varyantıdır

(4). Bu histolojik varyant günümüzde mesane, akciğer, kolorektum, pankreatikobiliyer sistem ve over gibi birçok organda raporlanmıştır (5,6). Ancak ampulla Vateri'nin primer mikropapiller adenokarsinomu son derece nadirdir. İlk kez 2005 yılında Khayyata ve ark. tarafından ampullo-pankreatikobiliyer bölgeyi içeren bir seri içerisinde tanımlanan bu antite ile ilgili literatürde sınırlı sayıda olgu bulunmaktadır (7-11). Bildirilen olguların önemli bir kısmı saf veya baskın mikropapiller patern gösteren tümörlerden oluşmaktadır.

Mikropapiller paternin ampuller bölgedeki insidansı yaklaşık %4,1 olarak bildirilmiş olup, tümörün büyük kısmının bu paternden oluştuğu olgular oldukça nadirdir (12). Bu varyantın tanınması, agresif klinik seyir ve yüksek lenf nodu metastazı riski nedeniyle kritik öneme sahiptir. Literatürde bildirilen olguların çoğunda tanı anında lenf nodu metastazı mevcuttur (7,9,10).

Bu çalışmada, koledok taşı ile birlikte seyreden ve benign bir süreci taklit eden bir ampulla Vateri mikropapiller adenokarsinom olgusunu sunmayı ve bu nadir antitenin klinik, endoskopik ve histopatolojik özelliklerini literatür eşliğinde tartışmayı amaçladık.

OLGU SUNUMU

Doksan iki yaşında kadın hasta, yaklaşık bir aydır devam eden ilerleyici sarılık, iştahsızlık ve kilo kaybı şikayetleri ile gastroenteroloji kliniğine başvurdu. Hastanın özgeçmişinde hipertansiyon dışında önemli bir özellik yoktu. İlaç kullanım öyküsünde ramipril 5 mg/gün mevcuttu. Sigara ve alkol kullanımı yoktu.

Fizik muayenede skleral ve mukozal ikter belirgindi; epigastrik bölgede hassasiyet dışında ek patolojik bulgu saptanmadı. Hepatosplenomegali izlenmedi. Hastanın vital bulguları stabildi.

Laboratuvar incelemesinde total bilirubin 11,4 mg/dL, direkt bilirubin 8,2 mg/dL, alkalen fosfataz 420 U/L, GGT 310 U/L, AST 96 U/L ve ALT 82 U/L olarak ölçüldü. CA 19-9 düzeyi hafif yüksek (85 U/mL) iken CEA normal sınırlarda bulundu (2,1 ng/mL). Tam kan sayımı ve koagülasyon parametreleri normaldi.

Manyetik rezonans kolanjiyopankreatografi incelemesinde intrahepatik ve ekstrahepatik safra yollarında belirgin dilatasyon ile birlikte distal koledokta yaklaşık 2,5 cm çapında taş saptandı. Pankreatik kanalda da belirgin dilatasyon izlendi.

Endosonografik incelemede ampulla düzeyinde, pankreatik kanala uzanım gösteren, 17 × 13 mm boyutlarında, düzensiz sınırlı hipoekoik bir lezyon izlendi. Lezyonun duodenal duvarın muskularis propriasını invaze ettiği değerlendirildi. Çevresel lenfadenopati saptanmadı.

Endoskopik retrograd kolanjiyopankreatografi sırasında papilla Vateri'nin belirgin şekilde genişlemiş, protrüde ve frajil görünümde olduğu izlendi (Şekil 1). Papilla yüzeyi yer yer ülsere ve kanamalıydı. Koledok taşı nedeniyle önce sfinkterotomi yapıldı ve taş balon ile ekstrakte edildi. Ardından papilla yüzeyinden ve ampulla bölgesinin farklı alanlarından hedeflenmiş biyopsiler alındı.

Histopatolojik incelemede tümörün, fibrovasküler kor içermeyen ve stromal retraksiyon boşlukları içinde yer alan mikropapilla yapılarından oluştuğu görüldü (Şekil 2A). Tümör hücrelerinin apikal yüzleri laküner boşluklara bakmakta olup, belirgin glandüler yapı izlenmedi. Hücrelerde nükleer pleomorfizm, belirgin nükleoller ve artmış mitotik aktivite dikkati çekti (Şekil 2B). Lenfovasküler invazyon alanları mevcuttu; perinöral invazyon izlenmedi.

İmmünohistokimyasal incelemede tümör hücrelerinde EMA ile belirgin boyanma izlendi (Şekil 3A). CK7 ile difüz ve güçlü pozitiflik, CK20 ile fokal pozitiflik saptanırken CDX2 negatifti. p53 ile yaygın nükleer boyanma izlendi (Şekil 3B).

Tüm bulgular birlikte değerlendirilerek lezyon, ampulla Vateri kaynaklı invaziv mikropapiller adenokarsinom olarak tanımlandı.

Hastanın ileri yaşı ve komorbiditeleri nedeniyle cerrahi rezeksiyon uygulanmadı. Palyatif amaçlı safra yolu drenajı için koledoka plastik stent yerleştirildi. Hasta tanı sonrası dönemde izlem altındadır.

TARTIŞMA

İnvaziv mikropapiller adenokarsinom, belirgin lenfovasküler invazyon ve lenf nodu metastazı eğilimi ile karakterize, agresif biyolojik davranış gösteren nadir bir adenokarsinom varyantıdır (13,14). İlk olarak meme karsinomlarında tanımlanmış olmakla birlikte (4), daha sonra üriner sistem, akciğer, kolorektal bölge ve pankreatikobiliyer sistem dahil olmak üzere çeşitli organlarda bildirilmiştir (5,6). Ampulla Vateri yerleşimli mikropapiller adenokarsinom ise oldukça nadirdir ve literatürde sınırlı sayıda olgu bulunmaktadır (7-11).

Sunulan olgu, ileri yaşta ortaya çıkması ve koledokolitiazis ile birlikte prezente olması nedeniyle dikkat çekmektedir. Koledokolitiazis obstrüktif sarılığın sık benign nedenlerinden biri olmakla birlikte, eşlik eden maligniteleri maskeleyebilmektedir (15). Literatürde bildirilen ampuller mikropapiller adenokarsinom olgularında koledok taşı birlikteliği belirgin olarak vurgulanmamıştır. Bu nedenle, papilla Vateri'de düzensizlik, frajil görünüm, ülserasyon veya kitle izlenmesi durumunda benign nedenler mevcut olsa bile dikkatli endoskopik değerlendirme ve hedeflenmiş biyopsi alınması önem taşımaktadır.

Mikropapiller adenokarsinom tanısında histopatolojik inceleme temel belirleyicidir. Morfolojik olarak fibrovasküler kor içermeyen mikropapiller hücre kümeleri ve stromal retraksiyon benzeri boşluklar karakteristiktir (13,14). Tümör hücrelerinde sıklıkla ters polarizasyon ("inside-out" pattern) izlenir. Sunulan olguda fibrovasküler kor içermeyen mikropapiller tümör kümeleri, laküner boşluklar içerisinde yerleşim ve apikal yüzeylerin laküner boşluklara dönük görünümü bu patern ile uyumlu bulunmuştur. EMA ile stromaya bakan yüzeylerde belirgin boyanma izlenmesi tanıyı desteklemiştir; ancak tanıda esas olan ışık mikroskobik morfolojidir.

Ampuller bölge tümörleri intestinal, pankreatikobiliyer veya mikst fenotip gösterebilmektedir (16). Sunulan olguda CK7 pozitifliği, CK20 fokal pozitifliği ve CDX2 negatifliği pankreatikobiliyer diferansiasyon lehine değerlendirilmiştir. Benzer immünofenotipik özellikler literatürde bildirilen bazı ampuller mikropapiller adenokarsinom olgularında da tanımlanmıştır (7-11). Bununla birlikte, ampuller bölgenin kompleks histogenezi nedeniyle immünofenotipik bulguların morfolojik özelliklerle birlikte değerlendirilmesi gereklidir.

Ayırıcı tanıda klasik tübüler adenokarsinom, intestinal tip adenokarsinom, nöroendokrin tümör, lenfoma ve metastatik mikropapiller karsinomlar düşünülmelidir (17,18). Özellikle meme ve over kaynaklı metastatik mikropapiller karsinomların dışlanması önemlidir. Sunulan olguda klinik, radyolojik ve endoskopik bulgular primer ampuller tümör lehine değerlendirilmiştir.

Literatürde bildirilen olgular Tablo 1'de özetlenmiştir. Olguların büyük kısmında tanı anında lenf nodu metastazı mevcut olup, bu durum mikropapiller paternin agresif biyolojik davranışı ile uyumludur (7-10). Tablo 1'de yer alan altı olgunun dördünde (%66,7) lenf nodu metastazı saptanmıştır. Buna karşın, sunulan olguda klinik ve radyolojik olarak belirgin lenfadenopati izlenmemiştir. Bu durum, olgunun nispeten erken evrede tanı almış olabileceğini düşündürmektedir. Ayrıca sunulan olgu, literatürde bildirilen ampuller mikropapiller adenokarsinom olguları arasında en ileri yaşlı hastalardan biri olması açısından da dikkat çekmektedir.

Mikropapiller paternin biyolojik davranışı üzerine yapılan çalışmalar, bu tümörlerin stromal etkileşim özelliklerinin klasik adenokarsinomlardan farklı olduğunu göstermektedir. Ters polarizasyon gösteren tümör hücrelerinde hücre membranı organizasyonu ve adezyon moleküllerine ilişkin değişikliklerin lenfovasküler invazyon eğilimine katkıda bulunduğu düşünülmektedir (13-15). Bu nedenle, ampuller adenokarsinomlarda mikropapiller komponentin tanınması yalnızca histolojik alt tiplendirme açısından değil, aynı zamanda prognostik değerlendirme açısından da önem taşımaktadır.

Tedavi açısından değerlendirildiğinde, literatürdeki olguların çoğunda pankreatikoduodenektomi uygulanmıştır. Yaygın lenf nodu metastazı bulunan olgularda ise palyatif yaklaşımlar tercih edilmiştir (9). Sunulan olguda ileri yaş ve eşlik eden komorbiditeler nedeniyle palyatif stentleme uygulanmıştır. Lenf nodu metastazı bulunmayan olgularda daha iyi klinik seyir bildirilmiş olmakla birlikte, mevcut olgu sayısının sınırlı olması nedeniyle prognoza ilişkin kesin çıkarımlar yapmak güçtür.

Sonuç olarak, ampulla Vateri'nin mikropapiller adenokarsinomu nadir görülmesine rağmen agresif biyolojik davranışı nedeniyle klinik açıdan önem taşıyan bir antitedir. Bu olgu, benign obstrüktif

süreçleri düşündüren klinik tablolarda dahi papilla Vateri'nin dikkatli değerlendirilmesi gerektiğini göstermekte ve mikropapiller morfolojinin doğru tanınmasının tanısal ve prognostik önemini vurgulamaktadır.

Tablo 1.

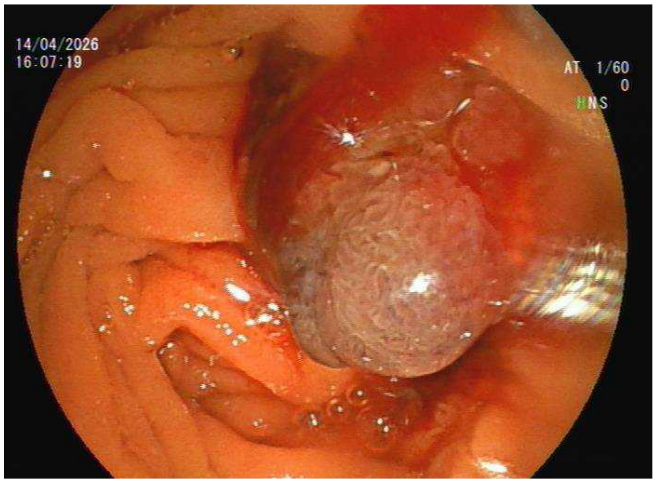
Yazar (Yıl)	Yaş/Cinsiyet	Tümör Boyutu	Lenf Nodu Metastazı	Tedavi	Prognoz
Khayyata ve ark. (2005)	66/K	2,0 cm	Evet	Pankreatikoduodenektomi	12 ay, nüks yok
Fujita ve ark. (2010)	64/E	1,8 cm	Evet	Pankreatikoduodenektomi + adjuvan KT	24 ay, hastalıksız
Michal ve ark. (2018)	71/K	2,2 cm	Evet (yaygın)	Palyatif	6 ay, exitus
Elghareeb ve ark. (2023)	29/K	1,5 cm	Hayır	Pankreatikoduodenektomi	18 ay, hastalıksız
Noguchi ve ark. (2021)	73/E	2,1 cm	Evet	Pankreatikoduodenektomi	10 ay, hastalıksız
Sunulan olgu	92/K	1,7 cm	Hayır	Palyatif stent	İzlem altında

K: Kadın, E: Erkek, KT: Kemoterapi

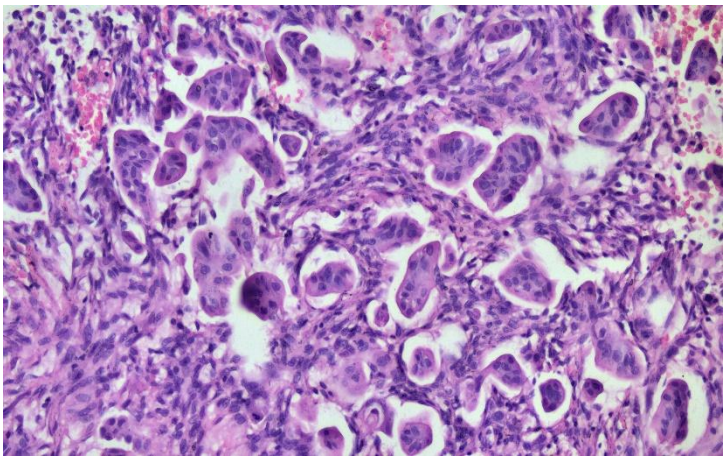
Kaynaklar

1. Adsay NV, et al. Ampullary region carcinomas: definition and classification. Semin Diagn Pathol. 2004.
2. Albores-Saavedra J, et al. Carcinoma of the ampulla of Vater. Hum Pathol. 2009.
3. Howe JR, et al. The management of adenocarcinoma of the ampulla of Vater. Ann Surg Oncol. 1998.
4. Siriaunkgul S, Tavassoli FA. Invasive micropapillary carcinoma of the breast. Mod Pathol. 1993.
5. Amin MB, et al. Micropapillary variant of transitional cell carcinoma. Am J Surg Pathol. 1994.
6. Nassar H. Carcinomas with micropapillary morphology. Adv Anat Pathol. 2004.
7. Khayyata S, et al. Micropapillary adenocarcinoma of the ampulla of Vater. Arch Pathol Lab Med. 2005.
8. Fujita T, et al. Micropapillary carcinoma of the ampulla of Vater. Pathol Int. 2010.
9. Michal M, et al. Invasive micropapillary carcinoma of the ampulla. Ann Diagn Pathol. 2018.
10. Noguchi H, et al. Ampullary micropapillary adenocarcinoma with mixed phenotype. Surg Case Rep. 2021.
11. Elghareeb M, et al. Micropapillary adenocarcinoma of the ampulla of Vater in a young patient. Int J Surg Case Rep. 2023.
12. Sangoi AR, et al. Micropapillary features in pancreatobiliary neoplasms. Am J Surg Pathol. 2010.
13. Luna-Moré S, et al. Importance of micropapillary pattern in adenocarcinomas. Histopathology. 1994.
14. Nassar H, et al. Clinicopathologic significance of micropapillary differentiation. Cancer. 2001.
15. Costi R, et al. Choledocholithiasis and hidden malignancy. World J Gastroenterol. 2012.
16. Ang DC, et al. Immunophenotypic classification of ampullary carcinomas. Arch Pathol Lab Med. 2014.
17. Rosai J. Rosai and Ackerman's Surgical Pathology. 11th ed.
18. Odze RD, Goldblum JR. Surgical Pathology of the GI Tract, Liver, Biliary Tract and Pancreas. 3rd ed.

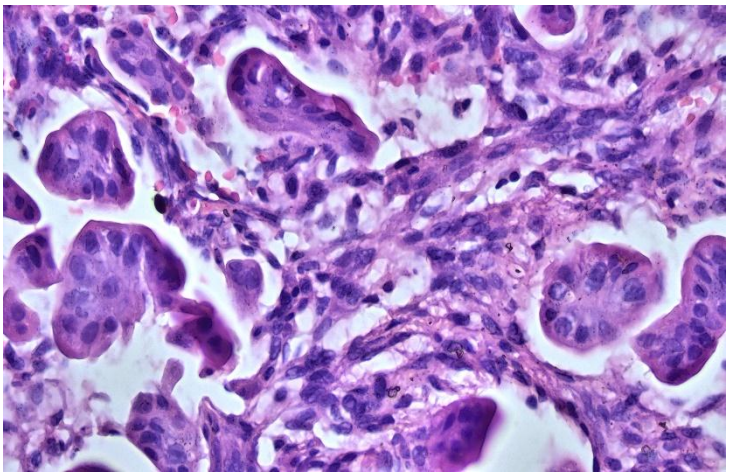
Şekil 1. ERCP sırasında papilla Vateri'de genişlemiş, protrüde ve frajil görünümde lezyon izlenmektedir. Lezyon yüzeyinde düzensizlik ve hemorajik alanlar dikkati çekmektedir.



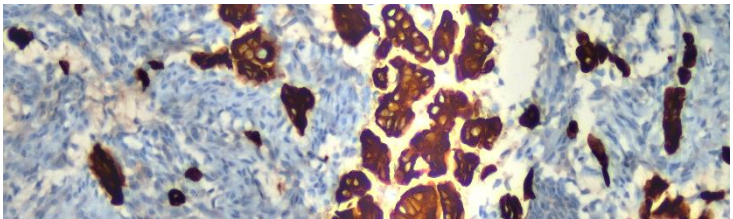
Şekil 2A. Desmoplastik stroma içerisinde retraksiyon artefaktı gösteren mikropapiller yapıda tümör hücre grupları izlenmektedir (H&E, ×100).



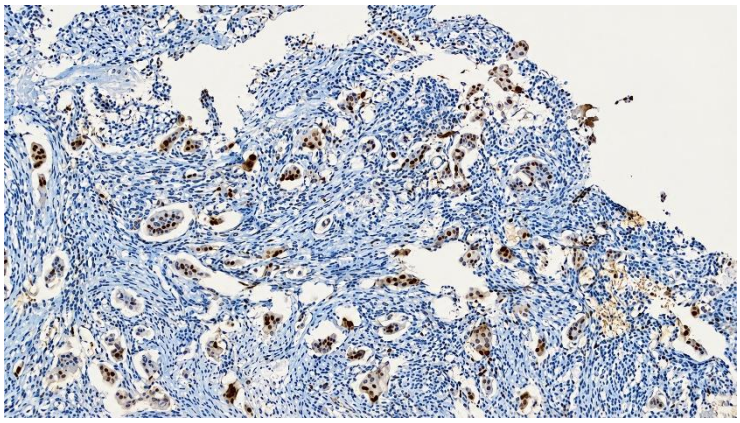
Şekil 2B. Nükleer atipi içeren, apikal dens sitoplazmaya sahip hücreler mikropapilla oluşturmaktadır. (H&E, ×400).



Şekil 3A. EMA ile apikal sitoplazmada yoğunlaşan kuvvetli membranöz boyanma (x200).



Şekil 3B. P53 ile tümör hücrelerinde kuvvetli nükleer boyanma (X100)



DECISION SUPPORT SYSTEMS IN POST-DISASTER HEALTH MANAGEMENT: MODELING THE FLOOD-HEALTH ACTION PLAN

Pınar Seçmen

Sakarya University, Institute of Business Administration, Fields of Expertise: Health Management, Disaster Management, Decision Support Systems, ORCID: https://orcid.org/0009-0002-1942-8333

ABSTRACT

Aim: The aim of this study is to rank the strategic factors influencing post-flood health management processes within a multi-criteria decision-making framework and to identify effective intervention strategies. Bartın, located in the Western Black Sea coastal region, represents a critical area in terms of health service continuity due to the increasing flood risk associated with climate change. In this context, a hybrid model integrating the SWOT and AHP methods has been developed.

Methods: A two-stage hybrid methodology was applied in the study. In the first stage, SWOT factors and 16 sub-criteria for the flood-health action plan of Bartın Province were systematically identified. In the second phase, a panel of five expert decision-makers (DM5; comprising a physician, a health administrator, an AFAD/UMKE specialist, and an academic) evaluated both the main SWOT categories and the sub-criteria of each category using AHP pairwise comparison matrices based on Saaty's (1980) 1–9 importance scale.

Results: According to the AHP analysis, in the "Strengths" category, AFAD/İSM institutional coordination (S2: 0.413) ranks first, followed by UMKE and 112 services (S1: 0.311). In the Weaknesses category, the negative impact on service continuity (W1: 0.344) and the hindrance to the timely provision of health services (W2: 0.326) stand out. In terms of opportunities, international funding support (O3: 0.276) and the possibility of establishing specialized mobile alert systems for healthcare personnel (O1: 0.266) rank first and second, respectively. Among the threats, the risk of epidemics caused by water pollution following floods (T2: 0.349) and the systemic pressure resulting from increased flood frequency (T1: 0.338) are the dominant factors.

Conclusion: The model presents five key policy recommendations: The central role of institutional coordination (S2) must be strengthened; infrastructure vulnerabilities (W1) that threaten service continuity during disasters must be addressed as a priority; early-phase post-disaster epidemic surveillance and water quality monitoring systems (T2) must be urgently strengthened, systematic use must be made of international funding and project support (O3), and all strategic dimensions must be addressed simultaneously. The findings provide a framework for an evidence-based flood-health action plan that can be implemented through coordination among the Ministry of Health, AFAD, and local governments.

Keywords: Post-Disaster Health Management, Decision-Making Processes, Climate Change, Bartın.

1. INTRODUCTION

Disasters, regardless of whether they are natural or man-made, are complex events that disrupt the normal functioning of societies, result in loss of life and property, and require emergency response and coordination[1] [2]. Globally, more than 500 natural disasters occur annually, claiming the lives of approximately 75,000 people and affecting over 200 million people[3]. These figures clearly highlight the critical importance of effective disaster preparedness and response mechanisms.

Floods are among the most common natural disasters both in our country and worldwide. In Turkey, there have been 389 recorded disaster events from 1948 to the present. Of these, 55 were floods, and 3,691 people in Turkey have lost their lives as a result of flooding. Due to their sudden and destructive effects, floods place significant strain on health systems; they lead to secondary health issues such as trauma, outbreaks of infectious diseases, psychosocial problems, and disruptions in access to basic

health services[4 5]. In particular, outbreaks of infectious diseases that emerge after disasters are cited as among the primary causes of morbidity and mortality[6].

Turkey's Western Black Sea Region has experienced a documented increase in the frequency and intensity of floods, landslides, and heavy rainfall events over the past decade.[7] In the 2021 Western Black Sea flood disaster, Bartın, Kastamonu, and Sinop were among the hardest-hit provinces.[8] As a result of the disaster, one person lost their life in Bartın, while the death toll across the region reached 97. In the district of Ulus, one of the most affected areas, approximately 16,703 people in 58 settlements were affected by the flood [8 9]. Additionally, damage to healthcare facilities, infrastructure disruptions, and disruptions in healthcare services were experienced. This disaster clearly highlighted the vulnerabilities and coordination gaps in the management of post-disaster healthcare services[10]. With the increasing frequency of floods, health systems are facing multiple interconnected pressures, including service disruptions, disruptions in the pharmaceutical supply chain, epidemiological risks, and interruptions in the follow-up of chronic patients[11]. At this point, decision support systems (DSS) emerge as a critical tool in post-disaster health management.

Decision support systems (DSS) are critical tools that enable decision-makers to generate rapid and accurate solutions in post-disaster health management. These systems strengthen the continuity and coordination of health services through functions such as data integration, risk assessment, scenario analysis, and resource allocation[12]. AYDES, developed in Turkey, supports the coordination of health service groups by providing access to and analysis of data during pre- and post-disaster processes through its spatial information system-based structure[13]. International literature emphasizes that artificial intelligence-based models and geographic information systems play a strategic role in modeling post-disaster health action plans, particularly regarding logistics planning, epidemiological forecasts, and early warning mechanisms[14].

This study aims to contribute to this gap by adopting a hybrid methodology that integrates SWOT analysis with the Analytic Hierarchy Process (AHP). SWOT analysis is a strategic tool widely used to assess an organization's internal and external environments[15]. However, while SWOT identifies factors qualitatively, it cannot determine their relative weights or priority rankings[16]. The AHP, developed by Saaty (1980), addresses this limitation by quantifying factor weights through pairwise comparisons; it integrates subjective expert judgment with consistency verification mechanisms[17].

The aim of this study is to rank the strategic factors influencing post-flood health management in Bartın Province using the AHP-SWOT hybrid model and to propose evidence-based policy recommendations. The selected region is a typical representative of Turkey's Western Black Sea coastal regions in terms of climate change risks, health system infrastructure, and challenges in institutional coordination[18].

2. METHODOLOGY

In this study, a two-stage hybrid methodology was applied. In the first stage, 16 sub-criteria of the SWOT factors were identified; in the second stage, AHP pairwise comparisons were conducted by five expert decision-makers.

2.1. Phase 1: Identification of SWOT Factors

The process of identifying SWOT factors involved a comprehensive literature review, an examination of disaster health legislation in Turkey, and a preliminary observational study of health facilities and emergency response agencies in Bartın. During this process, the literature on disaster health management and Turkey's AFAD coordination structure was systematically reviewed. The factors were validated through an expert panel; the final SWOT framework comprises a total of 16 elements, consisting of four sub-criteria in each category (Table 1).

Table 1. SWOT Sub-Criteria of the Bartın Province Flood-Health Action Plan

Category	Strengths (S)	Weaknesses (W)	Opportunities (O)	Threats (T)
Sub-Criterion 1	UMKE and 112 Services (S1)	Adverse Impact on Service Continuity (W1)	Mobile Alert Systems (O1)	Increasing Frequency of Floods (T1)
Sub-Criterion 2	AFAD/ISM Institutional Coordination (S2)	Delays in Healthcare Services (W2)	Digital Health Systems (O2)	Risk of an Outbreak Due to Water Pollution (T2)
Sub-Criterion 3	Medical Equipment Capacity (S3)	Lack of Digital Systems (W3)	International Fund Support (O3)	Climate Uncertainty (T3)
Sub-Criterion 4	Trained Staff (S4)	Budget Constraints (W4)	NGO Partnerships (O4)	Political Instability (T4)

2.2. Second Stage: Weighting Using the AHP

In the second stage, the expert panel evaluated the factors using AHP pairwise comparison matrices based on Saaty's (1980) 1–9 importance scale. The expert panel consisted of five decision-makers: a physician (KV1), a health administrator (KV2), an AFAD/UMKE expert (KV3), a UMKE expert (KV4), and an academic (KV5). Purposive sampling was used in the selection of experts; a minimum of five years of experience in disaster health management, institutional coordination, and health services planning was established as the criterion.

The experts conducted evaluations at two separate levels: (1) the relative weights of the four main SWOT categories and (2) the relative weights of the four subcriteria within each category. AHP pairwise comparison matrices were created separately for each expert; the individual weights were aggregated using the geometric mean method.[19]

The consistency of the ratings was verified by calculating the consistency ratio (CR). In accordance with Saaty's (1980) criteria, a threshold of CR < 0.10 was used as a reference for all matrices, and ratings exceeding this threshold were returned to the expert for re-evaluation. This process ensures the mathematical consistency and reliability of the weights[17].

3. FINDINGS

3.1. Weights of the Main SWOT Categories

The Strengths category ranked first with a weight of 0.536; this was followed, in order, by Opportunities (0.281), Weaknesses (0.115), and Threats (0.068). This distribution reflects the expert panel's consensus assessment that the existing institutional and operational strengths in the region outweigh the threats and vulnerabilities (Table 2).

Table 2. AHP Analysis - Weights for Main SWOT Categories

SWOT Category	AHP Weight	Ranking	Percentage (%)
Strengths (S)	0,536	1	53,6

Opportunities (O)	0,281	2	28,1
Weaknesses (W)	0,115	3	11,5
Threats (T)	0,068	4	6,8
Total	**1,000**	**—**	**100,0**

3.2. Sub-Criterion Weights for the Strengths Category

In the Strengths category, AFAD/ISM institutional coordination (S2: 0.413) emerges as a key factor. This finding aligns with the literature regarding the critical role of coordination in multi-agency disaster response on operational outcomes20 and reveals that experts perceive inter-organizational synergy as the most valuable strategic asset in the region. UMKE and 112 services (S1: 0.311), ranked second, reflect the region's emergency medical capacity.

Table 3. AHP Weights for Sub-Criteria in the Strengths Category

Sub-criterion	AHP Weight	Ranking
S2: AFAD/ISM Institutional Coordination	0,413	1
S1: UMKE and 112 Services	0,311	2
S3: Medical Equipment Capacity	0,142	3
S4: Trained Staff	0,134	4

3.3. Sub-Criterion Weights for the Weaknesses Category

Within the Weaknesses category, the negative impact on service continuity (Z1: 0.344) was identified as the most critical vulnerability. This finding is directly related to documented disruptions in chronic disease management and ongoing care services during the post-disaster period21. Together with the vulnerability caused by delays in health services (Z2: 0.326), these two sub-criteria highlight the importance of uninterrupted access to health care during the critical initial hours and days following a disaster.

Table 4. AHP Weights for Sub-Criteria in the Weaknesses Category

Sub-criterion	AHP Weight	Ranking
W1: Adverse Impact on Service Continuity	0,344	1
W2: Delays in Health Care	0,326	2

W3: Lack of Digital Systems	0,165	3
W4: Budget Constraints	0,165	4

3.4. Sub-criterion Weights for the Opportunities Category

In the Opportunities category, international funding support (O3: 0.276) was identified as the highest-priority opportunity. This finding highlights the potential to leverage EU framework programs, WHO funds, and international development resources for disaster management and climate adaptation[22]. The opportunity to establish specialized mobile alert systems for healthcare personnel (O1: 0.266) aligns with the growing institutional interest in digital health solutions.

Table 5. AHP Weights for Sub-Criteria in the Opportunities Category

Sub-criterion	AHP Weight	Ranking
O3: International Fund Support	0,276	1
O1: Mobile Alert Systems	0,266	2
O2: Digital Health Systems	0,247	3
O4: NGO Partnerships	0,211	4

3.5. Sub-criterion Weights in the Threats Category

In the Threats category, the risk of epidemics caused by post-flood water pollution (T2: 0.349) ranked first. This result is noteworthy: it is fully consistent with the literature indicating that diseases associated with water pollution, such as cholera, typhoid, and diarrhea, constitute a significant source of morbidity and mortality in the post-disaster period[23]. The systemic pressure caused by increasing flood frequency (T1: 0.338), however, highlights the underlying climate factor; this finding indicates that experts prioritize long-term structural challenges as highly as current immediate threats.

Table 6. AHP Weights for Sub-Criteria in the Threats Category

Sub-criterion	AHP Weight	Ranking
T2: Risk of an Outbreak Due to Water Pollution	0,349	1
T1: Increasing Frequency of Floods / Systemic Pressure	0,338	2
T3: Climate Uncertainty	0,155	3
T4: Political Instability	0,158	4

4. DISCUSSION

The findings of this study are consistent with the established literature regarding the central importance of human resources and institutional factors in post-disaster health management. The fact that AFAD/İSM coordination received the highest weight (0.413) as S2 directly reflects the initial response operations in Bartın following the flood; coordination mechanisms were comprehensively tested in the field. This demonstrates that Turkey's centralized coordination structure can be considered a strong advantage under appropriate conditions[24].

The identification of the risk of an epidemic (T2) as the highest-priority threat is a particularly noteworthy finding. This result highlights that the true scale of the epidemiological threat may be overlooked initially during a period when disaster response resources are initially focused on search-and-rescue and medical evacuation. The findings strongly support the inclusion of water quality monitoring protocols and epidemic prevention strategies in disaster response planning from the very beginning[23].

The fact that international funding (O3) emerges as a leading opportunity underscores the potential to leverage EU and WHO resources to enhance the climate resilience of health systems.[22] At the same time, this finding also indicates that existing domestic financing mechanisms are insufficient on their own; this observation is of direct relevance to policy discussions on climate health financing in Turkey.

From a methodological perspective, the AHS-SWOT hybrid approach offers several significant contributions: First, by converting subjective expert judgments into quantitative weights, it enables comparisons among multiple decision-makers. Second, the calculation of the consistency ratio reduces the risk of subjective judgment error. Third, the methodology is adaptable to different provinces and regions while maintaining the same methodological framework[25]. However, certain limitations of the study should be taken into account. Limiting the expert panel to five members restricts the generalizability of the weights; while this criterion is consistent with the current AHP methodology, it should not be forgotten that different expert compositions may lead to different weight profiles. On the other hand, while the study's structural validity is supported by conceptual frameworks found in the existing literature, the methodology has not been validated using quantitative field data or historical disaster morbidity statistics. Addressing these limitations offers a meaningful roadmap for future research[26].

5. CONCLUSION

This study presents an evidence-based strategic framework for post-flood health management in Bartın Province, based on an AHP-weighted SWOT analysis. The mixed-methods approach provides a comprehensive and systematic assessment in terms of operational strengths, infrastructural vulnerabilities, strategic opportunities, and structural threats.

Based on the findings, five key policy recommendations have been developed:

- ✓ The central role of AFAD/ISM coordination (S2: 0.413) must be systematically strengthened through unified command structures, joint exercises, and regular updates to inter-agency protocols.
- ✓ Infrastructure vulnerabilities threatening service continuity (W1: 0.344) must be addressed urgently by developing backup communication systems, backup power infrastructure, and alternative service delivery protocols.
- ✓ Capacity for epidemic surveillance and water quality monitoring during the early stages of a disaster (T2: 0.349) should be enhanced by strengthening on-site and community-based monitoring networks.
- ✓ International funding mechanisms (O3: 0.276) should be systematically utilized; a structured funding strategy should be developed for projects aimed at strengthening climate adaptation and disaster health capacities.

- ✓ All SWOT dimensions should be addressed simultaneously and systematically within the framework of an integrated, multi-stakeholder action plan to be developed in coordination among the Ministry of Health, AFAD, and local governments.

The developed framework is scalable to other coastal regions with similar climate and health system characteristics and provides a methodological contribution to evidence-based policymaking in disaster health management. It is recommended that future research validate this framework across multiple provinces, incorporate quantitative health outcomes, and monitor the implementation of the proposed interventions over time[27].

REFERENCES

1. Macit İ. (2018). Bütünleşik afet yönetim sistemleri için karar destek sistemi geliştirilmesi: Mobil uygulama örneği. Uluslararası Yönetim Bilişim Sistemleri ve Bilgisayar Bilimleri Dergisi, 2018, 2(1):23-41.

2. Khosravi, R. & Rabbani, M.A. Telemedicine-oriented framework for scenario-based disaster management: Integrating machine learning and multi-criteria decision making. Applied Soft Computing, 2026, 186, 114274.

3. World Health Organization. Climate change and health. WHO Fact Sheet. 2023. https://www.who.int/news-room/fact-sheets/detail/climate-change-and-health. Erişim tarihi: 15 Ocak 2025.

4. Tortumlu,M. & Altunci, Y.A. Türkiye'de meydana gelen sel afetlerinin analizi ve sağlık üzerine etkileri. Anatolian journal of emergency medicine 2024, 7(2): 74-80. DOI: 10.54996/anatolianjem.1376324 AFAD. (2021). Batı Karadeniz'de meydana gelen sel afetine ilişkin değerlendirme raporu.

5. Keskin G. Afetler ve travma, travmayı anlamak. In: Keskin G, ed. Afetlerde Ruhsal Sorunlar ve Psikiyatri Hemşireliği Yaklaşımları. 1st ed. Türkiye Klinikleri; 2023:1-6.

6. BMJ 2023; 383. Mortality risks associated with floods in 761 communities worldwide: time series study. doi: https://doi.org/10.1136/bmj-2023-075081 (Published 04 October 2023)

7. Türkiye afet ve acil durum yönetimi başkanlığı (AFAD). Türkiye doğal afet istatistikleri raporu 2022. Ankara: AFAD; 2023.

8. AFAD. Batı Karadeniz'de meydana gelen sel afetine ilişkin değerlendirme raporu, 2021.

9. BirGün. Bartın'da hasar tespit çalışmaları sona erdi: Zarar 23 milyon 107 bin 924 lira. (2021, Ağustos 16). https://www.birgun.net/haber/bartin-da-hasar-tespit-calismalari-sona-erdi-zarar-23-milyon-107-bin-924-lira-355955

10. Güner İ, & Özdemir M. Bartın-Bozkurt sel afetinin sağlık hizmetlerine etkisinin değerlendirilmesi. Türkiye Acil Tıp Dergisi. 2022;22(3):145-152.

11. Alderman K, Turner LR, & Tong S. Floods and human health: A systematic review. Environ Int. 2012;47:37-47. doi:10.1016/j.envint.2012.06.003

12. Sutton, J., Spiro, E., Butts, C., Fitzhugh, S., & Greer, J. Decision support systems in disaster health management: Applications of GIS and predictive analytics. Journal of Emergency Management, 1(2020), 8(4), 45–56.

13. AFAD. Afet yönetim ve karar destek sistemi (aydes). Afet ve acil durum yönetimi başkanlığı yayınları, 2023.

14. Karuppan Perumal, S., Kumar, R., & Singh, A. AI-based models for disaster health planning: Integrating epidemiological forecasting and logistics. International Journal of Disaster Risk Reduction, 2025, 78, 103–115.

15. Helms MM,& Nixon J. Exploring SWOT analysis – where are we now? A review of academic research from the last decade. J Strateg Manag. 2010;3(3):215-251. doi:10.1108/17554251011064837

16. Glaister KW. The usefulness of a SWOT analysis. Work study. 2003;6(4):39-44.

17. Saaty TL. The analytic hierarchy process: Planning, priority setting, resources allocation. New York: McGraw-Hill; 1980.

18. Türkiye İstatistik Kurumu (TÜİK). Bartın ili sosyoekonomik göstergeler. Ankara: TÜİK; 2023.

19. Forman E, & Peniwati K. Aggregating individual judgments and priorities with the Analytic Hierarchy Process. Eur J Oper Res. 1998;108(1):165-169. doi:10.1016/S0377-2217(97)00244-0

20. Waring SC,& Brown BJ. The threat of communicable diseases following natural disasters: A public health response. Disaster Manag Response. 2005;3(2):41-47. doi:10.1016/j.dmr.2005.02.003

21. Neria Y, Nandi A, & Galea S. Post-traumatic stress disorder following disasters:A systematic review. Psychol Med. 2008;38(4):467-480. doi:10.1017/S0033291707001353

22. Avrupa Komisyonu. Sağlık güvenliği ve afet direnci İçin ab finansman rehberi 2021-2027. Brüksel: Avrupa Komisyonu; 2021.

23. Ivers LC, Ryan ET. Infectious diseases of severe weather-related and flood disasters. Curr Opin Infect Dis. 2006;19(5):408-414. doi:10.1097/01.qco.0000244044.85393.9e

24. Türkiye Cumhuriyeti Sağlık Bakanlığı. Sağlık hizmetleri genel müdürlüğü afet ve acil durum planı. Ankara: Sağlık Bakanlığı Yayınları; 2022.

25. Kurttila M, Pesonen M, Kangas J, & Kajanus M. Utilizing the analytic hierarchy process (AHP) in SWOT analysis — A hybrid method and its application to a forest-certification case. For Policy Econ. 2000;1(1):41-52. doi:10.1016/S1389-9341(99)00004-0

26. Tavana M, Zareinejad M, Di Caprio D, & Kaviani MA. An integrated intuitionistic fuzzy AHP and SWOT method for outsourcing reverse logistics. Appl Soft Comput. 2016;40:544-557. doi:10.1016/j.asoc.2015.12.005

27. Cutter SL, Ash KD, & Emrich CT. The geographies of community disaster resilience. Glob Environ Change. 2014;29:65-77. doi:10.1016/j.gloenvcha.2014.08.005

AN ANALYSIS OF THE EFFECTS OF CLIMATE CHANGE ON HEALTH TOURISM

Pınar Seçmen

Sakarya University, Institute of Business Administration, Research Interests: Health Tourism, Climate Change and Health, Strategic Management, ORCID: https://orcid.org/0009-0002-1942-8333

ABSTRACT

Aim: The aim of this study is to quantitatively assess the health tourism potential of public and private healthcare institutions in the context of climate change and to identify strategic priorities. As extreme summer temperatures rise in Turkey's southern and inland regions, the cool climate of the Black Sea coastal belt presents a significant competitive opportunity for health tourism. With its extensive forested areas and low level of industrialization, Bartın Province stands out as a strategic area of focus in this context.

Methods: In the study, the A'WOT (AHP-Supported SWOT) method, which integrates the Analytic Hierarchy Process (AHP) to mitigate the subjective nature of the classical SWOT analysis, was employed. Five expert decision-makers (DMs)—comprising a physician, a healthcare administrator, a health tourism manager, and an academic—evaluated the four main SWOT categories and 16 sub-criteria using pairwise comparison matrices based on Saaty's 1–9 scale. All matrices were validated using a CR < 0.10 threshold.

Results: The Strengths (S) category ranked first with a weight of 53.6%; this was followed by Opportunities (28.1%), Weaknesses (11.5%), and Threats (6.8%). In the Strengths category, the thermal comfort of the Black Sea climate (S1: 0.353) is the dominant factor. In the Weaknesses category, the insufficient capacity for climate adaptation (W4: 0.402) stands out, while in the Opportunities category, the potential for active aging/rehabilitation targeting Europe's aging population (O1: 0.401) is prominent. Among the Threats, the risk of service disruptions caused by floods and landslides (T1: 0.510) alone accounts for more than half of the total weight of threats.

Conclusion: The A'WOT findings reveal that the region's competitive advantage is based on its climatic and environmental assets; however, the same climate system simultaneously constitutes the primary source of threat. This paradoxical relationship aligns with a structural pattern frequently observed in destination-based strategic analyses. Strengthening climate adaptation infrastructure (W4), increasing international patient reception capacity, and developing products focused on active aging are recommended as priority policy interventions. Digital health solutions (O4), meanwhile, remain in a complementary role. The findings present an evidence-based strategic framework that can be implemented through multi-stakeholder coordination involving the Ministry of Health, the Ministry of Culture and Tourism, and local governments.

Keywords: Decision-Making Processes, A'WOT Analysis, Climate Change, Medical Tourism, Bartın.

1. INTRODUCTION

Climate change is emerging as a multidimensional driving force that is transforming global tourism flows and destination preferences. As temperatures rise, precipitation patterns shift, and extreme weather events become more frequent, the appeal of many traditional tourism destinations is diminishing; this situation is triggering a redistribution process that is redirecting travel toward alternatives[1]. As a sub-sector that prioritizes thermal comfort and the quality of the natural environment as primary selection criteria, health tourism is disproportionately affected by this shift[2].

Turkey is a major destination for medical tourism; however, different regions within the country have unequal potential in this regard. While the Marmara and Mediterranean regions have well-established tourism economies, the need for new destinations is becoming increasingly evident due to climate change, which is causing summer temperatures in these areas to rise steadily.[3] In this context, the cool

and humid climate of the Black Sea coastline offers a comparative advantage in terms of thermal comfort, a factor that is attracting growing interest in European markets.[4]

Bartın Province presents a striking profile in terms of the characteristics that embody this potential: forested areas cover approximately 70% of the province's total land area, the level of industrialization remains significantly below the national average, and the province encompasses both continental and coastal microclimate characteristics. [5] However, systematic studies aimed at quantitatively documenting this potential and prioritizing it strategically have been quite limited.[6]

Strategic decision-making in the field of medical tourism typically requires a multidimensional assessment: internal capacity, market trends, competitive positioning, and potential risks must be addressed simultaneously.[7] While SWOT analysis provides an established framework for such assessments, its traditional application is qualitative and fails to quantitatively highlight the relative importance of these factors.[8] To overcome this limitation, Kurttila et al. (2000) developed the A'WOT method, which integrates AHP with SWOT analysis[9]. This hybrid approach significantly enhances the methodological rigor of strategic analysis by quantifying expert judgment through consistency verification mechanisms[7].

This study was designed to systematically and evidence-based assess Bartın's potential for health tourism in the context of climate change, document its competitive position stemming from its climate assets, identify structural vulnerabilities and development opportunities, and develop prioritized strategic recommendations for policymakers and health administrators. The findings are applicable to other coastal provinces with characteristics similar to those of Bartın and are therefore valuable for policy transfer.[10]

2. METHODOLOGY

This study employs a mixed-methods analytical design. The qualitative component covers SWOT factors through a systematic literature review and expert panel interviews, while the quantitative component involves weight calculations derived from AHP pairwise comparison matrices.

2.1. The Theoretical Basis of the A'WOT Method

The A'WOT method was first applied to strategic planning for forest certification.[9] The method consists of a three-step process: (1) Identification of SWOT categories and sub-criteria, (2) conduct of AHP pairwise comparisons by an expert panel, and (3) calculation and interpretation of composite weights. Saaty's (1980) 1–9 scale represents absolute equality (1) and the absolute superiority of one factor over another (9). On this scale, even numbers (2, 4, 6, 8) represent intermediate values.[7] The method's primary methodological strength lies in its ability to convert subjective expert judgments into quantitative priority values.[11]

2.2. Identification of SWOT Factors

The SWOT factors were identified through a systematic review of the health tourism literature, an examination of Turkey's health tourism legislation, and an assessment of Bartın's geographic and demographic characteristics. The review examined the climatic determinants of medical tourism,[12] Turkey's capacity to receive international patients,[13] and examples of disaster risk in the Western Black Sea region.[6] These factors were validated by a panel of experts, resulting in a final SWOT framework comprising a total of 16 factors, each consisting of four sub-criteria (Table 1).

Table 1. SWOT Analysis of Health Tourism in Bartın Province: SWOT Sub-Criteria

Category	Strengths (S)	Weaknesses (W)	Opportunities (O)	Threats (T)
Sub-Criterion 1	Black Sea Climate Thermal Comfort (S1)	Limited International Recognition (W1)	Active Aging / Rehabilitation Potential (O1)	Risk of Flood and Landslide Disruptions (T1)
Sub-Criterion 2	Forested Natural Environment (S2)	Inadequate Transportation Infrastructure (W2)	Digital Health Systems (O2)	Climate Uncertainty (T2)
Sub-Criterion 3	Low Industrialization / Clean Air (S3)	Shortage of Qualified Personnel (W3)	International Fund Support (O3)	Competition from Rival Destinations (T3)
Sub-Criterion 4	Natural Healing Waters and Mineral Water Sources (S4)	Insufficient Climate Adaptation Capacity (W4)	Digital Health Solutions (O4)	Economic Dependence on Foreign Countries (T4)

2.3. Expert Panel and Data Collection

The expert panel consists of five decision-makers: a physician (KV1), a healthcare administrator (KV2), a medical tourism manager (KV3), an AFAD expert (KV4), and an academic (KV5). Purposive sampling was used to select panel members; a minimum of five years of experience in the fields of health tourism management, climate health policy, or healthcare services in the Black Sea region was established as the primary criterion. Each expert completed separate pairwise comparison matrices at four main category levels and four sub-criteria levels within each category.[11] The individual weights were aggregated using the geometric mean method, which is the standard aggregation approach in the AHP methodology.[14]

2.4. Consistency Check

To minimize the risk of subjective judgment error, the consistency ratio (CR) was calculated for each matrix. Based on Saaty's (1980) threshold, a CR < 0.10 standard was established as the acceptance criterion; evaluations exceeding this threshold were returned to the relevant expert for review. This process ensures the mathematical validity of the weights and systematically controls for subjectivity[7].

3. FINDINGS

3.1. Main SWOT Category Weights

The "Strengths" category ranked first by a clear margin, with a weight of 0.536. This result indicates that the expert panel considers Bartın's natural climate and environmental assets to be more valuable than any vulnerabilities, opportunities, or threats; it demonstrates that the climate is perceived as a key competitive factor in terms of the destination strategy. The fact that the "Opportunities" category (28.1%) significantly outpaces the combined total of the "Weaknesses" (11.5%) and "Threats" (6.8%) categories reflects a generally optimistic strategic assessment of the region's external environment (Table 2).

Table 2. A'WOT Analysis - Weights of Main SWOT Categories

SWOT Category	AHP Weight	Ranking	Percentage (%)
Strengths (S)	0,536	1	53,6
Opportunities (O)	0,281	2	28,1
Weaknesses (W)	0,115	3	11,5
Threats (T)	0,068	4	6,8
Total	**1,000**	**—**	**100,0**

3.2. Sub-Criterion Weights for the Strengths Category

In the Strengths category, the thermal comfort of the Black Sea climate (S1: 0.353) ranked first. This weight indicates that the expert panel highlighted climatic comfort as the region's most significant competitive advantage. This finding aligns with the literature regarding the role of climate therapy and climate-based healing in determining health tourism destination selection.[15] The forested natural environment (G2: 0.285) ranked second; this result, which aligns with the growing global interest in forest bathing and nature-based health practices, points to a significant complementary advantage.[16]

Table 3. AHP Weights for Sub-Criteria in the Strengths Category

Sub-criterion	AHP Weight	Ranking
S1: Thermal Comfort in the Black Sea Climate	0,353	1
S2: Forested Natural Environment	0,285	2
S3: Low Industrialization / Clean Air	0,218	3
S4: Natural Healing Waters and Mineral Water Sources	0,144	4

3.3. Sub-Criterion Weights in the Weaknesses Category

In the Weaknesses category, insufficient climate adaptation capacity (W4: 0.402) has taken the top spot, clearly surpassing the other sub-criteria. This finding points to a striking paradoxical relationship: The region's primary competitive advantage (climate) is also the source of its most critical vulnerability, as the climate adaptation infrastructure is not yet at a level capable of preserving and sustaining this advantage. Limited international recognition (W1: 0.265) and inadequate transportation infrastructure (W2: 0.198) stand out as structural barriers that limit international patient access despite the region's comparative advantages.[13]

Table 4. AHP Weights for Sub-Criteria in the Weaknesses Category

Sub-criterion	AHP Weight	Ranking
W4: Insufficient Climate Adaptation Capacity	0,402	1
W1: Limited International Recognition	0,265	2
W2: Inadequate Transportation Infrastructure	0,198	3
W3: Shortage of Qualified Personnel	0,135	4

3.4. Sub-Criteria Weights for the Opportunities Category

Within the Opportunities category, the potential for active aging and rehabilitation (F1: 0.401) has been identified as the highest-priority opportunity. The aging demographic structure of the European population is creating an increasingly large demand base for long-term therapeutic stays in climatically favorable destinations.[17] Digital health systems (F2: 0.247), meanwhile, stand out as a significant complementary opportunity due to their potential to overcome geographical constraints through telemedicine and remote patient monitoring.[18]

Table 5. AHP Weights for Sub-Criteria in the Opportunities Category

Sub-criterion	AHP Weight	Ranking
O1: Active Aging / Rehabilitation Potential	0,401	1
O2: Digital Health Systems	0,247	2
O3: International Fund Support	0,218	3
O4: Digital Health Solutions	0,134	4

3.5. Sub-Criteria Weights for the Threats Category

In the Threats category, the risk of service disruption caused by floods and landslides (T1: 0.510) was assigned an exceptionally high weight; this single factor accounted for more than half of the category's total weight. This finding is significant: The participating experts have identified the existence of a single threat that is so dominant and potentially devastating as to render all other threats insignificant. This observation gains further significance when considering local officials' institutional memory of recent flood experiences, such as the Batın-Bozkurt event.[6] Climate uncertainty (T2: 0.248), meanwhile, reflects the challenges of long-term planning.

Table 6. AHP Weights for Sub-Criteria in the Threats Category

Sub-criterion	AHP Weight	Ranking
T1: Risk of Service Disruptions Caused by Floods and Landslides	0,510	1
T2: Climate Uncertainty	0,248	2
T3: Pressure from Competitor Destinations	0,148	3
T4: Economic Dependence	0,094	4

4. DISCUSSION

The most striking pattern emerging from the interpretation of the A'WOT findings is the structural paradox in which climate assets serve as the source of both competitive advantage (S1: 0.353) and the dominant threat (T1: 0.510). This paradox aligns with a pattern frequently observed in destination-based strategic analyses: It is possible that a region's most valuable assets also represent its greatest vulnerabilities.[19] In the case of Bartın, the climate system that makes the region attractive for tourism is also the very system that fuels disaster risk.

The fact that active aging and rehabilitation (O1: 0.401) emerge as the highest-priority opportunity is consistent with evidence-based projections. Demographic changes in Europe are driving an increasing demand for long-term stays focused on health and well-being; The region's climatic characteristics provide a suitable foundation for these services. To capitalize on this opportunity, however, a robust marketing strategy is required, backed by international accreditation, multilingual service delivery, and documented clinical expertise.[17]

The identification of insufficient climate adaptation capacity (W4: 0.402) as the highest-weighted weakness serves as an important indicator of how policy priorities are perceived in the region. Given that this sub-criterion ranks first among the weaknesses and is evaluated in conjunction with the T1 weight in the threat category, it is clear that climate resilience is an indispensable prerequisite for any health tourism development strategy. If healthcare facilities become inoperable during floods or landslides, this will not only have a direct negative impact on health outcomes but could also lead to significant reputational damage in terms of marketing the region's health tourism sector.[6]

The fact that digital health solutions (O4: 0.134) remain at a complementary priority level aligns with recent initiatives aimed at overcoming geographic and transportation barriers to market access through telemedicine services. However, the fact that they carry the lowest opportunity weight indicates that digital solutions cannot replace physical and in-person care; yet, they can significantly enhance service access and the patient experience.[18]

5. CONCLUSION

This study presents a structured, evidence-based, and quantitative strategic analysis of the impacts of climate change on health tourism in Bartın Province. The A'WOT methodology enabled the systematic prioritization of strategic factors, thereby overcoming the qualitative limitations of traditional SWOT analysis.

Based on the findings, the following policy recommendations have been developed:

- ✓ Climate adaptation infrastructure (W4: 0.402) should be an urgent investment priority. Structural reinforcement of high-risk facilities, flood-resistant design standards, and comprehensive business continuity planning are key areas requiring immediate action.
- ✓ Specialized service packages should be developed for active aging and rehabilitation products (O1: 0.401); in this context, international accreditation, the hiring of multilingual staff, and marketing initiatives targeting the European market should be implemented.
- ✓ Flood and landslide risk management (T1: 0.510) must be addressed with the utmost care at the healthcare facility level. Early warning systems, emergency evacuation protocols, and contingency plans for service delivery should be established as a priority in this context.
- ✓ Efforts to increase access for international patients should be expanded; priority should be given to targeted promotional campaigns that will introduce the region to EU health tourism markets, alongside projects to develop transportation infrastructure.
- ✓ A coordinated, multi-stakeholder management structure should be established among the Ministry of Health, the Ministry of Culture and Tourism, AFAD, and the Bartın Provincial Special Administration to ensure the comprehensive implementation of the regional health tourism strategy.

The primary methodological contribution of this study is the application of the A'WOT method to climate-focused health tourism planning in Turkey. The findings reveal that Bartın has high potential; however, they emphasize that this potential can only be realized through evidence-based management practices that directly address climate risks.[20] It is recommended that future research include a longitudinal assessment using time-series analysis, a comparative study of multiple provinces in the Black Sea region, and primary market research to assess the preferences of both domestic and foreign potential health tourists.

REFERENCES

1. Scott D, Hall CM, Gössling S. Global Tourism and Climate Change: A Review of Impacts, Adaptation Strategies and Future Challenges. J Sustain Tour. 2012;20(1):1-39. doi:10.1080/09669582.2011.630852

2. Lohmann M, Kaim A. Weather and Holiday Destination Preferences. Image, Attitude and Experience. Tour Rev. 1999;54(2):54-64. doi:10.1108/eb058299

3. Türkiye Kültür ve Turizm Bakanlığı. Sağlık Turizmi Strateji Belgesi 2023-2030. Ankara: Kültür ve Turizm Bakanlığı Yayınları; 2023.

4. Matzarakis A. Weather- and Climate-Related Information for Tourism. Tour Hosp Plan Dev. 2006;3(2):99-115. doi:10.1080/14790530600938279

5. Türkiye İstatistik Kurumu (TÜİK). Bartın İli Arazi Kullanımı ve Çevre İstatistikleri. Ankara: TÜİK; 2023.

6. Güner İ, Özdemir M. 2021 Bartın-Bozkurt Sel Felaketinin Değerlendirilmesi: Sağlık Hizmetlerine Etkileri ve Alınan Dersler. Türk Afet ve Acil Durum Dergisi. 2022;4(1):12-24.

7. Saaty TL. The Analytic Hierarchy Process: Planning, Priority Setting, Resources Allocation. New York: McGraw-Hill; 1980.

8. Helms MM, Nixon J. Exploring SWOT Analysis - Where Are We Now? A Review of Academic Research from the Last Decade. J Strateg Manag. 2010;3(3):215-251. doi:10.1108/17554251011064837

9. Kurttila M, Pesonen M, Kangas J, Kajanus M. Utilizing the Analytic Hierarchy Process (AHP) in SWOT Analysis - A Hybrid Method and Its Application to a Forest-Certification Case. For Policy Econ. 2000;1(1):41-52. doi:10.1016/S1389-9341(99)00004-0

10. Dwyer L, Edwards D, Mistilis N, Roman C, Scott N. Destination and Enterprise Management for a Tourism Future. Tour Manag. 2009;30(1):63-74. doi:10.1016/j.tourman.2008.04.002

11. Kajanus M, Kangas J, Kurttila M. The Use of Value Focused Thinking and the A'WOT Hybrid Method in Tourism Management. Tour Manag. 2004;25(4):499-506. doi:10.1016/S0261-5177(03)00120-1

12. Hein L, Metzger MJ, Moreno A. Potential Impacts of Climate Change on Tourism; A Case Study for Spain. Curr Opin Environ Sustain. 2009;1(2):170-178. doi:10.1016/j.cosust.2009.10.005

13. Lunt N, Smith R, Exworthy M, Green ST, Horsfall D, Mannion R. Medical Tourism: Treatments, Markets and Health System Implications: A Scoping Review. Paris: OECD; 2011.

14. Forman E, Peniwati K. Aggregating Individual Judgments and Priorities with the Analytic Hierarchy Process. Eur J Oper Res. 1998;108(1):165-169. doi:10.1016/S0377-2217(97)00244-0

15. Mucha W. Climatotherapy: Historical and Contemporary Overview. Balneol Pol. 2008;50(1):34-42.

16. Li Q. Effect of Forest Bathing Trips on Human Immune Function. Environ Health Prev Med. 2010;15(1):9-17. doi:10.1007/s12199-008-0068-3

17. Smith M, Puczko L. Health, Tourism and Hospitality: Spas, Wellness and Medical Travel. 2nd ed. London: Routledge; 2014.

18. Mechael P, Batavia H, Kaonga N, et al. Barriers and Gaps Affecting mHealth in Low and Middle Income Countries: Policy White Paper. New York: Columbia University Earth Institute; 2010.

19. Weihrich H. The TOWS Matrix: A Tool for Situational Analysis. Long Range Plan. 1982;15(2):54-66. doi:10.1016/0024-6301(82)90120-0

20. Jopp R, DeLacy T, Mair J. Developing a Framework for Regional Destination Adaptation to Climate Change. Curr Issues Tour. 2010;13(6):591-605. doi:10.1080/13683501003653379

ÇOCUKLARINI KAYBEDEN EBEVEYNLERİN DUYGUSAL VE DAVRANIŞSAL SORUNLARI VE YAŞAM SONU BAKIMDA PEDİATRİ HEMŞİRELERİN ROLÜ

Burcu YILMAZ

Ardahan Üniversitesi, Sağlık Bilimleri Fakültesi, Hemşirelik Bölümü, Çocuk Sağlığı Hastalıkları Hemşireliği, 0000-0001-6423-6483

Derya ŞİMŞEKLİ

Ardahan Üniversitesi, Sağlık Bilimleri Fakültesi, Hemşirelik Bölümü, İç Hastalıkları Hemşireliği, 0000-0002-3904-951X

ÖZET

Gelişmiş ülkelerde pediatrik ve yenidoğan ölümlerinin önemli bir bölümü yoğun bakım ünitelerinde gerçekleşmekte ve bu durum çoğu zaman yaşamı sürdürmeye yönelik tedavilerin sınırlandırılması kararlarıyla ilişkilendirilmektedir. Tıp ve teknolojideki ilerlemeler, yaşamı tehdit eden hastalıklara sahip çocukların bakım süresini uzatırken, ailelerin üstlendiği bakım rolünü de daha karmaşık ve çok boyutlu hale getirmiştir. Aileler, günlük bakımın ötesinde hastalığa özgü gereksinimleri karşılamak zorunda kalmakta; bu süreç hem fiziksel hem de duygusal açıdan yıpratıcı bir deneyim yaratmaktadır. Ayrıca birçok ebeveyn, çocuklarının hastalığının ölümle sonuçlanabileceğinin farkında olarak bakım vermekte ve bu durum bakım sürecinin belirsizlik, kaygı ve sürekli bir kayıp beklentisiyle sürdürülmesine neden olmaktadır. Ölüm, yaşamın evrensel bir gerçeği olmakla birlikte, bir çocuk söz konusu olduğunda çok daha derin ve sarsıcı bir anlam kazanmaktadır. Çocuğun kaybı, yalnızca bir bireyin kaybı değil; aynı zamanda geleceğe dair umutların, beklentilerin ve potansiyelin yitirilmesi anlamına gelmektedir. Bu nedenle çocuk ölümü, aileler üzerinde yoğun psikolojik ve varoluşsal etkiler bırakan en yıkıcı deneyimlerden biri olarak değerlendirilmektedir. Hastane ortamında gerçekleşen bu kayıp, ebeveynlerin ölüm anısına dair güçlü hatıralar geliştirmesine ve uzun süreli bir yas süreci yaşamasına yol açabilmektedir. Öte yandan, pediatrik ve yenidoğan yoğun bakım üniteleri aileler için çoğu zaman yabancı, belirsizliklerle dolu ve stresli bir ortamdır. Çocuğun kritik durumu, bilgiye erişimde yaşanan güçlükler ve sürecin öngörülemezliği, ebeveynlerin psikolojik yükünü artırmaktadır. Bu bağlamda, aile merkezli bakım yaklaşımı, ebeveynlerin ihtiyaçlarının fark edilmesi ve desteklenmesi açısından önemli bir çerçeve sunmaktadır. Bu süreçte pediatri hemşirelerinin rolü, yalnızca çocuğa bakım vermekle sınırlı olmayıp, aileyi de kapsayan bütüncül bir destek sağlamayı içermektedir.

Anahtar Kelimeler: yas, pediatrik yoğun bakım üniteleri, yenidoğan yoğun bakım üniteleri, palyatif bakım, pediatri hemşireliği

EMOTIONAL AND BEHAVIORAL ISSUES AMONG PARENTS WHO HAVE LOST THEIR CHILDREN: THE ROLE OF PEDIATRIC NURSES IN END-OF-LIFE CARE

ABSTRACT

In developed countries, a significant proportion of pediatric and neonatal deaths occur in intensive care units, and this situation is often associated with decisions to limit life-sustaining treatments. Advances in medicine and technology have extended the duration of care for children with life-threatening illnesses, while also making the caregiving role assumed by families more complex and multifaceted. Families are often required to meet disease-specific needs beyond daily care; this process creates an experience that is physically and emotionally draining. Additionally, many parents provide care while being aware that their child's illness may result in death, leading to a care process marked by uncertainty, anxiety, and a constant expectation of loss. While death is a universal reality of life, it takes on a much deeper and more shattering meaning when a child is involved. The loss of a child is not merely the loss of an individual; it also signifies the loss of hopes, expectations, and potential for the future. For this reason, the death of a child is considered one of the most devastating experiences, leaving profound

psychological and existential impacts on families. This loss, occurring in a hospital setting, can lead parents to develop strong memories of the moment of death and to experience a prolonged grieving process. On the other hand, pediatric and neonatal intensive care units are often unfamiliar, uncertain, and stressful environments for families. The child's critical condition, difficulties in accessing information, and the unpredictability of the process increase the parents' psychological burden. In this context, family-centered care provides a framework for recognizing and supporting parents' needs. Pediatric nurses' role extends beyond caring for the child to providing comprehensive family support.

Keywords: bereavement, pediatric ıntensive care units, neonatal ıntensive care units, palliative care, pediatric nursing

GİRİŞ

Pediatrik ve yenidoğan yoğun bakım üniteleri (PYBÜ), yaşamı tehdit eden hastalık veya yaralanmalar nedeniyle çocukların kritik bakım aldığı özel birimlerdir. Yenidoğan yoğun bakım ünitelerinde (YYBÜ)ise bakım gereksinimlerinin ve klinik karmaşıklığın yüksek olması nedeniyle ölüm, zaman zaman kaçınılmaz bir sonuç olarak ortaya çıkabilmektedir. Bu ölümlerin önemli bir bölümü, yaşamı sürdürmeye yönelik tıbbi tedavilerin sınırlandırılması veya sonlandırılması kararlarının ardından gerçekleşmektedir. Bu durum, ölümün çoğunlukla yoğun tedavi girişimlerinin sürdürülmesine rağmen meydana geldiği genel pediatrik hasta grubundan farklılık göstermektedir. [1] Bu ünitelerde tedavi gören bir çocuğun varlığı, ebeveynler için ani, beklenmedik ve son derece stresli bir deneyim olup, aileleri psikolojik olarak zorlayan bir süreci beraberinde getirmektedir.[2] Özellikle yoğun bakım ortamının yabancı ve teknolojik yapısı, ebeveynlerde kaygı, korku ve çaresizlik duygularını artırabilmektedir.[3].

Çocuğun yaşamı için verilen mücadele sürecinde ebeveynler yalnızca fiziksel değil, aynı zamanda yoğun duygusal yük altında kalmaktadır. Çocuğun kritik hastalığına tanıklık etmek, belirsizlik ve kontrol kaybı hissi ile birleştiğinde ebeveynlerde travmatik stres tepkilerine yol açabilmektedir.[4] Yapılan çalışmalar, bu süreçte ebeveynlerin yoğun anksiyete, depresif belirtiler, suçluluk duygusu ve uyku problemleri gibi duygusal ve davranışsal sorunlar yaşayabildiğini göstermektedir.[5]

Çocuk kaybı gerçekleştiğinde ise yas süreci daha da karmaşık hale gelmektedir. Ebeveynlerde derin üzüntü, öfke, inkâr, sosyal geri çekilme ve yaşam kalitesinde belirgin düşüş gibi durumlar gözlenebilmektedir. Ayrıca bazı ebeveynlerde uzun süre devam eden komplike yas, travma sonrası stres belirtileri ve günlük yaşam işlevlerinde bozulmalar ortaya çıkabilmektedir.[6]

Yaşam sonu bakım, çocuğun konforunu artırmayı, semptom kontrolünü sağlamayı ve aileyi bu sürece hazırlamayı amaçlayan bütüncül bir bakım yaklaşımıdır.[7] Yaşam sonu bakım sürecinde alınacak tıbbi kararların belirlenmesinde, sağlık profesyonelleri ile ailelerin birlikte yer aldığı ortak karar verme yaklaşımı günümüzde en uygun yöntemlerden biri olarak kabul edilmektedir. Bu yaklaşım, ailelerin bakım sürecine aktif katılımını desteklerken, alınan kararların çocuğun yararı ve ailenin değerleri doğrultusunda şekillendirilmesini amaçlamaktadır.[8] Bununla birlikte, tanı ve prognoza ilişkin belirsizlikler, gelecekteki sağlık sonuçlarının öngörülememesi ve aileler ile sağlık profesyonelleri arasındaki kültürel, dini ve sosyal farklılıklar karar verme sürecini zorlaştırabilmektedir. Ayrıca sağlık ekibinin tıbbi seçenekleri ve olası sonuçları ailelere hangi yöntemle ve ne ölçüde aktaracağı konusunda da farklı yaklaşımlar bulunmaktadır. Ailelerin geçmiş deneyimleri, yaşam öyküleri, inançları ve beklentileri karar alma süreçlerini etkileyebildiğinden, yaşam sonu bakım kararlarının her aile için bireysel gereksinimler doğrultusunda değerlendirilmesi gerekmektedir.[9]

Ebeveyn yasını desteklemeye yönelik uygulamaları değerlendiren güncel araştırmalar, yenidoğan yoğun bakım sürecinde ailelerin birçok açıdan yeterince desteklenemediğini ortaya koymaktadır.[1] Özellikle ebeveynlerin bebekleriyle anlamlı zaman geçirebilmeleri, bakım süreçlerine aktif olarak katılabilmeleri, sağlık ekibiyle açık iletişim kurabilmeleri ve palyatif ya da manevi destek hizmetlerinden yararlanabilmeleri yas sürecini etkileyen önemli unsurlar arasında yer almaktadır. Ancak mevcut bulgular, bu gereksinimlerin her zaman yeterli düzeyde karşılanamadığını göstermektedir. Ebeveynler, bebeklerini kucaklama, bakımına katılma ve bakım sürecine ilişkin düşüncelerini sağlık ekibiyle paylaşma konusunda zaman zaman sınırlı destek aldıklarını ifade etmektedir. Bu durum, yaşanan kaybın etkilerini derinleştirerek ebeveynlerin yas deneyimini daha karmaşık hale getirebilmektedir.

Çocuğun kaybı ya da kayıp olasılığıyla karşı karşıya kalmak, ebeveynlerde yoğun duygusal tepkilere yol açabilmektedir. Yas, çaresizlik, suçluluk, korku ve derin üzüntü bu süreçte sık karşılaşılan duygular arasında yer almaktadır. Özellikle anneler, bakım sürecinin çoğunlukla bebeğin klinik durumuna odaklanması nedeniyle kendi duygusal gereksinimlerinin göz ardı edildiğini hissedebilmektedir.[10] Bu durum ebeveynlerin ebeveynlik rollerini deneyimlemelerini ve kayıpla baş etme süreçlerini olumsuz etkileyebilmektedir. Bu nedenle yenidoğan yoğun bakım ünitelerinde ailelerle güvene dayalı ilişkilerin kurulması, düzenli ve anlaşılır bilgi paylaşımının sağlanması, ebeveynlerin bakım ve karar verme süreçlerine aktif katılımının desteklenmesi ve duygusal gereksinimlerinin dikkate alınması yaşam sonu bakımın temel bileşenleri arasında kabul edilmektedir.[11]

Bu süreçte pediatri hemşireleri, yalnızca klinik bakım sağlayan kişiler değil, aynı zamanda aile ile çocuk arasında iletişimi güçlendiren, duygusal destek sunan ve yas sürecini kolaylaştıran önemli sağlık profesyonelleridir.[7] Hemşireler, ebeveynlerin bilgi gereksinimlerini karşılamak, karar verme süreçlerine katılımlarını desteklemek ve çocuğun son döneminde anlamlı zaman geçirmelerini sağlamak gibi önemli roller üstlenmektedir.[8]

Bu nedenle çocuklarını kaybeden ebeveynlerin duygusal ve davranışsal tepkilerinin anlaşılması ve yaşam sonu bakım sürecinde pediatri hemşirelerinin rollerinin değerlendirilmesi, aile merkezli bakımın geliştirilmesi açısından büyük önem taşımaktadır.[12]

Güncel çalışmalar, yenidoğan yoğun bakım ünitelerinde ebeveynlerin bakım sürecine aktif katılımının hem aile hem de bebek açısından olumlu sonuçlar doğurduğunu göstermektedir.[13] Bu doğrultuda geliştirilen aile bütünleşik bakım yaklaşımı, ebeveynleri yalnızca bakımın alıcısı olarak değil, sağlık ekibinin önemli bir paydaşı olarak değerlendirmektedir. Bu model kapsamında ailelerin bakım planlamasına katılımı teşvik edilmekte, karar verme süreçlerinde söz sahibi olmaları desteklenmekte ve psikososyal gereksinimlerinin karşılanmasına önem verilmektedir. Ayrıca ebeveynlerin bebeklerinin günlük bakımına katılmaları ve sağlık profesyonelleriyle iş birliği içinde olmaları aile merkezli bakım anlayışının temel unsurları arasında yer almaktadır. Araştırmalar, bu yaklaşımın ebeveyn memnuniyetini artırdığını, ailelerin bakım sürecine uyumunu kolaylaştırdığını ve kayıp yaşayan ailelerin yas süreçlerini daha sağlıklı yönetmelerine katkı sağlayabildiğini bildirmektedir.[14]

Öte yandan yaşam sonu bakım kararlarının alınması ve yas sürecinin desteklenmesi, sağlık profesyonelleri ile aileler açısından karmaşık ve duygusal açıdan zorlayıcı bir süreç olarak değerlendirilmektedir. Yoğun bakım hemşireleri açısından bakıldığında, PYBÜ'de yaşam sonu bakımı oldukça zorlu bir süreçtir.[15] Hemşireler, çocuğun klinik gereksinimlerini karşılarken aynı zamanda bilgi paylaşımını kolaylaştırmak,[16] mahremiyet ve saygınlığı korumak,[15,17] ebeveynleri ve aileyi desteklemek,[15,18] yas bakımına katılmak ve anı oluşturma süreçlerini yürütmek durumundadır.[15,16,18]

Her ailenin kültürel özellikleri, yaşam deneyimleri, değerleri ve beklentileri farklı olduğundan, yaşam sonu bakım uygulamalarının bireysel gereksinimlere göre planlanması gerekmektedir. Ebeveynlerin yaşadıkları deneyimlerin daha iyi anlaşılması ve onların bakış açılarının ortaya konulması, yaşam sonu bakım uygulamalarının geliştirilmesi ve sağlık profesyonellerinin ailelere daha etkili destek sunabilmeleri açısından önem taşımaktadır.[1]

Bu nedenle, çocuk kaybı yaşayan ebeveynlerin yaşam sonu bakım sürecindeki deneyimlerinin anlaşılması ve bu süreçte karşılaştıkları duygusal ile davranışsal güçlüklerin belirlenmesi büyük önem taşımaktadır. Araştırmalar, yaşam sonu bakım sürecinde ebeveynlerin bebekleriyle zaman geçirebilmelerinin, bakım süreçlerine katılabilmelerinin, sağlık profesyonelleriyle açık iletişim kurabilmelerinin ve psikososyal destek alabilmelerinin yas sürecine uyumlarını olumlu yönde etkilediğini göstermektedir. Buna karşın iletişim eksiklikleri, karar verme sürecine yeterince katılamama ve destek hizmetlerine erişimde yaşanan yetersizlikler ebeveynlerin kayıp deneyimini daha da ağırlaştırabilmektedir. Bu noktada pediatri hemşireleri; aile merkezli bakımın sürdürülmesi, ebeveynlerin bakım ve karar verme süreçlerine katılımının desteklenmesi, etkili iletişimin sağlanması ve yas sürecine yönelik duygusal desteğin sunulmasında temel bir role sahiptir. Çocuk kaybının ebeveynlerde oluşturduğu uzun süreli psikolojik etkiler göz önünde bulundurulduğunda, yaşam sonu bakımda pediatri hemşirelerinin rolünün güçlendirilmesi ve kanıta dayalı uygulamaların geliştirilmesi gerekmektedir.[19-23]

Çocuklarda yaşam sonu bakım, hemşirelik araştırmalarında öncelikli alanlardan biri olarak kabul edilmektedir. Özellikle ebeveynler, aile üyeleri ve sağlık profesyonelleri arasındaki güven ve iletişim gibi yaşam sonu bakımın ilişkisel yönlerinin daha iyi anlaşılmasına ihtiyaç duyulmaktadır. [15] Bu kapsamda, "Çocuklarını Kaybeden Ebeveynlerin Duygusal ve Davranışsal Sorunları: Yaşam Sonu Bakımda Pediatri Hemşirelerinin Rolü" başlıklı bu derleme, çocuk kaybı sonrası ebeveynlerde ortaya çıkan psikolojik ve davranışsal etkileri ve bu süreçte pediatri hemşirelerinin üstlendiği destekleyici rolleri mevcut literatür doğrultusunda incelemeyi amaçlamaktadır. Derleme, yaşam sonu bakımın yalnızca klinik uygulamalarla sınırlı olmadığını, aynı zamanda aile merkezli bakım, etkili iletişim ve duygusal destek süreçlerini içeren bütüncül bir yaklaşım gerektirdiğini ortaya koymaktadır.

ÇOCUKLARINI KAYBEDEN EBEVEYNLERİN DUYGUSAL VE DAVRANIŞSAL SORUNLARI YAŞAM SONU BAKIMDA PEDİATRİ HEMŞİRELERİN ROLÜ

Gelişmiş ülkelerde pediatrik ve yenidoğan ölümlerinin büyük bir kısmı yoğun bakım ünitelerinde gerçekleşmekte ve bu durum çoğunlukla yaşamı sürdürmeye yönelik tedavinin sınırlandırılması kararının ardından ortaya çıkmaktadır. [12,24] Yaşamı sınırlayan ya da yaşamı tehdit eden hastalıklara sahip çocukların bakım süreci, tıp ve teknolojideki ilerlemelere paralel olarak daha uzun ve daha karmaşık bir hale gelmiştir. Bu durum, ailelerin üstlendiği bakım rolünü yalnızca süre açısından değil, içerik bakımından da derinleştirmekte ve çok yönlü bir sorumluluk alanına dönüştürmektedir. Günlük çocuk bakımına ek olarak hastalığa özgü gereksinimlerin karşılanması, aileler için hem fiziksel açıdan yorucu hem de duygusal açıdan yıpratıcı bir süreç yaratmaktadır.[25] Ayrıca birçok aile, çocuklarının hastalığının ölümle sonuçlanabileceğinin farkında olarak bakım vermekte; bu da bakım sürecinin sürekli bir belirsizlik, kaygı ve kayıp beklentisi eşliğinde sürdürülmesine neden olmaktadır. Bu yönüyle aileler, bir yandan yaşamı desteklemeye çalışırken diğer yandan olası kayba hazırlık yapmayı gerektiren oldukça zorlayıcı bir deneyim yaşamaktadır.[24] Ölüm, insan yaşamının kaçınılmaz ve evrensel bir gerçeği olmakla birlikte, özellikle bir çocuk söz konusu olduğunda anlamı çok daha derin ve sarsıcı bir boyut kazanmaktadır. Yaşam ve ölüm çoğu zaman birbirinin karşıtı gibi algılansa da, aslında iç içe geçmiş süreçlerdir; ancak bu döngü çocuklar için düşünüldüğünde, "erken" ve "beklenmedik" oluşu nedeniyle kabullenilmesi güçleşmektedir. Bir çocuğun ölümü, yalnızca biyolojik bir kayıp değil, aynı zamanda geleceğe dair umutların, hayallerin ve potansiyelin de yitirilmesi anlamına gelmektedir.[26] Bu durum, aileler ve toplum açısından kaybın duygusal yükünü daha da ağırlaştırır. Ölüm kavramı çoğu birey için zaten zorlayıcıyken, çocukla ilişkilendirildiğinde korku, çaresizlik ve kaçınma duygularını daha yoğun hale getirir. Bu nedenle çocukta ölüm olgusu, yalnızca bireysel değil, aynı zamanda derin psikososyal ve varoluşsal etkiler yaratan, yas sürecini daha karmaşık hale getiren bir deneyim olarak öne çıkmaktadır.[27].Hastane ortamında bir çocuğun kaybı, ebeveynler ve aile üyeleri üzerinde derin ve uzun süreli etkiler bırakmakta; özellikle ölüm anına ilişkin anılar ve buna eşlik eden yas süreci, bireylerin yaşamlarını önemli ölçüde şekillendirmektedir. Çocuk kaybı, çok katmanlı duygusal tepkiler ve varoluşsal sorgulamaları içeren, en yıkıcı kayıp türlerinden biri olarak değerlendirilmektedir. Bu nedenle yenidoğan ve pediatrik yoğun bakım hemşirelerinin, yalnızca çocuğa değil aynı zamanda ebeveynler ve geniş aileye yönelik yaşam sonu bakım sürecini de duyarlı ve bütüncül bir yaklaşımla yönetmesi gerekmektedir.[28]

Öte yandan, yaşamı tehdit eden hastalık ya da yaralanma nedeniyle pediatrik yoğun bakım ünitelerine yatırılan çocukların aileleri için bu süreç çoğu zaman ani, beklenmedik ve son derece stresli bir deneyimdir.[29] Yabancı bir ortam olarak algılanan yoğun bakım üniteleri, ebeveynler tarafından sıklıkla "duygusal bir iniş çıkış" şeklinde tanımlanmakta; çocuğun kritik durumu ile birlikte belirsizlikler ve zamanında bilgiye ulaşmadaki güçlükler bu stresi daha da artırmaktadır. Bu etkiler, yatışın ilk saatlerinden itibaren hissedilmekte ve uzun vadede ebeveynlerin psikolojik ve fiziksel sağlığını, baş etme becerilerini ve genel iyilik halini olumsuz yönde etkileyebilmektedir.[30-31]Bu bağlamda, aile merkezli bakım yaklaşımı, ebeveynlerin ve aile üyelerinin ihtiyaçlarının fark edilmesi ve karşılanmasında önemli bir rol oynamaktadır.

EBEVEYNLERDE KAYIP SONRASI RUHSAL TEPKİLER VE TRAVMA SONRASI BÜYÜME

Bir çocuğun kaybı, ebeveynler için son derece sarsıcı bir deneyim olup genellikle yoğun ve derin bir yas süreciyle sonuçlanır. Yas bazı durumlarda akut bazı durumlarda ise karmaşık olabilir. Ruhsal Bozuklukların Tanı ve İstatistik El Kitabı'nın (DSM) beşinci baskısına dahil edilecek yeni bir tanı birimi olarak önerilen karmaşık yas, kişilerin günlük işlevselliğini engellemekte 6 aydan fazla sürmektedir. Yoğun özlem, şok ,inanamama, öfke ve acı yaşayan ebevynler [32] Bu süreçte ebeveynlerin anksiyete, depresyon, travma sonrası stres belirtileri ve uzun süreli yas tepkileri geliştirme riski artmaktadır. Güncel tanı sınıflandırmalarında "uzamış yas bozukluğu" olarak ele alınan bu durum, kaybedilen çocuğa yönelik yoğun özlem, kaybın gerçekliğini kabullenmede güçlük ve günlük yaşam işlevselliğinde belirgin bozulmalar ile karakterizedir. ICD-11 ve DSM-5-TR'de yer alan Uzamış Yas Bozukluğu (PGD) kriterlerine ilişkin mevcut sınıflandırmaların büyük ölçüde Avrupa ve Kuzey Amerika merkezli araştırmalara dayandığı belirtilmektedir. Bu durum, PGD'ye ilişkin bilgilerin kültürlerarası geçerliliği konusunda önemli bir sınırlılık oluşturmaktadır.[33-34] Literatürde, yas tepkilerinin kültürler arasında hem ifade edilme biçimi hem de semptomların algılanması açısından farklılık gösterdiği vurgulanmaktadır.[35] Bu farklılıklar, bazı kültürel bağlamlarda anlamlı kabul edilen yas belirtilerinin mevcut PGD tanı ölçütleri içerisinde yeterince temsil edilmemiş olabileceğini düşündürmektedir.[36] Örneğin, Japonya'da yas sürecine ilişkin yapılan nitel çalışmalar, bireylerde somatik yakınmaların belirgin olduğunu ortaya koymuş, ancak bu belirtilerin mevcut PGD kriterlerinde yeterince yer almadığı görülmüştür.[34] Çocuk kaybı, en ağır yas deneyimlerinden biri olarak kabul edilmekte ve uzamış yas bozukluğu (PGD) riskini artırabilmektedir.[37-38] Özellikle Çin'de tek çocuğunu kaybeden "shidu ebeveynler", çocuk kaybını daha karmaşık bir süreç olarak yaşamakta ve bu grup kültürel, sosyal ve yapısal faktörler nedeniyle yüksek riskli kabul edilmektedir. Konfüçyüsçü kültürün etkisiyle çocuk, aile desteği ve yaşam anlamının temel kaynağı olarak görülmekte; çocuksuzluk ise toplumsal baskı ve damgalanma ile ilişkilendirilebilmektedir.[39] Bu durum, shidu ebeveynlerde PGD, depresyon ve travma sonrası stres gibi psikolojik sorunların daha sık görülmesine yol açmaktadır.[40-41] Mevcut bulgular, bu grubun kültürel bağlamının Batı temelli PGD kriterleriyle tam olarak açıklanamayabileceğini ve kültüre duyarlı yaklaşımlara ihtiyaç olduğunu göstermektedir. [38,42] Bu nedenle, PGD kavramının kültürel duyarlılık açısından yeniden değerlendirilmesi ve özellikle Batı dışı toplumlarda yas deneyimlerinin daha kapsamlı biçimde ele alınması gerektiği ifade edilmektedir.

Bununla birlikte, her ebeveyn bu süreci patolojik düzeyde yaşamaz; bazı ebeveynler derin bir yas deneyimi yaşasa da klinik bir bozukluk geliştirmeden süreci yönetebilmektedir.

Öte yandan, yaşanan büyük kayba rağmen bazı ebeveynler zamanla yaşamlarında olumlu değişimler fark edebilmektedir. Literatürde bu durum; stresle ilişkili büyüme, fayda bulma ya da travma sonrası büyüme kavramlarıyla açıklanmaktadır. Travma sonrası büyüme, bireyin ciddi bir travmatik yaşantı sonrasında anlam arayışı ve bilişsel-duygusal yeniden yapılanma süreciyle birlikte ortaya çıkan olumlu dönüşümleri ifade eder. Bu süreç; kişilerarası ilişkilerde güçlenme, yaşam önceliklerinin yeniden şekillenmesi, kişisel dayanıklılığın artması, manevi ya da varoluşsal farkındalık gelişimi ve yaşamın değerine yönelik daha derin bir anlayış kazanılması gibi alanlarda kendini gösterebilir.[43]

Farklı travmatik deneyimler yaşayan bireylerde olduğu gibi, çocuk kaybı yaşayan ebeveynlerde de travma sonrası büyüme gözlenebilmektedir. Ebevynlerin yas sürecinin ardından yaşamlarına ilişkin bakış açılarını yeniden şekillendirebilir ve yeni bir anlam arayışı geliştirebilirler. Bu süreçte yaşam önceliklerinde değişim yaşanması, yeni hedefler belirleme veya farklı ilgi alanlarına yönelme gibi bireysel dönüşümler görülebilmektedir. Ayrıca bazı ebeveynlerde, ilişkilerde daha fazla empati, yakınlık ve şefkat geliştirme gibi olumlu psikolojik değişimlerin ortaya çıkabildiği bildirilmektedir.[44] Bununla birlikte, özellikle pediatrik yoğun bakım ünitesinde çocuğunu kaybeden ebeveynlerde bu büyümenin düzeyi ve hangi faktörlerle ilişkili olduğu henüz tam olarak netleşmemiştir. Çocuk kaybı yaşayan ebeveynlerde ruh sağlığı belirtilerinin zaman içindeki seyrini inceleyen çalışmalar sınırlı sayıdadır.[29] Mevcut araştırmalar, birçok ebeveynde kaybın ilk yılı içerisinde psikolojik belirtilerde bir miktar azalma görülebileceğini ortaya koymakla birlikte, bu iyileşme sürecinin tüm bireyler için aynı şekilde ilerlemediğini de göstermektedir. Çocuk kaybının ebeveynler üzerindeki derin etkileri, bu sürece aktif olarak eşlik eden hemşirelerin de benzer şekilde duygusal, etik ve mesleki açıdan etkilenmesine neden olmaktadır. [6]

YAŞAM SONU BAKIMDA HEMŞİRELERİN ROLÜ: PEDİATRİK YOĞUN BAKIMDA DENEYİMLER VE ZORLUKLAR

Yoğun bakım üniteleri, yaşamı tehdit eden durumdaki hastaların ileri teknoloji ve yoğun izlem altında tedavi edildiği kritik bakım alanlarıdır. Bu ünitelerde temel hedef, hastaların yaşamsal fonksiyonlarını sürdürmelerini sağlamak ve akut sağlık sorunlarını kontrol altına almaktır. Ancak, pediatrik ve yenidoğan yoğun bakım üniteleri de dahil olmak üzere bu ortamlarda mortalite oranlarının diğer klinik birimlere kıyasla daha yüksek olduğu bilinmektedir. Nitekim çocuk ve bebek ölümlerinin önemli bir bölümü hastane içinde ve çoğunlukla yoğun bakım ünitelerinde gerçekleşmektedir.[15]

Hastalarla sürekli temas halinde olan hemşireler açısından bir çocuk ya da yenidoğanın kaybı, mesleki ve duygusal açıdan son derece zorlayıcı bir deneyimdir. Çocuğun ölümü, hemşirelerde üzüntü, kaygı, yetersizlik ve başarısızlık duygularına yol açabilmekte, bazı durumlarda kişisel bir yas sürecini de beraberinde getirebilmektedir. Ayrıca hemşireler, yaşam sonu bakım sürecinde çocuğun klinik gereksinimlerini karşılarken aynı zamanda ebeveynlerin ve aile üyelerinin duygusal ihtiyaçlarını destekleme sorumluluğunu da üstlenmektedir. Ancak yoğun bakım ortamındaki iş yükü, zaman baskısı ve iletişimle ilgili zorluklar bu süreci daha karmaşık hale getirebilmektedir. Araştırmalar, hemşirelerin yaşam sonu bakım ve ölüm sonrası süreçlerde kurumsal, mesleki ve psikolojik desteğe ihtiyaç duyduklarını; bu desteğin bulunmamasının duygusal yükü artırdığını göstermektedir.[12,15,18] Ayrıca yaşam sonu bakımda iletişim, karar verme süreçleri ve aile desteği konularındaki rol belirsizliklerinin hemşirelerin bakım deneyimlerini olumsuz etkileyebildiği bildirilmektedir. [45]

Pediatrik palyatif bakım, yaşamı tehdit eden hastalığı bulunan çocukların ve ailelerinin yaşam kalitesini artırmayı amaçlayan kapsamlı bir bakım yaklaşımıdır. Bununla birlikte, uygun hasta grubunun belirlenmesindeki güçlükler, uzman sağlık profesyoneli eksikliği ve palyatif bakımın çoğu zaman yalnızca yaşamın son dönemine özgü bir hizmet olarak algılanması, bu alanın gelişimini sınırlandırmaktadır. Ayrıca sağlık çalışanlarının ağrı yönetimi, semptom kontrolü ve yaşam sonu bakım konularında yeterli eğitim ve deneyime sahip olmamaları, bakımın niteliğini ve ailelerle kurulan iletişimi olumsuz etkileyebilmektedir.[18] Bu nedenle pediatrik palyatif bakım hizmetlerinin yaygınlaştırılması, uzmanlaşmış merkezlerin artırılması ve sağlık profesyonellerine yönelik yapılandırılmış eğitim programlarının güçlendirilmesi önemli bir gereksinim olarak öne çıkmaktadır.

Pediatrik yaşam sonu bakım sürecinde hemşireler, çocuk ve ailesiyle en fazla zaman geçiren sağlık profesyonelleri olarak merkezi bir role sahiptir. Ancak bir çocuk ya da yenidoğanın kaybına tanıklık etmek, hemşireler açısından yoğun duygusal ve mesleki yük oluşturabilmektedir. Çalışmalar, hemşirelerin bu süreçte üzüntü, kaygı, yetersizlik, başarısızlık ve tükenmişlik duyguları yaşayabildiğini, bazı durumlarda ise kişisel bir yas sürecine girebildiğini göstermektedir.[15] Yaşam sonu bakımda rol ve sorumlulukların net olmaması, iletişim güçlükleri ve verilen bakımın yeterliliğine ilişkin belirsizlikler bu yükü daha da artırabilmektedi.[45] Bunun yanı sıra hemşireler yalnızca çocuğun fiziksel bakımından değil, aynı zamanda ölüm öncesi ve sonrası dönemde ebeveynlerin ve aile üyelerinin duygusal gereksinimlerinin karşılanmasından da sorumludur. Ancak yoğun bakım ünitelerindeki yüksek iş yükü, zaman baskısı ve çakışan klinik öncelikler, aileye yeterli destek sunulmasını zorlaştırabilmektedir.[15] Bu nedenle hemşirelerin yaşam sonu bakım konusundaki bilgi ve becerilerinin geliştirilmesi, duygusal destek mekanizmalarının güçlendirilmesi ve kurumlar tarafından destekleyici uygulamaların hayata geçirilmesi, hem bakım kalitesinin artırılması hem de hemşirelerin psikolojik iyi oluşlarının korunması açısından önem taşımaktadır.[15,18]

Aile ile kurulan iletişimin niteliği, ebeveynlerin yaşam sonu bakım deneyiminden duydukları memnuniyeti ve yas sürecine uyumlarını doğrudan etkileyebilmektedir. Bu nedenle hemşirelerin, aileyle etkili iletişim kurabilmeleri, onları olası bir kayba hazırlayabilmeleri ve yas sürecinde uygun destek sağlayabilmeleri büyük önem taşımaktadır .[15,46] Bununla birlikte, özellikle yenidoğan ve pediatrik yoğun bakım ünitelerinde çalışan hemşirelerin yaşam sonu bakım ve yas desteği konusunda kendilerini yeterince hazırlıklı hissetmediklerini bildiren çalışmalar bulunmaktadır.[18,47]

Hemşireler, ölümle başa çıkabilmek için profesyonel mesafeyi koruma, durumu rasyonelleştirme ve duygularını kontrol altında tutma gibi çeşitli baş etme mekanizmaları geliştirebilmektedir. Ancak söz konusu bir çocuk ya da yenidoğan olduğunda, ölümün erken ve beklenmedik olarak algılanması bu

mekanizmaların etkisini azaltabilmekte ve kaybın daha yoğun duygusal yükle deneyimlenmesine neden olabilmektedir .[15,48]

Literatürde, pediatrik ve yenidoğan yoğun bakım hemşirelerinin çocuk ölümü karşısındaki deneyimlerini inceleyen çalışmaların sınırlı olduğu görülmektedir. Mevcut bulgular, hemşirelerin ölümle ilgili tutumlarının klinik deneyim ve mesleki olgunlaşma süreciyle şekillendiğini; ancak buna rağmen hasta kayıplarının mesleki başarısızlık algısı, üzüntü ve ölüm kaygısına yol açabildiğini göstermektedir.[15, 45] Ölüm kaygısı, ölüm ve ölme sürecine ilişkin korku ve endişeleri içeren çok boyutlu bir kavram olup, özellikle çocuk ölümlerinde daha belirgin şekilde ortaya çıkabilmektedir.[48] Bu nedenle çocuk kaybı karşısında hemşirelerin deneyimleri, yalnızca mesleki değil aynı zamanda insani boyutlarıyla da değerlendirilmesi gereken önemli bir konu olarak öne çıkmaktadır.

Bu zorlu süreçte yalnızca hastaya değil, aileye yönelik bakımın da yapılandırılması gerekmektedir. Özellikle çocuk kaybı gibi derin bir kriz durumunda ailelerin psikososyal açıdan desteklenmesi, karar verme süreçlerine katılımlarının sağlanması ve yas sürecinde güçlendirilmeleri hemşirelik bakımının temel bileşenleri arasında yer almaktadır.[15,25,46]

SONUÇ VE ÖNERİLER

Çocuk ve yenidoğan ölümleri, yalnızca ebeveynler için değil, bakım sürecinde aktif rol alan hemşireler için de derin etkiler bırakan yaşam olaylarıdır. Yaşam sonu bakım sürecinde kurulan hemşire-hasta-aile ilişkisi, ölüm deneyiminin nasıl algılandığını ve yas sürecinin nasıl şekillendiğini etkileyen temel unsurlardan biridir. Bu nedenle yaşam sonu bakımın başarısı yalnızca semptom yönetimi ve klinik uygulamalarla değil, aile ile kurulan ilişkinin niteliği, iletişim becerileri ve bakım ekibinin duygusal farkındalığı ile de yakından ilişkilidir.

Mevcut literatür, çocuk kaybının ardından ebeveynlerin uzun süre devam edebilen psikolojik, sosyal ve davranışsal sorunlar yaşayabildiğini göstermektedir. Bununla birlikte, yaşam sonu bakım sürecinin görünmeyen paydaşlarından biri olan hemşirelerin deneyimleri çoğu zaman yeterince ele alınmamaktadır. Oysa hemşireler, bir yandan aileye destek olmaya çalışırken diğer yandan kendi duygusal tepkilerini yönetmek zorunda kalmaktadır. Özellikle yoğun bakım ortamlarında yaşanan hasta kayıplarının, hemşirelerde mesleki sorgulamalara, duygusal tükenmeye ve ahlaki sıkıntıya neden olabileceği göz önünde bulundurulmalıdır.

Bu doğrultuda yaşam sonu bakım uygulamalarının yalnızca hasta ve aile odaklı değil, aynı zamanda bakım veren sağlık profesyonellerini de kapsayacak şekilde yapılandırılması gerekmektedir. Kurumlar tarafından çocuk ölümü sonrasında ekip üyelerinin deneyimlerini paylaşabilecekleri güvenli ortamların oluşturulması, meslektaş desteğinin teşvik edilmesi ve hemşirelerin yas süreçlerini sağlıklı biçimde yönetebilmelerine olanak tanınması önemlidir. Ayrıca yaşam sonu bakım eğitimlerinin yalnızca klinik uygulamaları değil; iletişim, kültürel duyarlılık, etik karar verme ve yas desteği konularını da kapsayacak şekilde geliştirilmesi gerekmektedir.

Sonuç olarak, yaşam sonu bakımın niteliğinin artırılabilmesi için hem ailelerin hem de hemşirelerin ihtiyaçlarının birlikte değerlendirilmesi gerekmektedir. Çocuk kaybı sonrasında ailelerin psikososyal olarak desteklenmesi kadar, bu sürece tanıklık eden hemşirelerin duygusal iyi oluşlarının korunması da sürdürülebilir ve nitelikli bakımın önemli bir bileşenidir. Gelecekte yapılacak çalışmaların, özellikle pediatrik ve yenidoğan yoğun bakım hemşirelerinin ölüm sonrası deneyimlerine, destek gereksinimlerine ve etkili kurumsal müdahalelere odaklanması alana önemli katkılar sağlayacaktır.

KAYNAKLAR

1. Lakhani J, Mack C, Kunyk D, van Manen M. Exploring and supporting parents' stories of loss in the NICU: a narrative study. Qual Health Res. 2023;33(14):1279-1290. doi:10.1177/10497323231201023
2. Abela KM, Wardell D, Rozmus C, LoBiondo-Wood G. Impact of pediatric critical illness and injury on families: an updated systematic review. J Pediatr Nurs. 2020;51:21-31. doi:10.1016/j.pedn.2019.10.013
3. Alzawad Z, Lewis FM, Kantrowitz-Gordon I, Howells AJ. A qualitative study of parents' experiences in the pediatric intensive care unit: riding a roller coaster. J Pediatr Nurs. 2020;51:8-14. doi:10.1016/j.pedn.2019.11.015
4. Dahav P, Sjöström-Strand A. Parents' experiences of their child being admitted to a paediatric intensive care unit: a qualitative study—like being in another world. Scand J Caring Sci. 2018;32(1):363-370. doi:10.1111/scs.12470
5. Ko MSM, Lee WK, Sultana R, Murphy B, Heng KYC, Loh SW, et al. Psychological outcomes in families of PICU survivors: a meta-analysis. Pediatrics. 2024;154(1):e2023064210. doi:10.1542/peds.2023-064210
6. Suttle M, Hall MW, Pollack MM, Berg RA, McQuillen PS, Mourani PM, Sapru A, Carcillo JA, Startup E, Holubkov R, Dean JM, Notterman DA; Eunice Kennedy Shriver National Institute of Child Health and Human Development Collaborative Pediatric Critical Care Research Network (CPCCRN). Complicated grief, depression and post-traumatic stress symptoms among bereaved parents following their child's death in the pediatric intensive care unit: a follow-up study. Am J Hosp Palliat Care. 2022;39(2):228-236. doi:10.1177/10499091211015913
7. Abukari AS, Schmollgruber S. Concepts of family-centered care at the neonatal and paediatric intensive care unit: a scoping review. J Pediatr Nurs. 2023;71:e1-e10. doi:10.1016/j.pedn.2023.04.005
8. Al-Motlaq M, Foster M, Zgambo M, Neill S. Assessing the maturity of the “family centered care” concept: a review of concept analyses studies. J Pediatr Nurs. 2024;79:150-156. doi:10.1016/j.pedn.2024.09.004
9. Gallegos C, Cacchillo N. Experiences of parents of children with medical complexity in the pediatric intensive care unit: a scoping review. Crit Care Nurse. 2023;43(4):20-28. doi:10.4037/ccn2023774
10. Baum N, Weidberg Z, Osher Y, Kohelet D. No longer pregnant, not yet a mother: giving birth prematurely to a very-low-birth-weight baby. Qual Health Res. 2012;22(5):595-606. doi:10.1177/1049732311422899
11. Caeymaex L, Jousselme C, Vasilescu C, et al. Perceived role in end-of-life decision making in the NICU affects long-term parental grief response. Arch Dis Child Fetal Neonatal Ed. 2013;98(1):F26-F31. doi:10.1136/archdischild-2011-301548
12. Bloomer MJ, Butler AE, Brooks LA, Coventry A, McKeever S, Ranse K, Rowe J, Thomas S, Thornton R. Parents’ and nurses’ experiences of end-of-life care in intensive care for children: a systematic review. Aust Crit Care. 2025;38:101455. doi:10.1016/j.aucc.2025.101455
13. Waddington C, van Veenendaal NR, O’Brien K, Patel N; International Steering Committee for Family Integrated Care. Family integrated care: supporting parents as primary caregivers in the neonatal intensive care unit. Pediatr Investig. 2021;5(2):148-154. doi:10.1002/ped4.12277
14. Sigurdson K, Profit J, Dhurjati R, Morton C, Scala M, Vernon L, Randolph A, Phan JT, Franck LS. Former NICU families describe gaps in family-centered care. Qual Health Res. 2020;30(12):1861-1875. doi:10.1177/1049732320932897
15. Bloomer MJ, Brooks LA, Coventry A, Ranse K, Rowe J, Thomas S. “You need to be supported”: an integrative review of nurses' experiences after death in neonatal and paediatric intensive care. Aust Crit Care. 2025;38(3):101149. doi:10.1016/j.aucc.2024.101149
16. Mu PF, Tseng YM, Wang CC, Chen YJ, Huang SH, Hsu TF, et al. Nurses' experiences in end-of-life care in the PICU: a qualitative systematic review. Nurs Sci Q. 2018;32(1):12-22. doi:10.1177/0894318418807936
17. Butler AE, Pasek TA, Clark TJ, Broden EG. Supported privacy: an essential principle for end-of-life care for children and families in the PICU. Pediatr Crit Care Med. 2024;25(5):e258-e262. doi:10.1097/PCC.0000000000003440

18.Adistie F, Neilson S, Shaw KL, Bay B, Efstathiou N. The elements of end-of-life care provision in paediatric intensive care units: a systematic integrative review. BMC Palliat Care. 2024;23:184. doi:10.1186/s12904-024-01512-5
19.Lakhani J, Mack C, Kunyk D, Kung J, van Manen M. Considerations for practice in supporting parental bereavement in the neonatal intensive care unit: a systematic review. J Palliat Care. 2024;39(2):138-160. doi:10.1177/08258597231158328
20.Barrett L, Fraser L, Noyes J, Taylor J, Hackett J. Understanding parent experiences of end-of-life care for children: a systematic review and qualitative evidence synthesis. Palliat Med. 2023;37(2):241-258. doi:10.1177/02692163221144084
21. Bartrug WC. Maintaining parental roles during neonatal end-of-life care: a review of the literature. Crit Care Nurs Clin North Am. 2024;36(2):289-294. doi:10.1016/j.cnc.2023.11.008
22.Xu D, Zhang G, Ding X, et al. Bereaved parents' perceptions of memory making: a qualitative meta-synthesis. BMC Palliat Care. 2024;23:24. doi:10.1186/s12904-024-01339-0
23.Cambonie G, Desage C, Thaller P, Lemaitre A, Bertran de Balanda K, Combes C, Gavotto A. Context of a neonatal death affects parental perception of end-of-life care, anxiety and depression in the first year of bereavement. BMC Palliat Care. 2023;22:58. doi:10.1186/s12904-023-01183-8
24.Kaya F, Kontaş A, Cin G, Gümüştekin Ö. Yenidoğan Yoğun Bakım Ünitesine Yatırılan Bebeklerin Ebeveynlerinde Stres Düzeyi ve İlişkili Faktörler. Yoğun Bakım Hemşireliği Dergisi . 2022;26(1):1-8. https://izlik.org/JA79BL97HJ
25.Üstüner Top F. Ölümcül hastalığı olan çocukların ailelerinin güçlendirilmesi. SBÜ Hemşirelik Dergisi. 2023;5(2):145-150. doi:10.48071/sbuhemsirelik.1213959
26.Özel Ş, Tayman C, Korkut S, Çakar EŞ, Üstün YE. Yenidoğan Yoğun Bakım Ünitelerinde Palyatif Bakımın Önemi ve Gerekliliği. Ahi Evran Med J. 2018;2(2):39-44. https://izlik.org/JA68NF23RD
27.O'Meara A, Akande M, Yagiela L, Hummel K, Whyte-Nesfield M, Michelson KN, et al. Family outcomes after the pediatric intensive care unit: a scoping review. J Intensive Care Med. 2022;37(9):1179-1198. doi:10.1177/08850666211056603
28.Shaw C, Connabeer K, Drew P, Gallagher K, Aladangady N, Marlow N. Initiating end-of-life decisions with parents of infants receiving neonatal intensive care. Patient Educ Couns. 2020;103(7):1351-1357. doi:10.1016/j.pec.2020.02.013
29.Pohlkamp L, Kreicbergs U, Sveen J. Bereaved mothers' and fathers' prolonged grief and psychological health 1 to 5 years after loss: a nationwide study. Psychooncology. 2019;29:1530-1536.
30. Lykke C, Ekholm O, Schmiegelow K, et al. Anxiety and depression in bereaved parents after losing a child due to life-limiting diagnoses: a Danish nationwide questionnaire survey. J Pain Symptom Manage. 2019;58:596-604
31.Baumann I, Kühnzel J, Goldbeck L, et al. Prolonged grief, posttraumatic stress, and depression among bereaved parents: prevalence and response to an intervention program. Omega (Westport). 2020;84(3):837-855. doi:10.1177/0030222820918674
32.Prigerson HG, Boelen PA, Xu J, Smith KV, Maciejewski PK. Validation of the new DSM-5-TR criteria for prolonged grief disorder and the PG-13-Revised (PG-13-R) scale. World Psychiatry. 2021;20(1):96-106. doi:10.1002/wps.20823
33.Hilberdink CE, Ghainder K, Dubanchet A, Hinton D, Djelantik AAAMJ, Hall BJ, Bui E. Bereavement issues and prolonged grief disorder: a global perspective. Cambridge Prisms Glob Ment Health. 2023;10:1-37. doi:10.1017/gmh.2023.28
34.Killikelly C, Hasenohrl A, Stelzer EM, Maercker A. The new ICD-11 prolonged grief disorder guidelines in Japan: findings and implications from key informant interviews. Cult Med Psychiatry. 2023;47(2). doi:10.1007/s11013-022-09781-6
35.Eisma MC. Prolonged grief disorder in ICD-11 and DSM-5-TR: challenges and controversies. Aust N Z J Psychiatry. 2023;57(7):944-951. doi:10.1177/00048674231154206
36.Stelzer, E. M., Zhou, N., Maercker, A., O'Connor, M. F., & Killikelly, C. (2020). Prolonged grief disorder and the cultural crisis. Frontiers in Psychology, 10, 2982. doi. org/10.3389/fpsyg.2019.0298
37.Reynolds T, Boutwell B, Shackelford TK, Weekes-Shackelford V, Nedelec J, Beaver K, Abed MG. Child mortality and parental grief: an evolutionary analysis. New Ideas Psychol. 2020;59:100798. doi:10.1016/j.newideapsych.2020.100798

38.Buur C, Zachariae R, Komischke-Konnerup KB, Marello MM, Schierff LH, O'Connor M. Risk factors for prolonged grief symptoms: a systematic review and meta-analysis. Clin Psychol Rev. 2024;107:102375. doi:10.1016/j.cpr.2023.102375
39.Xu X, Wen J, Skritskaya NA, Zou X, Mauro C, Wang J, Shear MK. Grief-related beliefs in shidu parents with and without prolonged grief disorder: psychometric properties of a Chinese version of the Typical Beliefs Questionnaire. Clin Psychol Psychother. 2022;29(2):512-523. doi:10.1002/cpp.2641
40.Yuan MD, Wang ZQ, Fei L, Zhong BL. Prevalence of prolonged grief disorder and its symptoms in Chinese parents who lost their only child: a systematic review and meta-analysis. Front Public Health. 2022;10:1016160. doi:10.3389/fpubh.2022.1016160
41.Wang Q, Zhang S, Wang Y, Jing Z, Zhou Y, Qi K, Wang X, Zhou C. Prevalence and risk factors of posttraumatic stress disorder among Chinese shidu parents: a systematic review and meta-analysis. J Affect Disord. 2021;282:1180-1186. doi:10.1016/j.jad.2021.01.017
42.Yuan MD, Liu JF, Zhong BL. Prevalence of prolonged grief disorder and its symptoms among bereaved individuals in China: a systematic review and meta-analysis. Gen Psychiatry. 2024;37(2):e101216. doi:10.1136/gpsych-2023-101216
43.Xu X, Wen J, Qian W, Zhou N, Jiang W. Living with grief and thriving after loss: a qualitative study of Chinese parents whose only child has died. Eur J Psychotraumatol. 2024;15(1):2418767. doi:10.1080/20008066.2024.2418767
44.Xu X, Wen J, Zhou N, Shi G, Wang J, Skritskaya NA. Psychometric properties of a revised posttraumatic growth inventory and its short form in Chinese shidu parents. Curr Psychol. 2023;42(7):6011-6021. doi:10.1007/s12144-021-01717-4
45. Dönmez ÇF, Kara R, Muslu GK, et al. Nurses' experiences of end-of-life communication with children who have life-threatening conditions in paediatric intensive care units: A qualitative descriptive study. *BMC Palliat Care*. 2026;25:47. doi:10.1186/s12904-026-02007-1
46. Snaman JM, Kaye EC, Torres C, Gibson DV, Baker JN. Helping parents live with the hole in their heart: the role of health care providers and institutions in bereaved parents' grief journeys. Cancer. 2016;122(17):2757-2765. doi:10.1002/cncr.30087
47. Gibson K, Hofmeyer A, Warland J. Nurses providing end-of-life care for infants and their families in the NICU: a review of the literature. Adv Neonatal Care. 2018;18(6):460-468. doi: 10.1097/ANC.0000000000000533
48.Almeida FA, de Moraes MS, Cunha MLR. Taking care of the newborn dying and their families: nurses' experiences of neonatal intensive care. Rev Esc Enferm USP. 2016;50(Spec):118-124. doi:10.1590/S0080-623420160000300018

ÇOCUK VE ERGENLERDE PROBLEMLİ DİJİTAL MEDYA KULLANIMININ FİZİKSEL VE PSİKOSOSYAL ETKİLERİ

Burcu YILMAZ

Ardahan Üniversitesi, Sağlık Bilimleri Fakültesi, Hemşirelik Bölümü, Çocuk Sağlığı Hastalıkları Hemşireliği, 0000-0001-6423-6483

Derya ŞİMŞEKLİ

Ardahan Üniversitesi, Sağlık Bilimleri Fakültesi, Hemşirelik Bölümü, İç Hastalıkları Hemşireliği, 0000-0002-3904-951X

ÖZET

Son yıllarda çocuk ve ergenlerin dijital medya kullanımında belirgin bir artış gözlenmektedir. Özellikle akıllı telefon ve tabletlerin yaygınlaşmasıyla birlikte ekran temelli etkinlikler erken çocukluk dönemine kadar inmiştir. Günlük internet kullanım süresinin artması, çocukların fiziksel aktivite düzeyini azaltırken dijital ortamlarda geçirilen zamanı belirgin şekilde artırmıştır. COVID-19 pandemisi ile birlikte uzaktan eğitim uygulamaları ve sosyal kısıtlamalar bu eğilimi daha da güçlendirmiştir. Problematik dijital medya kullanımı, yalnızca ekran süresi ile değil, bireyin sosyal, akademik ve günlük yaşam işlevlerinde bozulma ile karakterize edilen bir durumdur. Literatürde internet bağımlılığı, sorunlu internet kullanımı ve problemli medya kullanımı gibi farklı kavramlarla tanımlanmakta olup, ortak bir tanı birliği henüz oluşmamıştır. Araştırmalar, aşırı dijital medya kullanımının çocuklarda hem fiziksel hem de psikososyal birçok olumsuz sonuca yol açtığını göstermektedir. Fiziksel olarak uyku bozuklukları, fiziksel aktivite azalması, obezite riski ve genel sağlık durumunda bozulma ön plana çıkmaktadır. Psikososyal açıdan ise dikkat ve öğrenme güçlükleri, akademik başarıda düşüş, sosyal izolasyon, davranış problemleri ve duygusal düzenleme güçlükleri bildirilmektedir. Bu durumun gelişiminde bireysel özelliklerin yanı sıra aile yapısı, ebeveyn tutumları ve dijital çevre gibi çoklu faktörlerin etkili olduğu vurgulanmaktadır. Özellikle erken yaşta yoğun medya maruziyeti, ilerleyen dönemlerde daha ciddi dijital bağımlılık davranışları için risk oluşturmaktadır. Sonuç olarak, çocuk ve ergenlerde problemli dijital medya kullanımı giderek artan önemli bir halk sağlığı sorunudur. Bu nedenle fiziksel aktivite, uyku düzeni ve ekran süresi dengesinin sağlanması ile birlikte koruyucu ve önleyici müdahalelerin geliştirilmesi büyük önem taşımaktadır. Ayrıca aile, okul ve sağlık profesyonellerinin iş birliği içinde farkındalık artırıcı stratejiler geliştirmesi gerekmektedir.

Anahtar Kelimeler: problemli medya kullanımı, çocuk, ergen, fiziksel sağlık, psikososyal etki

THE PHYSICAL AND PSYCHOSOCIAL EFFECTS OF PROBLEMATIC DIGITAL MEDIA USE IN CHİLDREN AND ADOLESCENTS

ABSTRACT

In recent years, there has been a marked increase in the use of digital media among children and adolescents. With the widespread adoption of smartphones and tablets, screen-based activities have become increasingly common even in early childhood. The increase in daily internet use has reduced children's levels of physical activity while significantly increasing the time spent in digital environments. The COVID-19 pandemic, along with remote learning initiatives and social restrictions, has further intensified this trend. Problematic digital media use is a condition characterized not only by screen time but also by impairments in an individual's social, academic, and daily life functioning. In the literature, it is defined by various concepts such as internet addiction, problematic internet use, and problematic media use; however, a common diagnostic consensus has not yet been established. Research indicates that excessive digital media use leads to numerous adverse physical and psychosocial outcomes in children. Physically, sleep disorders, reduced physical activity, increased risk of obesity, and deterioration in overall health stand out. Psychosocially, attention and learning difficulties, a

reduction in academic performance, social isolation, behavioral problems, and difficulties with emotional regulation have been reported. It is emphasized that multiple factors, including individual characteristics, family structure, parental attitudes, and the digital environment, play a role in the development of this condition. In particular, intense media exposure at an early age poses a risk for more severe digital addiction behaviors in later stages. Consequently, problematic digital media use among children and adolescents is a growing public health issue. Therefore, developing preventive interventions and maintaining a balance between physical activity, sleep, and screen time are essential. Additionally, collaboration among families, schools, and healthcare professionals is needed to raise awareness.

Keywords: problematic media use, child, adolescent, physical health, psychosocial ımpact

GİRİŞ

Teknolojik gelişmelerin hız kazanmasıyla birlikte dijital teknolojiler bireylerin günlük yaşamının ayrılmaz bir parçası haline gelmiştir. Özellikle internet erişiminin yaygınlaşması, çocuk ve ergenlerin dijital ortamlara çok daha erken yaşlarda katılım göstermesine neden olmuştur. Son otuz yılda dünya genelinde dijital bağlantının hızla artmasıyla birlikte internet kullanımı milyarlarca insana ulaşmış, dijital medya çocukların yaşamında eğitim, iletişim, eğlence ve sosyal etkileşim açısından temel bir araç haline gelmiştir. Günümüzde internet yalnızca bir iletişim aracı değil; çocukların öğrenme süreçlerine katılımını destekleyen, dijital beceri geliştirmelerine katkı sağlayan ve gelecekteki mesleki yeterlilikleri açısından önem taşıyan bir gereksinim olarak değerlendirilmektedir. [1]

Bununla birlikte dijital medya kullanım süresinin artması ve sosyal medya, çevrim içi oyunlar ile akıllı telefon kullanımının yoğunlaşması, çocuk ve ergenlerin sağlık ve gelişimleri üzerindeki olası olumsuz etkiler konusunda endişeleri artırmıştır. Özellikle kontrolsüz, aşırı ve işlevselliği bozan kullanım biçimleri "problemli dijital medya kullanımı" olarak tanımlanmakta ve son yıllarda önemli bir halk sağlığı sorunu olarak ele alınmaktadır. [2] Problemli dijital medya kullanımı; bireyin dijital medya kullanımını kontrol etmekte güçlük yaşaması, günlük yaşam aktivitelerinin, akademik performansın ve sosyal ilişkilerin olumsuz etkilenmesi ile karakterizedir. [3]

Son yıllarda özellikle COVID-19 pandemisi sürecinde uzaktan eğitim uygulamaları, sosyal izolasyon ve çevrim içi iletişim süreçlerinin yaygınlaşması çocuk ve ergenlerin ekran başında geçirdiği süreyi belirgin şekilde artırmıştır. [4] Çocukluk ve ergenlik dönemi; bilişsel, sosyal ve duygusal gelişimin hızla sürdüğü kritik gelişim dönemleri olduğundan, bu süreçte yoğun dijital medya maruziyeti fiziksel, psikolojik ve sosyal açıdan çeşitli olumsuz sonuçlara yol açabilmektedir.

Araştırmalar, problemli dijital medya kullanımının çocuk ve ergenlerde uyku kalitesinde bozulma, yetersiz uyku süresi, göz yorgunluğu, dijital göz zorlanması, baş ağrısı, boyun ve sırt ağrıları, fiziksel aktivite düzeyinde azalma ve obezite riskinde artış gibi çeşitli fiziksel sağlık sorunlarıyla ilişkili olduğunu göstermektedir.[5-6] Ayrıca aşırı dijital medya kullanımının depresyon, anksiyete, yalnızlık, düşük benlik saygısı, dikkat sorunları, davranış problemleri ve sosyal izolasyon gibi psikososyal sonuçlarla da ilişkili olduğu bildirilmektedir.[7–9] Çocukluk ve ergenlik dönemi biyopsikososyal gelişim açısından kritik bir dönem olması nedeniyle problemli dijital medya kullanımının fiziksel ve psikososyal etkilerinin bütüncül bir yaklaşımla incelenmesi önem taşımaktadır.

Bu derlemenin amacı, çocuk ve ergenlerde problemli dijital medya kullanımının fiziksel, bilişsel ve psikososyal etkilerini güncel literatür doğrultusunda incelemek ve bu doğrultuda geliştirilebilecek koruyucu ve önleyici yaklaşımları değerlendirmektir.

ÇOCUK VE ERGENLERDE DİJİTAL MEDYA KULLANIMININ UYKU VE GÖZ SAĞLIĞINA ETKİSİ

Son yıllarda dijital teknolojilerin yaygınlaşmasıyla birlikte çocuk ve ergenlerin günlük yaşamlarında ekran temelli etkinliklere ayırdıkları zaman önemli ölçüde artmıştır. Akıllı telefonlar, tabletler, bilgisayarlar ve diğer dijital medya araçları eğitim, iletişim ve eğlence gibi alanlarda çeşitli olanaklar sunmakla birlikte, bu araçların uzun süreli ve kontrolsüz kullanımının çocuk ve ergenlerin fiziksel,

bilişsel ve psikososyal gelişimleri üzerinde çeşitli olumsuz sonuçlar doğurabileceği belirtilmektedir.[10-12] Bu durum, özellikle eğlence amaçlı ekran kullanımının sınırlandırılmasına yönelik ulusal ve uluslararası sağlık kuruluşlarının çeşitli öneriler geliştirmesine neden olmuştur. [13-16]

Çocukluk ve ergenlik dönemi, büyüme ve gelişmenin hız kazandığı, biyolojik, psikolojik ve sosyal değişimlerin yoğun olarak yaşandığı kritik yaşam evreleri arasında yer almaktadır. Bu süreçte yeterli ve kaliteli uyku; bilişsel performansın sürdürülmesi, duygusal dengenin korunması, akademik başarının desteklenmesi ve sağlıklı fiziksel gelişimin devamı açısından temel bir gereksinimdir. [17-18] Ancak dijital teknolojilerin kullanım sıklığındaki artış, özellikle sosyal medya etkileşimlerinin yoğunlaşması ve gece saatlerinde ekran kullanımının yaygınlaşması, çocuk ve ergenlerin uyku düzenlerini olumsuz yönde etkileyebilmektedir. Ekranlardan yayılan mavi ışığın melatonin hormonunun salgılanmasını baskılayarak biyolojik ritmi etkilediği, bunun da uykuya dalma süresinin uzamasına ve uyku düzeninin bozulmasına yol açtığı bildirilmektedir.[19-22]Bu durum toplam uyku süresinin azalması, uyku kalitesinin düşmesi ve gündüz saatlerinde yorgunluk hissinin artması gibi sonuçlarla ilişkilendirilmektedir.[23-25] Araştırmalar, ergenlerin önemli bir bölümünün önerilen günlük uyku süresine ulaşamadığını ve uyku sorunlarının giderek daha yaygın hale geldiğini göstermektedir.[26] Bunun yanı sıra uykuya dalmada güçlük, sık gece uyanmaları ve dinlendirici olmayan uyku gibi problemlerin de ergenlik döneminde sık görüldüğü belirtilmektedir.[27]

Dijital medya kullanımındaki artışın yalnızca uyku üzerinde değil, bilişsel işlevler üzerinde de etkili olduğu ifade edilmektedir. Uzun süreli ekran maruziyetinin dikkat, çalışma belleği ve yürütücü işlevler gibi bilişsel süreçleri olumsuz etkileyebileceği bildirilmektedir. [28-29] Sürekli değişen ve yoğun uyaran içeren dijital içeriklere maruz kalmak, bireylerin dikkatlerini belirli bir noktada sürdürmelerini zorlaştırabilmekte, bilişsel yükü artırabilmekte ve konsantrasyon becerilerinde azalmaya neden olabilmektedir.[1,5] Ayrıca yetersiz uyku ile birlikte değerlendirildiğinde, yoğun dijital medya kullanımının akademik performans ve günlük yaşam aktiviteleri üzerindeki olumsuz etkilerinin daha belirgin hale geldiği vurgulanmaktadır. [30]

Dijital cihazların aşırı kullanımına bağlı olarak ortaya çıkan önemli sağlık sorunlarından biri de göz sağlığı ile ilişkilidir. Uzun süre ekran karşısında kalmanın göz kuruluğu, yanma, batma hissi, kızarıklık, bulanık görme, göz yorgunluğu ve baş ağrısı gibi belirtilerin görülme sıklığını artırdığı bildirilmektedir.[31] Ayrıca ekranlardan yayılan mavi ışığın yalnızca uyku düzenini etkilemekle kalmayıp görsel konforu azaltarak göz yorgunluğunu da artırabileceği belirtilmektedir.[32,33] Bu nedenle çocuk ve ergenlerde dijital medya kullanım süresinin, kullanım zamanının ve maruz kalınan içeriklerin özelliklerinin dikkatle değerlendirilmesi; uyku hijyeninin korunması ve göz sağlığının desteklenmesine yönelik önlemlerin geliştirilmesi büyük önem taşımaktadır.[6] Bu bağlamda çocuk ve ergenlerde dijital medya kullanımının uyku ve göz sağlığı üzerindeki etkilerinin incelenmesi, koruyucu sağlık uygulamalarının planlanması açısından değerli bilgiler sunacaktır.

ÇOCUK VE ERGENLERDE DİJİTAL MEDYA KULLANIMININ KAS-İSKELET SİSTEMİNE ETKİSİ

Dijital medya kullanımının artmasıyla birlikte çocuk ve ergenlerde uzun süreli hareketsizlik ve yanlış postür alışkanlıkları önemli bir sağlık sorunu haline gelmiştir. Özellikle akıllı telefon, tablet ve bilgisayar kullanım süresinin artması; boyun, sırt, omuz ve bel bölgelerinde kas-iskelet sistemi yakınmalarının görülme sıklığını artırmaktadır.[34] Çocuk ve ergenler dijital cihazları kullanırken çoğunlukla başın öne eğildiği, omuzların yuvarlandığı ve omurganın doğal hizasının bozulduğu uygunsuz postürlerde uzun süre kalmaktadır. Bu durum kaslarda aşırı yüklenmeye, kas spazmlarına ve postür bozukluklarına yol açabilmektedir. Özellikle “text neck” olarak tanımlanan öne eğik baş pozisyonu, servikal omurgada mekanik stresin artmasına neden olmakta ve kronik boyun ağrısıyla ilişkilendirilmektedir.[34]

Bununla birlikte uzun süreli ekran maruziyeti, çocuk ve ergenlerde fiziksel aktivite düzeyini azaltarak kas-iskelet sistemi sağlığını dolaylı olarak da olumsuz etkilemektedir. Sedanter yaşam tarzının artması kas kuvvetinde azalma, esneklik kaybı ve duruş bozukluklarına yol açabilmektedir.[35] Büyüme ve gelişmenin hızlı olduğu çocukluk ve ergenlik döneminde fiziksel aktivite yetersizliği, kas ve kemik gelişimini olumsuz etkileyerek ilerleyen yaşlarda kronik kas-iskelet sistemi problemlerine zemin hazırlayabilmektedir. Ayrıca uzun süreli dijital cihaz kullanımının üst ekstremite kaslarında ve el

bileğinde tekrarlayıcı zorlanmalara neden olduğu, bunun da ağrı ve fonksiyonel kısıtlılık riskini artırdığı bildirilmektedir. [36]

Literatürde çocuk ve ergenlerde günlük ekran süresi arttıkça kas-iskelet sistemi ağrılarının görülme sıklığının da arttığı gösterilmiştir. Özellikle pandemi döneminde uzaktan eğitim uygulamalarıyla birlikte masa başında geçirilen sürenin artması, ergonomik olmayan çalışma düzeni ve fiziksel aktivite azalması boyun, sırt ve bel ağrılarında belirgin artışa neden olmuştur.[37] Bu nedenle çocuk ve ergenlerde dijital medya kullanımının sınırlandırılması, ergonomik duruş alışkanlıklarının kazandırılması ve düzenli fiziksel aktivitenin teşvik edilmesi kas-iskelet sistemi sağlığının korunmasında önemli bir koruyucu yaklaşım olarak değerlendirilmektedir.

ÇOCUK VE ERGENLERDE DİJİTAL MEDYA KULLANIMININ OBEZİTE VE SEDANTER YAŞAM"COVİBESİTY" ÜZERİNE ETKİSİ

Dijital teknoloji kullanımı, çocukların günlük rutinlerini bozarak fiziksel aktivite düzeylerini düşürmekte ve obezite riskini kritik düzeyde artırmaktadır. Yapılan çalışmalar, çocuklarda obezite oranlarının arttığını ortaya koymaktadır. Teknolojiyi yoğun olarak kullanan gençlerin fiziksel egzersiz düzeyleri, teknolojiyi az kullanan akranlarına göre anlamlı derecede düşüktür; özellikle haftada altı saatten fazla elektronik cihaz kullanımı ile fiziksel aktivitedeki azalma arasında doğrudan bir ilişki saptanmıştır.[38]

Ekran başında geçirilen sürenin artması, sadece hareketsizlikle değil, aynı zamanda beslenme alışkanlıklarının bozulmasıyla da karakterizedir. Çocuklar ekran karşısındayken sosyal medya platformları üzerinden yüksek kalorili, yağ oranı yüksek ve besleyici değeri düşük olan "junk food" (abur cubur) reklamlarına yoğun şekilde maruz kalmaktadır[38-39] Bu durum; meyve-sebze tüketiminin azalmasına, enerji içecekleri, şekerli atıştırmalıklar ve fast food tüketiminin artmasına yol açarak kalori alımını kontrolsüz hale getirmektedir. Ayrıca, ekran karşısında yemek yeme alışkanlığı, dikkat dağıtıcı mekanizmalar nedeniyle beyindeki tokluk mekanizmasının bozulmasına ve çocukların doyma sinyallerini fark edemeyerek daha fazla enerji tüketmesine neden olmaktadır. [38-39]

Pandemi döneminde, sosyal izolasyon, uzaktan eğitim zorunluluğu ve ekran süresindeki dramatik artışın etkisiyle ortaya çıkan kilo artışı olgusu literatürde "Covibesity" (Covid Obezitesi) olarak adlandırılmıştır.[39-40] Bu dönemde gıda endüstrisinin çocuklara yönelik çevrimiçi reklamlarını yoğunlaştırması, bu riski daha da tetikleyebilmektedir. [39] Yatak odasında televizyon veya bilgisayar bulundurmanın obezite artışında bağımsız bir risk faktörü olabileceği ve Vücut Kütle İndeksi (VKİ) düzeylerini doğrudan yükseltebileceği vurgulanmaktadır. Bu bağlamda, Dünya Sağlık Örgütü, gelişme çağındaki gençlerin her gün en az bir saat orta ila yoğun fiziksel egzersiz yapmalarını önermektedir.[38]

ÇOCUK VE ERGENLERDE DİJİTAL MEDYA KULLANIMININ PSİKOSOSYAL VE RUH SAĞLIĞINA ETKİSİ

Depresyon, Anksiyete ve Özgüven Aşırı dijital medya kullanımı; yalnızlık, düşük benlik saygısı ve duygusal sorunlarla güçlü bir korelasyon içindedir. [39,41]

Özellikle sosyal medya platformlarında yapılan "olumsuz sosyal karşılaştırmalar", çocukların ve gençlerin kendi yaşamlarını ve fiziksel görünümlerini başkalarının "idealize edilmiş" hayatlarıyla kıyaslamalarına, bu da yetersizlik hissi ve depresif semptomların gelişmesine yol açmaktadır.[40,42] Literatürde "Facebook Depresyonu" olarak adlandırılan bu durum, sosyal izolasyon riskini artırmakta ve bireyi agresif veya kendine zarar verici davranışlara yönlendirebilmektedir. [39]

Araştırmalar, günde 2 saatten fazla sosyal medya kullanan ergenlerin depresyon hissetme olasılığının, daha az kullanan akranlarına göre anlamlı derecede yüksek olduğunu göstermektedir. [38-39] Pandemi döneminde okul kapanışları ve sosyal izolasyon, ekran süresini artırarak bu psikolojik sıkıntıları ve anksiyete düzeylerini daha da tetiklemiştir.[27,40] Ayrıca, dijital cihazların beyindeki ödül-ceza sistemini bozarak "ödül yetmezliği sendromuna" yol açtığı ve bu durumun madde bağımlılığına benzer bir bağımlılık döngüsü yarattığı vurgulanmaktadır. [38]

Siber Zorbalık ve Sosyal İzolasyon Dijital platformlar; anonimlik, fiziksel mesafenin sağladığı sahte cesaret ve sürekli erişilebilirlik özellikleri nedeniyle siber zorbalık için zemin hazırlamaktadır. Siber zorbalığa maruz kalmak; anksiyete, depresyon, paranoia ve intihar düşünceleri gibi ciddi ruh sağlığı sorunlarıyla ilişkilendirilmiştir. Yapılan çalışmalar, siber zorbalığın intihar ideasyonunu geleneksel zorbalığa göre daha fazla artırdığını ortaya koymaktadır.[39]

Ayrıca, sosyal izolasyon olgusu dijital dünyayla derinleşmektedir. İnterneti yoğun kullanan çocukların, kullanmayanlara göre aile ve arkadaş çevreleriyle gerçek zamanlı olarak 100 dakika daha az zaman geçirdikleri saptanmıştır. [38] Bu durum, çocukların gerçek dünyadaki sosyal becerilerini geliştirmelerini engellemekte ve onları sanal arkadaşlıklara mahkûm ederek "Shakaiteki Hikikomori" (sosyal geri çekilme) gibi uç durumlara sürükleyebilmektedir. [39]

Beden İmajı ve Yeme Bozuklukları Instagram ve Snapchat gibi görsel odaklı mecralar, filtreler ve düzenleme araçları ile gerçeklikten uzaklaştırılmış görseller sunarak çocukların benlik algısını bozmaktadır. [39,42] Bu platformlardaki görsellere uyum sağlama çabası; vücut dismorfik bozukluğu, düşük özgüven ve yeme bozukluklarını (anoreksiya, bulimia) teşvik eden içeriklere maruz kalma riskini artırmaktadır.[40] Araştırmalar, görsel içerikli sosyal medya kullanımının, özellikle kız çocuklarında beden memnuniyetsizliğini ve zayıflama takıntısını anlamlı şekilde yükselttiğini doğrulamaktadır.[39-40]

ÇOCUK VE ERGENLERDE DİJİTAL MEDYA KULLANIMININ BİLİŞSEL GELİŞİM VE AKADEMİK BAŞARIYA ETKİSİ

Aşırı teknoloji kullanımı, çocukların bilişsel gelişiminin temel taşları olan "Yürütücü İşlevlerini" (dikkat kontrolü, çalışma belleği, dürtü kontrolü ve zihinsel esneklik) olumsuz etkilemektedir. [30,41] Hızlı tempolu, sürekli değişen ve aşırı uyarıcı dijital içerikler, çocukların beynini düşük stimülasyonlu ortamlara (okul, kitap okuma) karşı duyarsızlaştırmakta, bu da dikkat sürelerinin kısalmasına ve odaklanma güçlüğüne neden olmaktadır.[30,42]

Nörolojik açıdan, erken yaşlarda yoğun ekrana maruz kalan çocuklarda prefrontal korteks gelişiminin yavaşladığı ve dil/okuryazarlık becerilerini destekleyen beyindeki beyaz madde organizasyonunda (miyelinleşme) azalma olduğu saptanmıştır.[30,42] Bu durum, çocukların bilgiyi işleme yeteneklerini yavaşlatmakta ve "Zihin Kuramı" (başkalarının düşüncelerini anlama becerisi) gelişiminde gecikmelere yol açmaktadır.[40]

Akademik başarı açısından ise; çoklu görev (multitasking) davranışı (örneğin ödev yaparken sosyal medyada vakit geçirme) öğrenme derinliğini azaltarak yüzeysel bir bilgi edinimine neden olmaktadır.[39,41] Gece geç saatlere kadar dijital cihaz kullanımı, uyku kalitesini bozarak ertesi gün okulda uykulu hissetmeye, dikkat dağınıklığına ve sonuç olarak ders başarısında düşüşe yol açmaktadır.[27,30] Özellikle 11-14 yaş arası erken ergenlik dönemindeki çocukların bilişsel olgunlaşma süreçleri devam ettiği için bu negatif etkilere karşı daha savunmasız oldukları vurgulanmaktadır.[30]

ÇOCUK VE ERGENLERDE DİJİTAL MEDYA KULLANIMINDA AİLE DİNAMİKLERİ VE "TECHNOFERENCE"

"Technoference", dijital ve mobil cihazların günlük yüz yüze iletişimi, paylaşılan zamanı ve ebeveyn-çocuk etkileşimini kesintiye uğratması veya bozması olarak tanımlanır.[46] Ebeveynlerin kendi cihazlarına aşırı odaklanması, literatürde "phubbing" (telefonla meşguliyet nedeniyle karşısındakini görmezden gelme) olarak adlandırılmakta ve çocuk gelişimini hem doğrudan hem de dolaylı yollarla etkilemektedir .[39,43]

Teorik açıdan bu durum üç temel mekanizmayla açıklanır: Birincisi, "Kabul-Reddetme Teorisi" uyarınca, ebeveynleri teknolojiyle meşgul olan çocuklar kendilerini ihmal edilmiş veya reddedilmiş hissederek bu duygusal boşluğu doldurmak için aşırı medya kullanımına yönelebilirler.[44] İkincisi, "Sosyal Öğrenme Teorisi" kapsamında çocuklar ebeveynlerinin problemli teknoloji kullanım davranışlarını model alarak benzer alışkanlıklar geliştirirler.[38,43]Üçüncüsü ise, "arka plan televizyonu" gibi faktörlerin ebeveyn-çocuk arasındaki sözel etkileşimi ve oyun kalitesini düşürmesidir. Yapılan

meta-analizler, özellikle her iki ebeveynin de dijital dikkat dağınıklığı yaşadığı ailelerde, çocukların ekran bağımlılığı ve psikososyal uyum sorunları riskinin çok daha yüksek olduğunu kanıtlamaktadır.[43]

Ebeveynlerin çocuklarının dijital dünyadaki varlığına yönelik yaklaşımları; kısıtlayıcı, eğitici ve birlikte izleme olmak üzere farklılık gösterir. [38,42] Kısıtlayıcı denetim tek başına internet bağımlılığını azaltmada yetersiz kalabilmekte; buna karşın ebeveynlerin içerik hakkında çocukla tartışması, eleştirel düşünmeyi teşvik etmesi ve dijital içerikleri birlikte tüketmesi daha koruyucu sonuçlar vermektedir.[38]

Ancak günümüzde çocukların dijital becerilerinin ebeveynlerinden daha ileri olması, denetim süreçlerini zorlaştırmakta ve ebeveynlerde "dijital yetersizlik" hissine yol açmaktadır.[43-44] Ebeveynlerin sadece yasak koyan bir otorite değil, aynı zamanda sağlıklı dijital alışkanlıklar sergileyen birer "rol model" olmaları kritiktir; çünkü ebeveynin ekran süresi, çocuğun ekran süresinin en güçlü öngörücüsüdür.[38]

SONUÇ VE ÖNERİLER

Çocuk ve ergenlerde problemli dijital medya kullanımı, çok boyutlu etkileri nedeniyle acilen ele alınması gereken küresel bir halk sağlığı sorunudur.[38] Literatür verileri ve uluslararası rehberler ışığında şu somut öneriler sunulmaktadır:

Yaş Gruplarına Göre Sınırlar: 18 ayın altındaki çocuklar (görüntülü sohbet hariç) ekrandan tamamen uzak tutulmalı; 18-24 ay arası çocuklar yalnızca yüksek kaliteli içerikleri ebeveyn eşliğinde izlemeli; 2-5 yaş arası çocuklar için ise ekran süresi günde en fazla 1 saat ile sınırlandırılmalıdır.[38,42] 6 yaş ve üzeri çocuklar için ise ekran süresi uyku, fiziksel aktivite ve diğer sağlıklı alışkanlıkları engellemeyecek şekilde kişiselleştirilmiş bir plan dahilinde yönetilmelidir.

Dijital Hijyen ve Cihazsız Alanlar: Yatak odalarından televizyon, bilgisayar ve akıllı telefonlar çıkarılmalıdır.[43] Uyku kalitesini korumak adına yatmadan en az bir saat önce "ekran yasağı" uygulanmalı ve yemek zamanları cihazsız bölge ilan edilmelidir.[27,38]

Fiziksel Aktivite Teşviki: Sedanter yaşam riskini azaltmak için çocukların günde en az bir saat orta ila yoğun fiziksel egzersiz yapmaları ve dijital olmayan yaratıcı hobiler (kitap okuma, sanat, spor) geliştirmeleri sağlanmalıdır .[38,45]

Kurumsal ve Profesyonel Destek: Pediyatristler ve okul sağlığı hemşireleri, rutin kontrollerde ailenin dijital medya kullanım alışkanlıklarını sorgulamalı ve ailelere özel "Aile Medya Kullanım Planı" (Family Media Use Plan) oluşturulması konusunda rehberlik etmelidir.Okullarda dijital okuryazarlık ve siber zorbalık farkındalık programları müfredata entegre edilmelidir.[39,41]

Sonuç olarak; dijital teknolojiler eğitim ve sosyal bağlantı açısından yadsınamaz fırsatlar sunsa da, kontrolsüz ve aşırı kullanımın fiziksel (obezite, uyku bozuklukları) ve psikososyal (depresyon, siber zorbalık, yürütücü işlevlerde gerileme) bedelleri oldukça ağırdır.[30,38]Çocukların sağlıklı bir dijital çevre içinde büyümeleri; ebeveynlerin bilinçli denetimi, eğitimcilerin rehberliği ve sağlık profesyonellerinin kararlı iş birliği ile mümkündür.[38]

KAYNAKLAR

1. de Barros EC. Understanding the influence of digital technology on human cognitive functions: A narrative review. IBRO Neurosci Rep. 2024;17:415-422. doi:10.1016/j.ibneur.2024.11.006
2. Domoff SE, Borgen AL, Foley RP, Maffett A. Excessive use of mobile devices and children's physical health. Hum Behav Emerg Technol. 2019;1(2):169-175. doi:10.1002/hbe2.145.
3. Domoff SE, Harrison K, Gearhardt AN, Gentile DA, Lumeng JC, Miller AL. Development and validation of the problematic media use measure: A parent report measure of screen media "addiction" in children. Psychol Pop Media Cult. 2017;8(1):2-11. doi:10.1037/ppm0000163.
4. Nagata JM, Singh G, Yang JH, Smith N, Kiss O, Ganson KT, Testa A, Jackson DB, Baker FC. Bedtime screen use behaviors and sleep outcomes: findings from the Adolescent Brain Cognitive Development (ABCD) Study. Sleep Health. 2023;9(4):497-502. doi:10.1016/j.sleh.2023.02.005.
5. Huang P, Chan SY, Ngoh ZM, et al. Screen time, brain network development and socioemotional competence in childhood: moderation of associations by parent-child reading. Psychol Med. 2024;54(9):1992-2003. doi:10.1017/S0033291724000084
6. Aykutlu MS, Aykutlu HC, Ozveren M, Garip R. Digital media use and its effects on digital eye strain and sleep quality in adolescents. PLoS One. 2024;19(12):e0314390. doi:10.1371/journal.pone.0314390.
7. Keles B, McCrae N, Grealish A. A systematic review: the influence of social media on depression, anxiety and psychological distress in adolescents. Int J Adolesc Youth. 2019;25(1):79-93. doi:10.1080/02673843.2019.1590851.
8. Boer M, Stevens GWJM, Finkenauer C, de Looze ME, van den Eijnden RJJM. Social media use intensity, social media use problems, and mental health among adolescents. Int J Environ Res Public Health. 2021;18(13):6959 doi.org/10.1016/j.chb.2020.106645.
9. Odgers CL, Jensen MR. Annual research review: adolescent mental health in the digital age. J Child Psychol Psychiatry. 2020;61(3):336-348. doi:10.1111/jcpp.13190.
10. Dong N, Zhou Y, Lei L, Lee TMC, Lam CLM. The longitudinal impact of screen media activities on brain function, architecture and mental health in early adolescence. Int J Clin Health Psychol. 2025;25:100589. doi:10.1016/j.ijchp.2025.100589
11. Clemente-Suárez VJ, Beltrán-Velasco AI, Herrero-Roldán S, Rodriguez-Besteiro S, Martínez-Guardado I, Martín-Rodríguez A, Tornero-Aguilera JF. Digital device usage and childhood cognitive development: exploring effects on cognitive abilities. Children. 2024;11(11):1299. doi:10.3390/children11111299
12. Marciano L, Camerini AL, Morese R. The developing brain in the digital era: a scoping review of structural and functional correlates of screen time in adolescence. Front Psychol. 2021;12:671817. doi:10.3389/fpsyg.2021.671817
13. Martins J, Tapia-Serrano MÁ, Nogueira T, Sánchez-Miguel PA. Compliance with the 24-h movement guidelines for Portuguese children: differences between boys and girls. Sci Rep. 2024;14:11926. doi:10.1038/s41598-023-49227-6
14. Muppalla SK, Vuppalapati S, Reddy Pulliahgaru A, Sreenivasulu H. Effects of excessive screen time on child development: an updated review and strategies for management. Cureus. 2023;15(6):e40608. doi:10.7759/cureus.40608
15. McArthur BA, Volkova V, Tomopoulos S, Madigan S. Global prevalence of meeting screen time guidelines among children 5 years and younger: a systematic review and meta-analysis. JAMA Pediatr. 2022;176(4):373-383. doi:10.1001/jamapediatrics.2021.6386
16. Friel CP, Duran AT, Shechter A, Diaz K. U.S. children meeting physical activity, screen time, and sleep guidelines. Am J Prev Med. 2020;59(4):513-521. doi:10.1016/j.amepre.2020.05.007.
17. Lewien C, Genuneit J, Meigen C, Kiess W, Poulain T. Sleep-related difficulties in healthy children and adolescents. BMC Pediatr. 2021;21(1):82. doi:10.1186/s12887-021-02522-2
18. Gradisar M, Wolfson AR, Harvey AG, Hale L, Rosenberg R, Czeisler CA. The impact of technology use on sleep quality and sleep disorders in adolescents. Sleep Health. 2020;6(2):145-155. doi:10.1016/j.sleh.2019.12.003

19. Höhn C, Hahn MA, Gruber G, Pletzer B, Cajochen C, Hoedlmoser K. Effects of evening smartphone use on sleep and declarative memory consolidation in male adolescents and young adults. Brain Commun. 2024;6(3):fcae173. doi:10.1093/braincomms/fcae173
20. Hartstein LE, Mathew GM, Reichenberger DA, et al. The impact of screen use on sleep health across the lifespan: a National Sleep Foundation consensus statement. Sleep Health. 2024;10(4):373-384. doi:10.1016/j.sleh.2024.05.001
21. Dos Santos AB, Prado WL, Tebar WR, et al. Screen time is negatively associated with sleep quality and duration only in insufficiently active adolescents: a Brazilian cross-sectional school-based study. Prev Med Rep. 2023;37:102579. doi:10.1016/j.pmedr.2023.102579
22. Silvani MI, Werder R, Perret C. The influence of blue light on sleep, performance and wellbeing in young adults: a systematic review. Front Physiol. 2022;13:943108. doi:10.3389/fphys.2022.943108
23. Iglesias-Vázquez L, Garcidueñas-Fimbres TE, Gómez-Martínez C, et al. Sleep duration moderates association between screen time and emotional and behavioural problems in young children. World J Pediatr. 2025;21(11):1140-1151. doi:10.1007/s12519-025-00963-x
24. Torres P, Pablos A, Elvira L, Ceca D, Chia M, Huertas F. Associations between screen time, physical activity, and sleep patterns in children aged 3–7 years: a multicentric cohort study in urban environment. Sports. 2025;13(4):91. doi:10.3390/sports13040091
25. van den Eijnden RJJM, Geurts SM, ter Bogt TFM, van der Rijst VG, Koning IM. Social media use and adolescents' sleep: a longitudinal study on the protective role of parental rules regarding internet use before sleep. Int J Environ Res Public Health. 2021;18(3):1346. doi:10.3390/ijerph18031346
26. Paulus FW, Joas J, Gerstner I, Kühn A, Wenning M, Gehrke T, et al. Problematic internet use among adolescents 18 months after the onset of the COVID-19 pandemic. Children. 2022;9(11):1724. doi:10.3390/children9111724
27. Ateş E, Korkmaz Konal E. Early adolescence in the shadow of the digital world: effects on eye health and sleep. J Public Health Nurs. 2026;8(1):1-7. doi:10.54061/jphn.1714799
28. Lakicevic N, Manojlovic M, Chichinina E, Drid P, Zinchenko Y. Screen time exposure and executive functions in preschool children. Sci Rep. 2025;15:1839. doi:10.1038/s41598-024-79290-6
29. Namazi SA, Sadeghi S. The immediate impacts of TV programs on preschoolers' executive functions and attention: a systematic review. BMC Psychol. 2024;12:226. doi:10.1186/s40359-024-01738-1
30. Toth C, Osser B, Bondar LI, Fazakas R, Marcu FM, Pascalau NA, Suciu RN, Dogaru BG. Associations between screen time, sleep, and executive function in school aged children and adolescents: the moderating role of digital content and age. J Clin Med. 2025;14:8842. doi:10.3390/jcm14248842
31. Mehra D, Galor A. Digital screen use and dry eye: a review. Asia Pac J Ophthalmol (Phila). 2020;9(6):491-497. doi:10.1097/APO.0000000000000328
32. Mataftsi A, Seliniotaki AK, Moutzouri S, Prousali E, Darusman KR, Adio AO, Haidich AB, Nischal KK. Digital eye strain in young screen users: a systematic review. Prev Med. 2023;170:107493. doi:10.1016/j.ypmed.2023.107493
33. Straker L, et al. Conflicting guidelines on children's screen time. J Paediatr Child Health. 2018;54(6):660-666. doi: 10.1016/j.jpeds.2018.07.019
34. Hansraj KK. Assessment of stresses in the cervical spine caused by posture and position of the head. Surg Technol Int. 2014;25:277-279. PMID:25393825
35. World Health Organization. *WHO guidelines on physical activity and sedentary behaviour*. Published 2020. Accessed June 1, 2026. https://www.who.int/publications/i/item/9789240015128
36. Thorburn, E., Pope, R., & Wang, S. (2021). Musculoskeletal symptoms among adult smartphone and tablet device users: a retrospective study. Archives of Physiotherapy, 11(1), 1. https://doi.org/10.1186/s40945-020-00096-6.
37. Nagata JM, et al. Screen time use among adolescents during COVID-19 pandemic. JAMA Pediatr. 2022;176(1):94-96. doi:10.1001/jamapediatrics.2021.4334

38. Mustafaoğlu R, Zirek E, Yasacı Z, Özdinçler AR. The negative effects of digital technology usage on children's development and health. Addicta Turk J Addict. 2018;5:227-247. doi:10.15805/addicta.2018.5.2.0051
39. Bozzola E, Spina G, Agostiniani R, et al. The use of social media in children and adolescents: scoping review on the potential risks. Int J Environ Res Public Health. 2022;19:9960. doi:10.3390/ijerph19169960
40. Eddy Ives LS, Huertas Patón A, Forti Buratti MA, Álvarez Pitti J, Salmerón-Ruiz MA, Rodríguez Hernández PJ, Real-López M. Impact of screen and social media use on mental health. An Pediatr (Engl Ed). 2025;103(2):503909. doi:10.1016/j.anpede.2025.503909
41. Liu J, Riesch S, Tien J, Lipman T, Pinto-Martin J, O'Sullivan A. Screen media overuse and associated physical, cognitive, and emotional/behavioral outcomes in children and adolescents: an integrative review. J Pediatr Health Care. 2022;36(2):99-109. doi:10.1016/j.pedhc.2021.06.003
42. Kar SS, Dube R, Goud BKM, Gibrata QS, El-Balbissi AA, Al Salim TA, Fatayerji RNMAK. Impact of screen time on development of children. Children. 2025;12:1297. doi:10.3390/children12101297
43. Zhang J, Zhang Q, Xiao B, Cao Y, Chen Y, Li Y. Parental technology mediation and children's problematic media use: a meta-analysis. J Med Internet Res. 2025;27:e57636. doi:10.2196/57636
44. Ünal Tokpunar Ş, Koçak H. Küçük ekranların büyük etkileri: çocuklar ve dijital dünyanın etkileşimi. AKÜSBD. 2025;27(Aile Özel Sayısı):502-520. doi:10.32709/akusosbil.1728767
45. Sharaf N, Bahez A, Akhtary E. Negative effects of digital technology on children's health. Int J Multidiscip Res Anal. 2024;7(11):5249-5255. doi:10.47191/ijmra/v7-i11-34

ASTIMLI HASTALARDA UYKU SORUNLARI VE HEMŞİRELİK BAKIMI

Derya ŞİMŞEKLİ

Ardahan Üniversitesi, Sağlık Bilimleri Fakültesi, Hemşirelik Bölümü, İç Hastalıkları Hemşireliği, 0000-0002-3904-951X

Burcu YILMAZ

Ardahan Üniversitesi, Sağlık Bilimleri Fakültesi, Hemşirelik Bölümü, Çocuk Sağlığı Hastalıkları Hemşireliği, 0000-0001-6423-6483

ÖZET

Astım akciğerin kronik inflamatuar geri dönüşümlü hastalıklarından biridir. Özellikle allerjenler kaynaklı ortaya çıkarak bronşlarda, bronşiallerde hipersensitiviteyle kendini gösterir. Mortalite ve morbidite oranı yüksek bir hastalıktır. Astım, hastaların fiziksel, psikolojik ve sosyal açıdan zorlanmalarına ve yaşam kalitelerinde azalmaya neden olabilmektedir. Astımda semptomların kontrol altına alınabilmesi, atakların ve akciğer fonksiyon kaybının önlenebilmesi amacıyla farmakolojik ve nonfarmakolojik tedaviler uygulanmaktadır. Farmakolojik tedavide hava yollarındaki kronik inflamasyonu azaltmak amacıyla inhale ve sistemik kortikosteroidler, uzun etkili bronkodilatörler ve hedefe yönelik tedaviler uygulanmaktadır. Nonfarmakolojik tedavisinde ise tetikleyicilerden uzak durmak, yaşam tarzı değişiklikleri, solunum egzersizleri, eşlik eden hastalıkların tedavisi, koruyucu önlemler yer almaktadır. Astım hastalarında uyku sırasında vücutta meydana gelen çeşitli değişimler nedeniyle astım semptomları etkilenebilir ve bu semptomlara uyku sorunları eklenebilir. Astım hastalarında sirkadiyen ritme bağlı olarak gece saatlerinde vücuttaki kortizol seviyesinin düşmesi ve histamin seviyesinin artması, gece solunan havanın soğuk olmasına bağlı bronkospazm, sırt üstü yatış pozisyonunun mukusu akciğerlere indirmesi ve hacimde hafif azaltma meydana getirmesi ve uyku sırasında mide asidinin yemek borusuna kaçması gibi nedenlerle uyku sorunları meydana gelebilir. Bu sorunlar gece öksürmeye, uykunun bölünmesine, gündüz sersemliğine ve uyku apnesine neden olabilir. Bu sorunlarla mücadelede hastanın ilaç dozlarının uygun şekilde ayarlanması, yatak odasının toz ve akarlardan temizlenmesinin sağlanması, hastanın uygun pozisyonda uyumasının sağlanması ve odanın uygun şekilde nemlendirilmesi büyük önem taşımaktadır. Astımlı hastaların yaşadıkları uyku sorunlarına yönelik hemşirelik bakımında hastanın uyku düzeninin uygun şekilde değerlendirilmesi gerekmektedir. İnhaler ilaç eğitimi, uyku hijyeni, reflü yönetimi, semptom takibi ve psikolojik destek verilerek uyku sorunları en azami düzeye çekilebilir.

Anahtar Kelimeler: astım, uyku sorunları, hemşirelik

SLEEP DISORDERS AND NURSING CARE IN PATIENTS WITH ASTHMA

ABSTRACT

Asthma is a chronic, reversible inflammatory disease of the lungs. It is often triggered by allergens and manifests as hypersensitivity in the bronchi and bronchial tubes. It is a disease associated with high rates of mortality and morbidity. Asthma can lead to physical, psychological, and social challenges for patients and may result in a reduced quality of life. Pharmacological and non-pharmacological treatments are used to control symptoms, prevent attacks, and mitigate the loss of lung function. Pharmacological treatment involves the use of inhaled and systemic corticosteroids, long-acting bronchodilators, and targeted therapies to reduce chronic inflammation in the airways. Non-pharmacological treatments include avoiding triggers, lifestyle modifications, breathing exercises, managing comorbid conditions, and preventive measures. In asthma patients, various physiological changes occurring during sleep can affect asthma symptoms, and sleep disturbances may also contribute to these symptoms. In asthma patients, sleep problems may arise due to a drop in cortisol levels and an increase in histamine levels at night in accordance with the circadian rhythm; bronchospasm caused by

the coldness of the air inhaled at night; the supine sleeping position causing mucus to drain into the lungs and resulting in a slight reduction in lung volume; and the reflux of stomach acid into the esophagus during sleep. These issues can lead to nighttime coughing, disrupted sleep, daytime drowsiness, and sleep apnea. In addressing these issues, it is crucial to ensure that the patient's medication doses are appropriately adjusted, the bedroom is kept free of dust and dust mites, the patient sleeps in an appropriate position, and the room is properly humidified. In nursing care for sleep issues experienced by patients with asthma, it is essential to properly assess the patient's sleep patterns. By providing inhaler medication education, sleep hygiene guidance, reflux management, symptom monitoring, and psychological support, sleep issues can be minimized to the greatest extent possible.

Keywords: asthma, sleep problems, nursing

GİRİŞ

Astım sık karşılaşılan, genellikle bronşial hiperaktiviteye bağlı meydana gelen kronik solunumsal bir hastalıktır. Astımda hastalar solunum sistemiyle ilişkili birçok belirti ve bulgu yaşar. Bunlar hışıltılı solunum, dispne, öksürük, göğüste sıkışma hissidir. Bunların sıklığı ve şiddeti hastalığın gidişatına ve maruz kalınan solunum irritanlarına göre değişiklik gösterebilir. Hastalığın semptomları ekspiratuvar hava akımı kısıtlamasıyla ilişkilidir.[1]

Astımın prevalansı ülkeden ülkeye bölgeden bölgeye değişmekle birlikte, ülkemizde yapılan prevalans çalışmalarına bakıldığında %1.2-9.4 arasında değiştiği görülmektedir. Astım mortalite ve morbidite oranlarını arttıran bir hastalıktır. Hastalık alevlenmelerle seyrettiği için acil servis ve hastane yatışlarında da artış meydana getirmektedir. Astımın ortaya çıkmasında genetik ve çevresel birçok risk faktörünün rol oynadığı görülmektedir. Bu faktörlerin bir veya birkaçının akciğerlerde meydana getirdiği kronik hava yolu inflamasyonu bronşlarda aşırı duyarlılığa neden olur ve bu da geri dönüşlü ve değişken bir hava yolu obstrüksiyonu olan astımla sonuçlanır. Astımda semptomların kontrol altına alınması ve gelecek riskler açısından hastanın uygun şekilde değerlendirilmesi önemlidir. Astımın tedavisinde, astımın kontrol altına alınmasını sağlamak üzere kontrol edici, semptomları azaltabilmek için semptom giderici ve ağır astımlılarda kullanılan ilave ilaçlar olmak üzere üç grup ilaç kullanılmaktadır. İlaç tedavisinin ana amacı semptomları kontrol altına alıp, komplikasyonları önleyerek hastalığın iyi yönde gitmesini sağlamaktır.[1]

Astım hastalarında geceleri öksürük, hırıltı ve dispne düzeyinde artış meydana gelebilmektedir. Hastaların büyük bir kısmı en az bir kere gece bu semptomlardan bir veya birkaçını deneyimlemektedir. Acil başvurularının birçoğu gece meydana gelmekte ve astıma bağlı ölümlerin çoğu da gece meydana gelmektedir. Bu durumun nedeni uyku sırasında hava yolu direncinin artması, akciğer fonksiyonlarının azalması, maksimum ekspiratuvar akımın düşmesi olarak açıklanabilir. Ayrıca vagal aktivite artışının bronkokonstrüksiyon yapması, gece inflamasyonda artışın meydana gelmesi akciğer hacimlerinin uyku sırasında azalması da uyku sorunlarının ortaya çıkmasındaki diğer nedenler arasında yer almaktadır.[2,3] Bu nedenlerle hastalarda görülen uyku sorunları arasında insomnia, uykuya dalmada zorlanma, gece uyku bölünmesi, öksürük, gün içinde uyku hali ve uyku kalitesinde azalma gibi sorunlar ortaya çıkabilir. Bu sorunların erken dönemde tespit edilip uygun tedavi ve hemşirelik girişimlerinin yapılması hastalığın gidişatı açısından ve hastanın yaşam kalitesi açısından oldukça önemlidir.[4]

Astımlı hastaların uyku ile ilgili sorunlarının çözümünde astım semptomlarının etkin şekilde kontrol altına alınması önemlidir. Semptomların kontrol altında tutulabilmesi uykuyla ilgili sorunlarında azalmasına yardımcı olacaktır. İlaçların uygun şekilde kullanılması, çevresel düzenlemelerin yapılması, yaşam tarzı değişikliklerinin yapılması ve bireyselleştirilmiş hemşirelik yaklaşımlarının uygulanması uyku sorunlarının çözümünde etkili faktörlerdendir. Özellikle uyku hijyeninin sağlanması, gece semptomlarını arttırabilme ihtimali olan allerjenlerin ve tetikleyicilerin ortamdan uzaklaştırılması, hastaların hastalık yönetimi konusunda eğitilmesi uyku kalitesinin arttırılmasına katkı sağlayabilmektedir. Ayrıca düzenli semptom izlemi, ilça uyumunun desteklenmesi ve ailenin bakım sürecine entegre edilmesi de gece semptomlarının kontrol altına alınmasında etkili olabilecek diğer faktörlerdendir. Sergilenen bu yaklaşım sayesinde astımın uygun şekilde kontrol altına alınması, hastalığın ilerlemesinin önlenmesi, ortaya çıkabilecek komplikasyonların engellenmesi ve hastaların yaşam kalitesinin arttırılmasında önemli katkılar sunmaktadır. Bunun yanı sıra uyku ile ilgili sorunların

erken dönemde tespit edilmesi, uygun hemşirelik girişimlerinin belirlenmesi, uygulanması ve değerlendirilmesine fırsat sunacaktır. Bu sayede hastane ve acil başvuru oranlarında azalma, buna paralel olarak tedavi ve bakım maliyetlerinde bir azalmada meydana gelebilecektir.[1,4–6] Bu nedenle bu derleme de astım hastalarının yaşadıkları uyku sorunları ve bunlara yönelik olarak yapılması gereken hemşirelik girişimlerine yer verilmesi amaçlanmıştır.

ASTIM TANIMI VE EPİDEMİYOLOJİSİ

Astım, sık karşılaşılan çeşitli mekanizmalarla ortaya çıkabilen, genetik ve çevresel faktörlerin rol oynadığı heterojen bir hastalıktır. Hastalığın özellikleri astım tiplerine göre farklılıklar gösterebilmektedir.

Astım hırıltılı solunum, dispne, öksürük, göğüste sıkışma hissi gibi semptomlarla seyretmektedir. Semptomların sıklığı ve şiddeti ekspiratuvar hava akımı kısıtlamasının düzeyine bağlıdır. Hastalık birçok hücre ve mediatörün rol aldığı kronik hava yolu inflamasyonu ve hava yollarındaki aşırı duyarlılıkla ilişkilidir. Hastalığın belirtileri ve hava akımı kısıtlaması enfeksiyonlar, solunum yolu irritanları ya da alerjenlere maruziyet, egzersiz gibi faktörlerle tetiklenebilir. Tedavi ile veya tedaviye gerek kalmadan kendiliğinden düzelme meydana gelebilir.

Astımın epidemiyolojisine bakıldığında dünya genelinde nüfusun %1-20'sini etkileyen ve tahminen 300 milyon kişiyi etkilemiş olan bir hastalık olduğu görülmektedir. Türkiye'de yapılan prevalans çalışmalarına bakıldığında astım prevalansının %1.2-9.4 olduğu tespit edilmiştir. [7–11] Türkiye'de Türk Toraks Derneği tarafından 14 ayrı şehirde gerçekleştirilen bir prevalans çalışmasında astım sıklığının erkeklerde %7.1, kadınlarda %9.0 olduğu tespit edilmiştir.[9] Dünya Sağlık Örgütü (DSÖ)'ne dahil olan ülkeler arasında yer alan aralarında Türkiye'nin de yer aldığı 70 ülke verilerinin değerlendirildiği bir çalışmada doktor tanılı astım prevalansının %4.27 ve hışıltı prevalansının ise %8.61 olduğu belirlenmiştir.[8]

ASTIMIN BELİRTİLERİ

Astım dispne, hışıltılı solunum, öksürük ve göğüste daralma hissi semptomlarıyla kendini gösteren kronik bir hastalıktır. Hastalığın semptomlarının şiddeti ve sıklığı hastalık seyri ile doğrudan ilişkilidir. Hava akımı kısıtlamasının artması hastalığın seyrinin kötüleştiğini gösterir ve semptomlarda da artma meydana gelebilir.[12]

Astım hastalarında irritanların solunması, egzersiz, hava değişimi, solunum yolu enfeksiyonlarının yaşanması, ani duygu durum değişimleri ve duyarlı bireylerde alerjene maruziyet yakınmaların başlamasına neden olur. Ortaya çıkan yakınmalar ise tedaviyle veya bazen tedavisiz şekilde uzun süre ortaya çıkmayabilir.[12]

ASTIM TEDAVİSİ

Astım tedavisinde hastaların uygun şekilde klinik özelliklerinin belirlenmesi oldukça önemlidir. Klinik özellikleri bakımından öncelikle hastaların yakınmaları sorgulanmaktadır. Bu kapsamda hırıltı, öksürük, dispne, öksürük, kilo kaybı, gece terlemesi, ateş basması, ishal, psikososyal durum ve alışkanlıklarının sorgulanması gerekmektedir. Semptomların başlangıç yaşı, hastanın fizik muayene bulgularının değerlendirilmesi, alerjik öyküsü, aile öyküsü, geçirilmiş hastalık ve operasyonel öyküsü sorgulanmalıdır. Hava yolu kısıtlamasının düzeyini belirlemek amacıyla spirometrik ölçümlerden FEV1 ve FVC değerleri ve PEF metre ile ölçülen PEF değerine de bakılıp değerlendirme yapılmalıdır. Tetikleyici, semptom ya da biyobelirteçlere göre astım tipleri belirlendikten sonra uygun bir tedavi kararı verilmelidir.[1,13]

Astım tedavisinde kontrol edici, semptom giderici ve ağır astımda kullanılan ilave ilaçlar kullanılmaktadır. Bu kapsamda inhale steroidler, uzun etkili beta-2 agonistler, antilökotrien, kısa etkili inhale antikolinerjikler, kısa etkili lökotrien gibi ilaçlar yer almaktadır.[1,13]

Astımın nonfarmakolojik tedavisinde ise sigaranın bıraktırılması, pasif içiciliğin önlenmesi, mesleki maruziyetten kaçınma, aspirin ve diğer nonsteroidal antiinflamatuvar ilaçlardan yani ağır astım atağına yol açabilecek ilaçlardan kaçınma, iç ortam alerjenleriyle mücadele, fiziksel aktivite ve sağlıklı diyet, emosyonel stresle başa çıkma, besin ve besin katkı maddelerinden kaçınma yer almaktadır.[1,13]

ASTIMLI HASTALARDA GÖRÜLEN UYKU SORUNLARI

Astımlı hastalarda çeşitli nedenlerle birçok farklı uyku sorunu ortaya çıkabilmektedir. En sık karşılaşılan uyku sorunu uykunun sürdürülmesinde meydana gelen güçlüktür. Özellikle gece sık sık uyanma, uyandıktan sonra tekrar uykuya dalamama, gece bronşlardaki spazma bağlı uyanmaların olması sık karşılaşılan sorunlardan biridir. Astım hastalarında gece sonuna doğru semptom sıklığı ve şiddetinin artmasına bağlı olarak hatsalar erken saatlerde uyanabilmektedir. Bu durum uykudan istenen verimin alınamamasına da neden olmaktadır. Ayrıca sabah erken saatlerde nefes darlığının yaşanması, öksürükle uyanma ve yorgun kalkma bu duruma eşlik eden diğer sorunlardandır. Gece uykusunun alamayan, düşük kalitede bir uyku süreci yaşayan hastalarda özellikle gün içinde aşırı uykululuk gözlenebilmektedir. Bu durum dikkat, algı ve konsantrasyonda azalma, öğrenme güçlüğü ve günlük yaşam aktivitelerine katılımda azalmaya neden olabilmektedir. Astım kontrol düzeyinin düşmesinin de hastalarda uyku kalitesinin bozan bir neden olduğu bildirilmiştir. [2,14–20]

Astımla birlikte sıkça karşılaşılan sorunlardan biri de obstrüktif uyku apne sendromudur. Özellikle kontrolü zor olan astımda daha sık karşılaşılmaktadır. Noktürnal astım durumunda gece dispnesi, hırıltı, öksürük ve göğüste sıkışma gibi semptomların sıklığı ve şiddetinde bir artış meydana gelir ve bu durumda hastanın uykusunun bölünmesine neden olabilir. Yapılan araştırmalarda astımlı bireylerin sağlıklı bireylere göre çok daha fazla uyku bölünmesi yaşadığı belirlenmiştir.[2,14–20]

Yetişkin astım hastalarında yaşanan bu uyku sorunları benzer şekilde çocuklarda da yaşanabilmektedir. Uyku sorunu yaşayan çocuklarda hafıza, dikkat ve öğrenme performansında azalma meydana gelmekte, bu doğrultuda okul performansında da düşme yaşanabilmektedir.[4]

Yapılan bir çalışmada astımlı hastalarda uykuyu sürdürmede güçlüğün %44, erken sabah uyanmasının %51 ve gündüz uykululuğunun %44 oranında görüldüğü bildirilmiştir.[15]

Yukarıda bahsedilen bu uyku sorunlarının nedenlerine bakıldığında temelde sirkadiyen ritim değişiklikleri, gece meydana gelen bronkokonstrüksiyon, geceleri inflamasyonda artma, hastaların astım kontrolünün düşük olması, obstrüktif uyku apne sendromu, astık şiddetinin artması, gece semptomları ve psikolojik faktörlerdir. Astım ataklarının gece daha fazla ortaya çıkmasının ve semptomların geceleri daha fazla ortaya çıkmasının en önemli nedenlerinden biri sirkadiyen ritimle ilgili fizyolojik değişikliklerdir. Gece saatlerinde hava yollarında doğal fonksiyonel bir azalma meydana gelebilmektedir. Bronş çaplarında, hava yolu direncinde ve akciğer fonksiyonlarında azalma meydana gelmektedir. Bu semptomlar kaynaklı gece yarısından sonra astım semptomlarında artma meydana gelmekte, bu durumda uyku sürekliliğini bozarak uyanmaya, uykunun bölünmesine neden olmaktadır.[3,18,20] Literatürde astım ile uyku bozuklukları arasında güçlü bir ilişki olduğu ve özellikle obstrüktif uyku apnesinin bu ilişkiyi güçlendiren önemli bir faktör olduğu bildirilmiştir.[17]

Uyku sırasında artan parasempatik aktivite artışı bronkokonstrüksiyon meydana getirerek hava yollarını daraltır ve bu duruma bağlı olarak da nefes darlığı, hırıltı, gece öksürüğü, göğüste sıkışma meydana gelebilir. Bu da hastanın aralıklarla uyanmasına neden olabilir.

Astımda temel fizyopatolojik mekanizma kronik hava yolu inflamasyonudur. Bu mekanizma özellikle gece saatlerinde artış gösterebilmektedir. Bu durum geceleri inflamatuar mediatörlerin artmasına paralel olarak hava yolu hassasiyetinin artmasıyla meydana gelmektedir. Eozonofil aktivitesi, inflamatuar sitokinlerin yükselmesi ve hava yolu hiperaktivitesinde artma meydana gelir. Bu süreç özellikle kontrolsüz astım hastalarında daha belirgin olarak seyrederek hastanın uyku sorunları yaşamasına, uyku kalitesinin bozulmasına yol açabilir.[20]

ASTIMLI HASTALARDA GÖRÜLEN UYKU SORUNLARINDA HEMŞİRELİK BAKIMI

Astımın tedavi ve bakımı içerisinde yer alan uyku sorunlarının uygun şekilde ele alınması astım kontrolü açısından oldukça önemlidir. Hastaların gece semptomlarının artması, gece sık sık uyanma, gündüz yorgunluk hastaların gün içerisinde yapacakları aktiviteleri yapamamasına neden olabilmektedir. Bu nedenle hemşireler, astımlı hastalarda uyku sorunlarının değerlendirilmesi, önlenmesi ve yönetilmesinde anahtar role sahiptir. Uygun hemşirelik girişimleri ile hastaların uyku sorunları azami düzeye çekilebilir, tedavi ve bakıma uyumları arttırılabilir ve yaşam kaliteleri arttırılabilir.[3,14,19,20]

Astım hastalarında uyku sorunlarının yönetiminin ilk adımı sorunların değerlendirilmesidir. Hemşire hastanın uyku düzenini, gece semptomları ve gündüz yorgunluk düzeyini ayrıntılı olarak değerlendirmelidir. Bu amaçla çeşitli ölçekler kullanılabilir. Dikkat edilmesi gereken en önemli noktalar hastanın uykuya dalma süresi, gece uyanma sıklığı, gece öksürük ve nefes darlığı, sabah yorgun kalkma durumu, gündüz aşırı uykululuk, astım kontrol düzeyi, ilaç kullanım düzeyidir. Uyku sorunları erken dönemde tespit edilirse, hem hastalık yönetimi açısından hem de hastanın günlük yaşam aktivitelerine katılımı açısından iyi bir yol alınmış olur. [3,14,19,20]

Uyku sorunları uygun şekilde değerlendirildikten sonra hastalara uyku hijyeni eğitimi verilmelidir. Bu eğitim sayesinde uyku kalitesinde artma meydana gelebilmektedir. Uyku hijyeni eğitimi kapsamında hastaya her gün aynı saatte yatıp her gün aynı saatte kalkmaya çalışması gerektiği bildirilmelidir. Yatmadan önce yemek yememesi gerektiği, kafein içeren içecekleri içmemesi gerektiği söylenmelidir. Uyku ortamının sessiz, karanlık ve uygun sıcaklıkta olması gerektiği ifade edilmelidir. Elektronik cihaz kullanımının sınırlandırılması gerektiği ve uyku öncesi gevşeme tekniklerini kullanabileceği, bunun uyukuya dalmasını kolaylaştıracağı söylenmelidir. [3,14,19,20]

Astımlı hastaların uyku sorunları yaşamalarının en önemli nedenleri gece semptomlarıdır. Bu açıdan astım semptomlarının kontrol altına alınması ve uygun şekilde yönetilebilmesi uyku sorunlarının çözümünde büyük önem arz etmektedir. Bu açıdan hastaların gece semptomlarının düzenli olarak takip edilmesi, solunum seslerinin değerlendirilmesi, ilaç kullanımlarının düzenli kontrolünün sağlanması ve astım atağı belirtilerinin erken dönemde tanımlanması gerekmektedir. Hastanın tedavi ve bakıma uyumunun arttırılması da gece semptomlarının azalmasına katkı sunacaktır. Bu doğrultuda inhaler ilaç kullanım tekniğinin öğretilmesi, ilaçların doğru zamanlarda kullanılmasının sağlanması, yan etkilerin izlenmesi, hastanın tedaviye uyumunun değerlendirilmesi gerekmektedir. [3,14,19,20]

Çevresel faktörlerin düzenlenmesi hasta odasının havalandırılması, akarlarla mücadele, iç ortam kirliliğinin önlenmesi, sigara dumanından kaçınılması, allerjenlerin kontrol altına alınması, evcil hayvanların yatak odalarından uzak tutulması gerekmektedir. Hastaların uygun pozisyonda, başları hafif yüksek, yan yatış pozisyonunda yatması, solunumu zorlaştıran pozisyonlardan kaçınılması, gece semptomlarının azaltılması açısından önemlidir. [3,14,19,20]

Hastaların kaygı düzeylerinin azaltılması, gevşeme tekniklerinin öğretilmesi, güven verici bir yaklaşım sergilenmesi, gerektiğinde psikolojik veya psikiyatrik destek almasının sağlanması da uyku sorunlarıyla mücadelede gereklidir. [3,14,19,20]

SONUÇ

Astım hastalarında uyku sorunları sık gözlenen sorunlar arasında yer almaktadır. Hastaların günlük yaşam aktivitelerine katılımlarında azalma meydana getirmekte, aktivitelerini azaltmaktadır. Bu duruma bağlı olarak astımlı hastalarda uyku sorunlarının değerlendirilmesi, çözüm yollarının aranması ve uygun hemşirelik girişimlerinin yapılması gerekmektedir.

KAYNAKÇA

1. Çelik GE, ed. *Astım Tanı ve Tedavi Rehberi 2020 Güncellemesi*.; 2020.

2. Khan WH, Mohsenin V, D'Ambrosio CM. Sleep in asthma. *Clin Chest Med*. 2014;35(3):483-493. doi:10.1016/j.ccm.2014.06.004

3. Kavanagh J, Jackson DJ, Kent BD. Sleep and asthma. *Curr Opin Pulm Med*. 2018;24(6):569-573. doi:10.1097/MCP.0000000000000526

4. Reiter J, Ramagopal M, Gileles-Hillel A, Forno E. Sleep disorders in children with asthma. *Pediatr Pulmonol*. 2022;57(8):1851-1859.

5. Crespo-Lessmann A. Enhancing the Management of Severe Asthma in Spain: The CARABELA Initiative Disclosed. *Open Respir Arch*. 2025;7(1):100378. doi:https://doi.org/10.1016/j.opresp.2024.100378

6. Mersal F, El-Awady S. Evaluation of bronchial asthma educational package on asthma self-management among school age children based on Orem's self-care model in Zagazig city. *Int J Adv Nurs Stud*. 2017;7(1):8-16. doi:10.14419/ijans.v7i1.8648

7. Noweir A, Abusamra A, Al Zarooni A, et al. Prevalence of benign prostatic hyperplasia among the adult general population of five Middle Eastern Countries: Results of the SNAPSHOT programme. *Arab J Urol*. 2022;20(1):14-23. doi:10.1080/2090598X.2021.2010451

8. To T, Stanojevic S, Moores G, et al. Global asthma prevalence in adults: Findings from the cross-sectional world health survey. *BMC Public Health*. 2012;12(1):204. doi:10.1186/1471-2458-12-204

9. Kurt E, Metintas S, Basyigit I, et al. Prevalence and risk factors of allergies in turkey (PARFAIT): Results of a multicentre cross-sectional study in adults. *Eur Respir J*. 2009;33(4):724-733. doi:10.1183/09031936.00082207

10.Özdemir N, Uçgun I, Metintas S, Kolsuz M, Metintas M. The prevalence of asthma and allergy among university freshmen in Eskisehir, Turkey. *Respir Med*. 2000;94(6):536-541. doi:10.1053/rmed.1999.0728

11.Saraçlar Y, Çetinkaya F, Tuncer A, et al. The prevalence of self-reported asthma and respiratory symptoms in Ankara, Turkey. *Respir Med*. 1997;91(8):461-463. doi:10.1016/S0954-6111(97)90110-4

12.Krishnan JA, Lemanske RF, Canino GJ, et al. Asthma outcomes: Symptoms. *J Allergy Clin Immunol*. 2012;129(3 SUPPL.):S124-S135. doi:10.1016/j.jaci.2011.12.981

13.Papi A, Blasi F, Canonica GW, Morandi L, Richeldi L, Rossi A. Treatment strategies for asthma: Reshaping the concept of asthma management. *Allergy, Asthma Clin Immunol*. 2020;16(1):1-11. doi:10.1186/s13223-020-00472-8

14.Braido F, Baiardini I, Ghiglione V, et al. Sleep Disturbances and Asthma Control : A Real Life Study. Published online 2008:27-33.

15.Janson C, Gislason T, Boman G, Hetta J, Roos B. Sleep disturbances in patients with asthma. Published online 1990.

16.Cukic V, Lovre V, Dragisic D. Sleep Disorders in Patients with Bronchial Asthma. 2011;23(September):235-237. doi:10.5455/msm.2011.23.235-237

17.Liu X, Hong C, Liu Z, Fan L, Yin M, Chen Y. Association of sleep disorders with asthma : a meta- - analysis. Published online 2023:1-12. doi:10.1136/bmjresp-2023-001661

18.Braido F, Baiardini I, Ferrando M, et al. The prevalence of sleep impairments and predictors of sleep quality among patients with asthma. *J Asthma*. 2021;58(4):481-487. doi:10.1080/02770903.2019.1711391

19.Mastronarde JG, Wise RA, Shade DM, Christopher O. Sleep Quality in Asthma : Results of a Large Prospective Clinical Trial Sleep Quality in Asthma : Results of a Large Prospective Clinical Trial. 2009;0903. doi:10.1080/02770900801890224

20.Luyster FS, Teodorescu M, Bleecker E, et al. Sleep quality and asthma control and quality of life in non-severe and severe asthma. *Sleep Breath*. 2012;16:1129-1137. doi:10.1007/s11325-011-0616-8

DİYABETLİ HASTALARDA TEDAVİYE UYUMU ETKİLEYEN FAKTÖRLER VE HEMŞİRELİK BAKIMI

Derya ŞİMŞEKLİ

Ardahan Üniversitesi, Sağlık Bilimleri Fakültesi, Hemşirelik Bölümü, İç Hastalıkları Hemşireliği, 0000-0002-3904-951X

Burcu YILMAZ

Ardahan Üniversitesi, Sağlık Bilimleri Fakültesi, Hemşirelik Bölümü, Çocuk Sağlığı Hastalıkları Hemşireliği, 0000-0001-6423-6483

ÖZET

Diabetes mellitus, insülin eksikliği, yokluğu veya hücrelerin insüline duyarsızlığı sonucunda ortaya çıkan kan şekeri yüksekliği ile seyreden kronik bir hastalıktır. Genetik, çevresel ve yaşam tarzı değişikliklerinin etkisiyle ortaya çıkan bu hastalık temelde Tip 1 ve Tip 2 Diabetes mellitus olmak üzere ikiye ayrılmaktadır. Diyabet hastalığında kan şekeri yüksekliği, aşırı susama, aşırı idrara çıkma, halsizlik, yorgunluk, yara iyileşmesinde gecikme, uyku sorunları, aşırı kilo alma veya zayıflama gibi birçok semptom meydana gelebilir. Hastalığın tedavisinde ise türüne ve kan şekeri düzeyine bağlı olarak oral antidiyabetikler ve insülin yer almaktadır. Ayrıca hastaların diyet, egzersiz, stresten uzak durma, alkol ve sigaranın bıraktırılması gibi farmakolojik tedaviyi destekleyici nonfarmakolojik yöntemlere de uyması beklenmektedir. Diyabetli hastalarda hastalık ve tedavi sürecine uyum oldukça önemlidir. Diyabet yaşam boyu tedavi ve bakıma uyum sürecinin gerekli olduğu bir hastalıktır. Bu durum özellikle ciddi komplikasyonların önlenmesi açısından gereklidir. Diyabette tedaviye uyum birçok faktörden etkilenebilir. Hastaların eğitim seviyesi, sosyal destek ağları, ekonomik durumları, psikolojik durumları, sağlık sistemine ulaşımları hastaların tedaviye uyumlarını etkileyebilir. Tedavinin karmaşık olması, hastanın ilaç yan etkilerinden korkması, hastalık algısının yetersizliği, kültürel ve sosyal bazı engeller ise diyabetli hastanın tedaviye uyumunun zorlaşmasına neden olabilir. Hastaların tedavi ve bakıma uyumlarını arttırabilmek adına hasta eğitimi, psikososyal destek, teknolojik destek ve terapötik iletişimin sağlanması ile tedaviye uyum arttırılabilir.

Anahtar Kelimeler: diyabet, tedaviye uyum, hemşirelik bakımı

FACTORS AFFECTING TREATMENT ADHERENCE IN PATIENTS WITH DIABETES AND NURSING CARE

ABSTRACT

Diabetes mellitus is a chronic condition characterized by high blood sugar levels resulting from insulin deficiency, absence, or cellular insulin resistance. This condition, which arises due to the combined effects of genetic, environmental, and lifestyle factors, is primarily classified into two types: Type 1 and Type 2 diabetes mellitus. In diabetes, high blood sugar levels can lead to various symptoms, including excessive thirst, frequent urination, weakness, fatigue, delayed wound healing, sleep disturbances, and significant weight gain or loss. Treatment for the disease involves oral antidiabetic medications and insulin, depending on the type of diabetes and blood sugar levels. In addition, patients are expected to adhere to non-pharmacological methods that support pharmacological treatment, such as diet, exercise, stress management, and quitting alcohol and smoking. Adherence to the disease and treatment process is particularly important in patients with diabetes. Diabetes is a condition that requires lifelong adherence to treatment and care. This is particularly necessary to prevent serious complications. Adherence to treatment in diabetes can be influenced by many factors. Patients' educational level, social support networks, economic status, psychological state, and access to the healthcare system can all affect their adherence to treatment. The complexity of treatment, the patient's fear of medication side effects,

insufficient understanding of the disease, and certain cultural and social barriers can make it difficult for patients with diabetes to adhere to treatment. To improve patients' adherence to treatment and care, adherence can be enhanced by providing patient education, psychosocial support, technological support, and therapeutic communication.

Keywords: diabetes, treatment adherence, nursing care

GİRİŞ

Diyabetes mellitus halk arasında şeker hastalığı olarak bilinen, insülin eksikliği, yokluğu veya insüline karşı duyarlılığa bağlı olarak gelişen kan şekeri yüksekliği ile seyreden kronik bir hastalıktır. Hastalığın birçok tipi vardır. Bu tipler insülin miktarıyla ilişkilidir. Diyabetes mellitus tüm dünyada ve Türkiye'de mortalite ve morbidite oranları yüksek olan bir hastalıktır [1].

Diyabetes mellitus'da çok su içme, çok idrara çıkma, aşırı yemek yeme, ağızda kuruma, gece idrara çıkma, bulanık görme, ayaklarda uyuşma, karıncalanma gibi birçok belirti ortaya çıkmaktadır. Diyabetes mellitus da diyabetin türüne göre temelde hastalara oral antidiyabetik ilaçlar ve insülin verilmektedir. Egzersiz, kan şekeri regülasyonu, beslenme, aktivite hastaların dikkat etmeleri gereken tedavinin diğer bileşenleridir. Hastaların oral antidiyabetik, insülin, egzersiz ve beslenme önerilerine uyumlarında yaşanan bozulmalar kan şekerinin regüle olmasını engelleyerek hastaların ciddi sorunlarla karşılaşmalarına neden olabilir. Bu sorunlar hipoglisemi, diyabetik ketoasidoz, hiperosmolar nonketotik koma gibi akut komplikasyonlar olabileceği gibi, kontrolsüz kan şekerine bağlı diyabetik retinopati, diyabetik nöropati, diyabetik nefropati, diyabetik ayak, kardiyovasküler ve serebrovasküler hastalıklar gibi birçok komplikasyon ortaya çıkabilir. Bu komplikasyonların ortaya çıkmasının önlenmesindeki en önemli nokta hastaların tedavi ve bakıma uyum sağlayabilmesidir [1].

Tedaviye uyum diyabetli hastaların oral antidiyabetiklerini ve insülini doğru dozda, doğru zamanda, doğru şekilde kullanmasıdır. Hastaların tedaviye uyum sağlamaları hastalık sürecinin uygun şekilde kontrol edilmesine yardımcı olabilmektedir. Hastaların tedaviye uyumlarının arttırılmasında hasta eğitimi, teknolojik aletlerin kullanılması, telefonlarda yer alan uygulamaların kullanılması oldukça önemlidir. Hastaların tedaviye uyumlarını ise yaş, cinsiyet, eğitim düzeyi, sağlık okur yazarlığı, ek kronik hastalıklar, alkol ve sigara kullanma durumu gibi faktörler etkileyebilmektedir. Diyabetli hastalarda bireylerin psikolojik ve sosyal durumları, ekonomik düzeylerinin de etkili olabileceği düşünülmektedir. Hastaların tedavi ve bakıma uyumlarının sağlanmasında ve bu uyumun arttırılmasında hemşireler anahtar rol oynamaktadır. Hemşireler yalnızca klinik bakımla sınırlı kalmayıp, eğitim, danışmanlık, izlem ve destek bakım hizmetlerini de kapsamaktadır. Hemşirelerin temel rollerinden biri hasta ve ailesine yönelik eğitim sağlamaktır. Diyabetli hastaların yeterli bilgiye sahip olmaları, tedaviye uyumlarının arttırılmasında önemli bir belirleyicidir [2–4]. Bu literatür derlemesinde diyabetli hastalarda tedaviye uyumu etkileyen faktörler ve buna yönelik uygulanan hemşirelik bakımına yer verilmiştir.

DİYABETES MELLİTUS'UN TANIMI VE EPİDEMİYOLOJİSİ

Diyabetes mellitus, insülinin salınımında meydana gelen eksiklik, insülin yokluğu veya insüline karşı dirence karşı ortaya çıkan kronik bir hastalıktır. Hastalık karbonhidrat, protein ve yağ metabolizmasıyla ilgili sorunlara yol açmaktadır [1].

Diyabetes mellitusun görülme sıklığı yaş, cinsiyet, aile öyküsü, etnik köken ve coğrafi bölgelere göre farklılık göstermektedir. Dünya genelinde hızlıca artan bir prevalansa sahip olan bir halk sağlığı sorunudur. Diyabet görülme sıklığı kentleşme, yaşam süresinin uzaması, obezite prevalansının artması ve fiziksel aktivite azalması ile ilişkili olarak artmaktadır. Uluslararası Diyabet Federasyonu (IDF) 2021 verilerine göre dünya genelinde yaklaşık 537 milyon yetişkinin diyabetli olduğu, bu sayının 2030 yılında 643 milyona ulaşacağı öngörülmektedir. Ayrıca dünya genelindeki diyabet prevalansının 2021 yılında %10.5 olduğu ve artış göstereceği bildirilmiştir [5].

Diyabetin oluşturduğu bu yük yalnızca hastalık sıklığındaki artmayla sınırlı değildir, aynı zamanda komplikasyonlara bağlı mortalite ve morbidite oranlarını da arttırmaktadır. Diyabet hem sinir, hem damar hasarı meydana getirerek kalp, böbrek, göz ve nöronlarda çeşitli sorunlara yol açabilmektedir. Bu

açıdan izlem oldukça önemlidir. Sağlık politikalarının oluşturulmasında ve koruyucu sağlık hizmetlerinin geliştirilmesinde diyabetin epidemiyolojisinin izlenmesi önemlidir [5].

Türkiye'de diyabet görülme sıklığının belirlenebilmesi açısından Türkiye Diyabet Epidemiyoloji Çalışması (TURDEP-I) sonuçlarına göre 1997-1998 yılları arasında %7.2 olduğu, bu çalışmanın ikincisinde ise prevalansın %16.5'e yükseldiği belirlenmiştir. Türkiye'de IDF verilerine bakıldığında 2024 yılında 20-79 yaş arası yetişkinlerde %16.5 olduğu ve 9.6 milyon diyabetli bireyin olduğu tahmin edilmektedir. Türkiye'de bu diyabet artışının en önemli nedeni obezite sıklığındaki artıştır. Sedanter yaşam, sağlıksız beslenme alışkanlıkları ve nüfusun yaşlanması da prevalans artışına kaynaklık etmektedir [6,7].

DİYABETES MELLİTUS TÜRLERİ VE BELİRTİLERİ

Diyabetes mellitus farklı nedenlere bağlı olarak gelişebilen heterojen bir hastalıktır. Patogenezine ve klinik özelliklerine bağlı olarak Tip 1, Tip 2, gestasyonel ve diğer spesifik diyabet tipleri olarak sınıflandırılabilmektedir. Her diyabet türü farklı nedenlerle ortaya çıkabilmekte ve belirtiler benzerlik göstermektedir [1,8].

Tip 1 diyabetes mellitus, pankreasın beta hücrelerinin otoimmün yıkımı sonucu insülin üretiminin ciddi şekilde azalması veya tamamen durmasıyla ilişkilidir. Genellikle çocukluk veya adölesan dönemde ortaya çıkmakla birlikte her yaşta ortaya çıkabilmektedir. Tip 1 diyabetli bireylerde insülin eksikliğine bağlı meydana geldiğinden insülin tedavisi gerekmektedir [1,8].

Tip 2 diyabetes mellitus insülin direnci ve insülin sekresyonundaki yetersizlik sonucunda ortaya çıkan diyabet türüdür. Tüm diyabet vakalarının %90-95'ini oluşturmaktadır. Genellikle yaşla birlikte artan bir prevalansı vardır. Obeziteyle ilişkilidir. Genetik yatkınlık, fiziksel inaktivite ve sağlıksız beslenmede diğer risk faktörlerindendir [1,8].

Gestasyonel diyabetes mellitus gebelik sürecinde meydana gelen, genel olarak doğum sonrasında düzelen glikoz intoleransı olarak tanımlanmaktadır. Gebelikteki hormonal değişimlerin insülin direncine yol açması buna neden olmaktadır. Gebelik sonrasında tip 2 diyabetes mellitusa neden olabilmektedir [1,8].

Diğer spesifik diyabet türleri, genetik defektlere bağlı diyabetler pankreas hastalıklarına bağlı diyabetler, endokrin hastalıklar veya bazı ilaçların kullanımına bağlı gelişen diyabet türlerini kapsamaktadır. Nadir görülmektedirler [1,8].

Diyabetes mellitus belirtilerine bakıldığında hiperglisemiye bağlı olarak ortaya çıkan, poliüri, polidipsi, polifaji diyabetin üç klasik belirtisidir. Diğer belirtiler kilo kaybı, yorgunluk, halsizlik, bulanık görme, ağız kuruluğu, yaraların geç iyileşmesi ve tekrarlayan enfeksiyonlardır. Tip 1 diyabetes mellitus da belirtiler ani başlar, bulantı, kusma, karın ağrısı, hızlı solunum ve bilinç durumu değişiklikleri gibi belirtiler ketoasidoz komasını gösterebilmektedir. Tip 2 diyabette belirtiler daha yavaş ortaya çıkmaktadır ve genellikle sağlık taramaları esnasında tesadüfen ortaya çıkabilmektedir [1,8].

DİYABETES MELLİTUS KOMPLİKASYONLARI

Kontrolsüz diyabet ve kan şekeri regülasyonunun sağlanamaması sonucunda akut ve kronik komplikasyonlar gelişebilmektedir. Bu komplikasyonlar diyabetli bireyin yaşam kalitesini ciddi düzeyde düşüren ve bazen hızlı müdahale gerektiren hayatı tehlikeye atan nitelikte olabilmektedirler. Diyabetin komplikasyonları akut ve kronik olmak üzere ikiye ayrılmaktadır. Diyabetin akut komplikasyonları ani gelişen, acil müdahale gerektiren komplikasyonlardır. Diyabetin akut komplikasyonlarına aşağıda yer verilmiştir [9–11].

- Diyabetik ketoasidoz
- Hiperosmolar hiperglisemik nonketotik koma
- Hipoglisemi

Diyabetin kronik komplikasyonları uzun süreli hiperglisemiye bağlı olarak yavaş yavaş gelişen komplikasyonlardır. Kendi içinde mikrovasküler ve makrovasküler komplikasyonlar olarak

ayrılmaktadır. Diyabetik ayak da diyabetin kronik uzuv kaybına neden olabilen ciddi bir komplikasyonudur [9–11].

Mikrovasküler komplikasyonlar

- Diyabetik retinopati
- Diyabetik nefropati
- Diyabetik nöropati

Makrovasküler komplikasyonlar

- Koroner arter hastalıkları
- Serebrovasküler hastalıklar
- Periferik arter hastalıkları

DİYABETES MELLİTUS TEDAVİSİ VE BAKIMI

Diyabetes mellitus tedavisinin amacı kan glikoz düzeylerinin normal aralıkta tutulmasının sağlanması ve komplikasyon gelişiminin önlenmesi yoluyla yaşam kalitesinin arttırılması ve hastalığa bağlı mortalitenin azaltılmasıdır. Diyabet tedavisinde farmakolojik, tıbbi beslenme tedavisi, düzenli fiziksel aktivite, kan glikoz düzeylerinin izlenmesi ve hasta eğitimi gibi yaklaşımları içermektedir [1,12].

Farmakolojik tedavi, diyabetin farmakolojik tedavisi diyabet türüne göre değişiklik göstermektedir. Tip 1 diyabette insülin üretimi olmadığından tedavide insülin yer almaktadır. İnsülinin uygun dozda uygun zamanlarda yapılması oldukça önemlidir. Doz atlanması, eksik veya fazla dozun uygulanması ciddi yan etkilerin oluşmasına neden olabilmektedir. Tip 2 diyabette oral antidiyabetik ilaçlar, yaşam tarzı değişiklikleri uygulanmaktadır. Tip 2 diyabette oral antidiyabetiklerin yanı sıra uygun bir diyet, egzersiz, stresten uzak bir yaşamın sürdürülmesi de oldukça önemlidir [1,12].

Tıbbi beslenme tedavisinde düzenli ve dengeli beslenmenin sağlanması gerekmektedir. Düzenli ve dengeli beslenme ve glisemik indeksi düşük besinlerin tüketilmesi kan glikoz düzeyinin normal aralıkta tutulmasını sağlayabilmektedir. Diyabetli bireyin beslenme planı oluşturulurken, bireyin yaşı, cinsiyeti, fiziksel aktivitesi, beden kitle indeksi ve metabolik gereksinimleri baz alınmalıdır. Hastaların karbonhidrat tüketiminin düzenlenmesi, lifli posalı besinlerin tercihi, basit şekerler yerine kompleks karbonhidratların tüketilmesi önemlidir [1,12].

Düzenli fiziksel aktivite diyabet tedavisinde önemlidir. Egzersiz yoluyla insülin duyarlılığında artma meydana gelerek kan glikoz düzeylerinde düşme meydana gelebilmektedir. Kilo kontrolüne de yardımcı olarak kardiyovasküler risk faktörleri azalabilmektedir. Fakat egzersizin kan şekeri kontrolünde uygun şekilde kontrollü biçimde yapılması hipoglisemi riskinin önlenmesi açısından değerlidir [1,12].

Kan glikoz düzeylerinin izlenmesi diyabet tedavisinin etkinliğinin değerlendirilmesi açısından gereklidir. İnsülin kullanan bireylerde düzenli kan şekeri ölçümünün yapılması, hipoglisemi ve hiperglisemi riskinin azalmasına yardımcı olacaktır. Ayrıca belirli aralıklarla HBA1c düzeylerinin değerlendirilmesi de uzun süreli glisemik kontrol açısından gereklidir [1,12].

Diyabette hastanın tedavi ve bakım sürecine aktif katılımının sağlanması, tedaviye uyumun artmasına yardımcı olacaktır. Bu açıdan hasta eğitimi ve öz bakım uygulamaları temel unsurlardır. Hastaların kan şekeri izlemi, ilaç kullanımı, beslenme, egzersiz, ayak bakımı ve komplikasyonlar hakkında hasta bilgilendirilmelidir [1,12].

DİYABETES MELLİTUS'DA TEDAVİYE UYUMU ETKİLEYEN FAKTÖRLER VE HEMŞİRELİK GİRİŞİMLERİ

Diyabette tedaviye uyum bireyin tedavi planını uygun şekilde ve düzenli biçimde yapması ile ilişkilidir. Birçok faktörden etkilenebilmektedir. Bu faktörler bireysel, sosyal, ekonomik, tedaviye ilişkin ve sağlık sistemiyle ilişkili olabilmektedir [13–15].

Hastanın yaşı, cinsiyeti, eğitim düzeyi, hastalık süresi, sağlık okuryazarlığı ve diyabet hakkındaki bilgi düzeyi gibi bireysel faktörler hastaların tedavi ve bakıma uyum süreçleri üzerinde etkili olabilmektedir.

Diyabet hakkında yeterli bilgiye sahip olunmaması öz bakım davranışlarında azalmaya ve buna bağlı tedaviye uyumda azalmaya neden olabilir. Hastaların psikolojik durumları stres, anksiyete ve depresyon gibi durumlar bireyin tedaviye uyumunu azaltabilir. Tedavi ve bakımın kabullenme sürecini uzatabilir. Bu durumda motivasyonu azaltarak tedaviye uyumun azalmasına neden olabilir. Hastaların gelir düzeyi, sosyal desteklerinin varlığı, sağlık hizmetlerine erişim imkanları ve tedavi maliyeti gibi sosyoekonomik faktörler tedaviye uyumu doğrudan etkileyebilir. Hastalara verilen sağlık hizmetlerinin yeterli olması, kurulan iletişimin kalitesi, sağlık hizmetlerinin sürekliliği de tedaviye uyumu etkileyen faktörler arasında yer almaktadır [13–15].

Diyabet yönetiminde tedaviye uyumun sağlanması, hastalığın kontrol altına alınması ve komplikasyonların önlenmesi kritik öneme sahiptir. Bu süreçte hemşireler diyabetli bireylerin bakımında sürekli hasta ile iletişim halinde olan sağlık profesyonelleri olarak önemli sorumluluklar almaktadır. Hemşirenin rolü yalnızca klinik bakım uygulamalarıyla sınırlı değil, aynı zamanda hastalara ve yakınlarına eğitim, danışmanlık, izlem ve destek vermektir [13–15].

Hemşirenin temel rollerinden biri hasta ve ailesine yönelik eğitim sağlamaktır. Diyabetli bireylerin hastaların yeterli düzeyde bilgi sahibi olması, tedaviye uyumun arttırılmasında önemlidir. Hemşireler, kan şekeri takibi, ilaç ve insülin uygulamaları, beslenme düzeni, fiziksel aktivite ve komplikasyonların erken belirtileri hakkında hastalara düzenli bireyselleştirilmiş bir eğitim verilmelidir. Bu eğitimler hastanın bilgi düzeyi, kültürel özellikleri ve öğrenme gereksinimleri doğrultusunda planlanmalıdır [13–15].

Hemşirelerin bu noktadaki diğer rolü ise hastalara ve yakınlarına diyabet ve komplikasyonlarına ilişkin danışmanlık ve rehberlik etmektir. Diyabetli bireyler, yaşam tarzı değişikliklerine uyum sağlamada oldukça fazla zorlanmaktadırlar. Hemşireler hastaların karşılaştıkları güçlükleri belirleyerek uygun çözüm önerileri sunmalı, hastaların öz bakım becerilerinin gelişmesine yardımcı olmalıdır. Hastaların motivasyonlarının arttırılmaya çalışılması da önemli noktalardan biridir. Ayrıca hemşireler, hasta izlemi ve değerlendirme sürecinde de aktif rol almaktadırlar. Hastaların düzenli şekilde izlenmeleri tedaviye uyumlarını arttırmakta, kan şekeri kontrolü, ilaç kullanım alışkanlıkları ve yaşam tarzı değişiklikleri takip edilmelidir. İzlem sonuçlarına göre bakım planı güçlenmeli, gerektiğinde diğer sağlık profesyonelleri ile iş birliği sağlanmalıdır [13–15].

Diyabetli bireye psikososyal desteğin sağlanması da tedaviye uyumun arttırılmasında önemlidir. Diyabetli birey tedavi ve bakım sürecinde stres, kaygı, depresyon gibi psikolojik sorunlarla karşı karşıya kalabilir, bu sorunlar onun tedaviye uyumunu bozabilir. Bu anlamda hemşireler hastaların yaşadıkları psikososyal sorunların tespit edilmesini sağlayarak destek vermelidir. Gerekli hallerde ise uzmana yönlendirmelidir. Diyabetli bireylerde tedaviye uyumun arttırılmasında aşağıda yer alan hemşirelik girişimleri uygulanabilir [13–15].

- Diyabetli hastaya ve ailesine tedavi ve bakım sürecine ilişkin bireyselleştirilmiş eğitim verilmelidir.
- Hastaya kan şekeri izlemi, ilaç ve insülin uygulaması konusunda doğru teknikler öğretilmelidir.
- Hastaların beslenme ve fiziksel aktivite alışkanlıkları değerlendirilerek uygun yaşam tarzı değişiklikleri konusunda bilgi verilmelidir.
- Hastanın tedaviye uyumunu etkileyen faktörler belirlenmeli ve uyumu azaltan faktörler ortadan kaldırılmaya çalışılmalıdır.
- Hastaların öz bakım becerilerini arttırması sağlanmalı ve bu yönde desteklenmelidir.
- Motivasyonlarını arttırmaya yönelik destekleyici iletişim teknikleri kullanılmalıdır.
- Hastanın kan şekeri, ilaç kullanım alışkanlıkları ve yaşam tarzı değişiklikleri değerlendirilmelidir.
- Diyabetin akut ve kronik komplikasyonlarıyla ilgili hasta bilgilendirilmeli ve erken aşamada başvurunun gerekli olduğu durumlar bildirilmelidir.
- Hasta ve ailesine psikososyal destek sağlanmalı ve gerektiğinde psikolog desteği alması için yönlendirilmelidir.
- Teknoloji destekli görsel, işitsel eğitim materyalleri kullanılmalıdır.

SONUÇ

Diyabetli hastalarda tedaviye uyum kan şekeri regülasyonunun sağlanması, komplikasyonların önlenmesi ve yaşam kalitesinin arttırılmasında oldukça önemlidir. Bu süreçte hemşireler eğitici, bakım verici, danışman ve destekleyici olarak rol almaktadır. Bu rollerin etkin şekilde yerine getirilmesi, diyabetin başarılı bir şekilde yönetilebilmesine, komplikasyonların önlenmesine ve hastaların yaşam kalitesinin arttırılmasına katkı sağlamaktadır. Diyabetli bireylerin tedaviye uyumları ve etkileyen faktörlerin belirlenmesi adına daha fazla çalışmalar yapılması, tedaviye uyumu arttırmak üzere randomize kontrollü deneysel çalışmaların yapılması önerilmektedir.

KAYNAKÇA

1. Ulusal Diyabet Konsensus Grubu. *Diyabet Tanı ve Tedavi Rehberi*. 13th ed.; 2024.

2. Ülker Y. Tip 2 Diyabetli Bireylerde Tedaviye Uyum ve Öz Yeterlilik Düzeyinin Glukoz Regülasyonu İle İlişkisinin İncelenmesi. *Turkish J Diabetes Nurs*. 2023;3(2):60-65. doi:10.29228/tjdn.73736

3. Dağdelen M, Muz G, Çırpan R. Diyabet Tanısı Almış Bireylerde Parmak Delme Ve İnsülin Enjeksiyonu Yapma Korkusunun Tedaviye Uyum Üzerine Etkisi. *Sağlık Bilim Derg*. 2022;31(1):51-59. doi:10.34108/eujhs.904283

4. Çorak B, Uysal N. Tip 2 Diyabetes Mellituslu Bireylerde Sağlık Algısı Ve Aile Desteğinin Tedaviye Uyum Düzeyine Etkisi. *Ankara Eğitim ve Araştırma Hastan Tıp Derg*. 2022;56(1):125-129. doi:10.20492/aeahtd.1098831

5. *Diabetes Atlas*. 10th ed. International Diabetes Federation; 2021. https://idf.org/about-diabetes/resources/idf-diabetes-atlas-2021/

6. Satman I, Yilmaz T, Sengul A, Salman S, Salman F, Uygur S. Population-based study of diabetes and risk characteristics in Turkey: results of the turkish diabetes epidemiology study (TURDEP). *Diabetes Care*. 2002;25(9):1551-1556.

7. Satman I, Omer B, Tutuncu Y, et al. Twelve-year trends in the prevalence and risk factors of diabetes and prediabetes in Turkish adults. *Eur J Epidemiol*. 2013;28(2):169-180.

8. Taslipinar A, Corakci A, Kaya A, Uysal AR. *TURKDIAB Diyabet Tanı ve Tedavi Rehberi 2017*.; 2017. http://www.turkdiab.org/admin/PICS/webfiles/Diyabet_tani_ve_tedavi__kitabi.pdf

9. Keskin O, Balci B. Diabetes Mellitus ve Kardiyovasküler Komplikasyonlar. *Kafkas J Med Sci*. 2011;1(2):81-85. doi:10.5505/kjms.2011.09797

10.Önmez A. Diabetes Mellitus'ta Mikrovasküler Komplikasyonların Yönetimi. *Düzce Üniversitesi Sağlık Bilim Enstitüsü Derg*. 2017;7(2):117-119.

11.Eroğlu N. Diabetes Mellitus'un Komplikasyonları. *İZMİR Democr Univ Heal Sci J*. Published online 2018.

12.Dinççağ N. Diabetes Mellitus Tanı ve Tedavisinde Güncel Durum. *İç Hast Derg*. 2011;18:181-223.

13.Yapar SN, Özkan Tuncay F. Tip 2 Diyabet Tanılı Bireylerde Hastalık Algısı Ve Tedaviye Uyum. *YOBU Sağlık Bilim Fakültesi Derg*. 2025;6(2):202-213.

14.Baykal A, Kapucu S. Tip 2 diyabetes mellituslu hastaların tedavilerine uyumlarının değerlendirilmesi. *Hacettepe Üniversitesi Hemşirelik Fakültesi Derg*. 2015;2(2):44-58.

15.Çapan S, Yılmaz E. Tip 2 Diyabetes Mellitus Yönetiminde Yaşam Kalitesi ve Hemşirenin Destekleyici Rolü. *KTO Karatay Üniversitesi Sağlık Bilim Derg*. 2025;6(3):596-605. doi:10.59244/ktokusbd.1821167

EXAMINATION OF STUDIES ON THERAPEUTIC TOUCH: A BIBLIOMETRIC STUDY

Melike DEMİR DOĞAN

[a]BSc., MSc, PhD., Professor, Department of Nursing, Gümüşhane University Faculty of Health Sciences, Gümüşhane, Turkey, Orcid ID: 0000-0001-7051-2202

ABSTRACT

Aim: This study aims to examine bibliometric indicators—such as growth rate, most cited authors, countries, and journals—in publications related to Therapeutic Touch.

Methods: A comprehensive search was conducted in the Web of Science database covering the period from 1970 to April 28, 2025. A total of 5,134 articles were identified and evaluated. The obtained data were subsequently analyzed utilizing the Bibliometrix program.

Results: The analysis revealed an average document age of 11 years, accompanied by an annual growth rate of 8.72%. On average, each document received 21.35 citations, and the total number of references across all documents was 185,043. The Journal of Alternative and Complementary Medicine was determined to be the leading journal in terms of article count. The United States emerged as the country with the highest number of publications in this field. Furthermore, based on publication count, the top 10 institutions were identified as follows: University of Miami, University of Toronto, Duke University, Ohio State University, University of Washington, Johns Hopkins University, Tel Aviv University, University of Alberta, University of Pittsburgh, and University of Haifa.

Conclusion: The findings demonstrate robust growth and considerable scholarly interest in the field of Therapeutic Touch. This bibliometric approach not only underscores key trends and influential contributors but also provides valuable insight to guide future research, foster international collaboration, and inform policy development in complementary medicine.

Keywords: Therapeutic Touch, bibliometric analysis, complementary medicine, growth rate, academic publications, Web of Science, Bibliometrix

1. INTRODUCTION

In recent years, the growing interest in complementary therapeutic modalities has paved the way for the widespread adoption of these practices in the healthcare sector (1). Therapeutic Touch (TT), recognized as one of these complementary treatment methods, was developed in the early 1970s by Dolores Krieger and Dora Kunz. This approach is designed to correct imbalances in an individual's energy field and to facilitate the healing process, relying on the principle of transmitting universal energy via the practitioner's hands. Sessions, which typically last between 15 and 20 minutes, constitute a fundamental component of this intervention. Although this method does not involve physical contact, its primary focus is on the regulation of the energy field (2,3,4).

Therapeutic Touch (TT) is regarded as an integrative therapeutic approach based on the assumption that individuals can achieve inner balance, restructure their energy fields, and utilize universal energy with a specific intention and compassion (5). Diseases and symptoms can not only lead to disturbances, blockages, and deformations in these energy fields but also affect their natural rhythm. Both psychological conditions and physical factors, such as fatigue and sleep disturbances, may contribute to imbalances within the energy field (3,6,7).

Studies have reported that Therapeutic Touch interventions contribute positively to quality of life by reducing anxiety, facilitating relaxation, enhancing positive affect, and improving both fatigue and sleep quality (8,9,10,11). Moreover, evidence suggests that TT is effective in reducing pain and anxiety (2,8,10,11,12). One study posited that touch may improve sensory parameters—such as pain and stress—by modulating central nervous system functions (13), while a meta-analysis indicated that TT has moderate effects on both physical and mental health (14).

Bibliometric analysis, through the examination of thousands of studies on the subject, enables the identification of the highest-quality publications, the most influential authors, the countries and institutions with the greatest output, the collaborative networks among these entities, as well as the most impactful journals (15,16). Consequently, this study was conducted with the aim of delineating the research topics that necessitate further scientific inquiry within the domain of Therapeutic Touch. It also seeks to provide valuable insights for the further development of this already expanding field, thereby fostering future interdisciplinary collaborations by outlining bibliometric indicators such as publication trends, the most active countries in terms of article output, and related metrics.

2. METHODS

2.1. Search strategy

2.2.

Our study is based on a selection protocol, composed of an established checklist, that was adopted to determine the collection of articles used in the systematic literature review. This protocol was developed on the basis of the PRISMA guidelines[17] to ensure the methodological rigor of the literature review, as well as the reproducibility and transparency of the selection process. The Web of Science (WOS) database was selected due to its advantages—such as high quality, rapid updates, and a low rate of data errors and the search was conducted from the inception of the database in 1970 until April 28, 2025. The following keywords were utilized in the search: "touch therapy (All Fields) and Therapeutic Touch (OR – Search within topic) and Healing Touch (OR – Search within topic) and Touch Therapy (OR – Search within topic)."

The search conducted in the Web of Science (WOS) database yielded a total of 5,134 records, all of which were subjected to a detailed evaluation process. This process is illustrated in Figure 1.

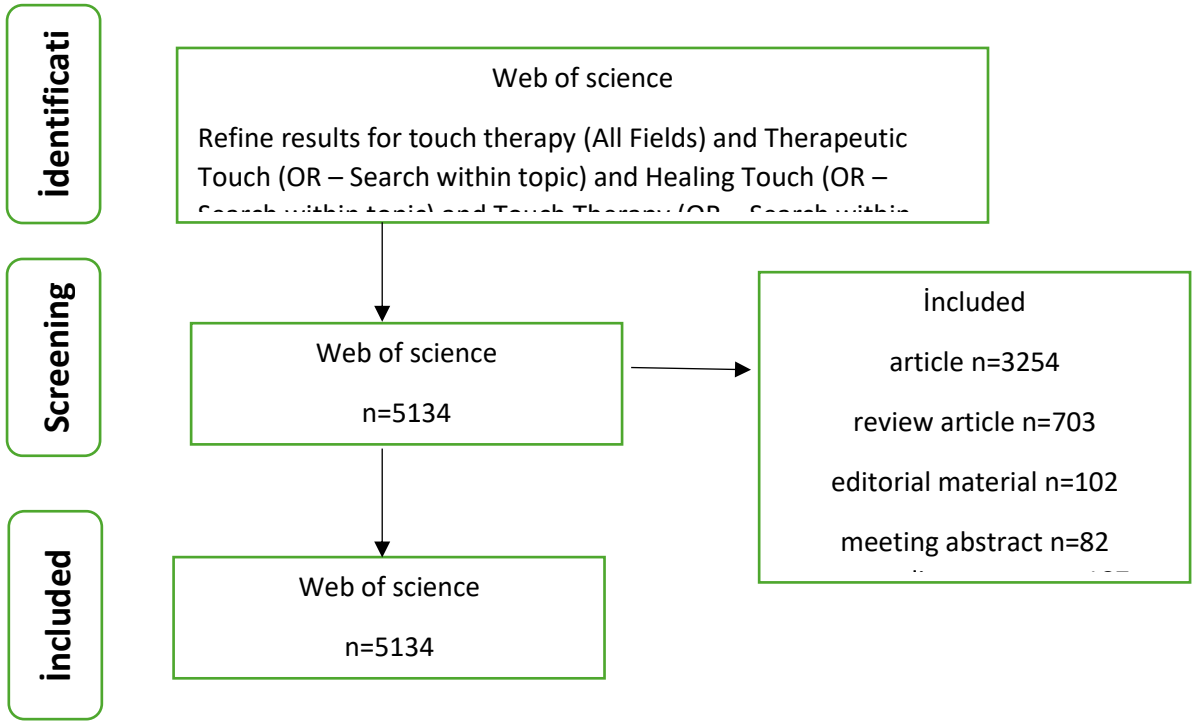


Figure 1: PRISMA Flow diagram

2.3. Data analysis

The results obtained from the search were exported from the WOS database in BibTeX format. The analysis outcomes offered by WOS served as the foundation for delineating the research area. For a

comprehensive science mapping analysis, Bibliometrix a novel R tool developed to import bibliographic data from scientific databases and to perform bibliometric analyses on various elements was employed (18).

3. RESULT

The study analyzed 5,134 documents spanning from 1980 to 2025. The average age of these documents was determined to be 11 years, while an annual growth rate of 8.72% was observed. On average, each document received 21.35 citations, and the total number of references amounted to 185,043. Moreover, with regard to the content analysis, Keywords Plus (ID) accounted for 10,132 entries, and the author-assigned keywords (DE) totaled 10,938 (Table 1).

Regarding author contributions, a total of 21,521 distinct authors were involved in the publications. The number of authors contributing to single-authored works was 675; however, the identification of 731 single-authored documents indicates that some authors produced multiple solo publications. Additionally, an average of 4.98 authors per document was recorded, highlighting the prevalence of teamwork and interdisciplinary collaboration in these studies. The international co-authorship rate was determined to be 15.19%, reflecting global collaborative dynamics (Table 1).

When examining the publication types, it was found that the documents consisted of articles (n=3,254), review articles (n=703), editorial materials (n=102), meeting abstracts (n=82), proceedings papers (n=187), book reviews (n=22), corrections (n=7), and letters (n=40) (Table 1).

Table 1: Characteristics of the general information in this study

Description	**Results**
MAIN INFORMATION ABOUT DATA	
Timespan	1980:2025
Sources (Journals, Books, etc)	2480
Documents	5134
Annual Growth Rate %	8.72
Document Average Age	11
Average citations per doc	21.35
References	185043
DOCUMENT CONTENTS	
Keywords Plus (ID)	10132
Author's Keywords (DE)	10938
AUTHORS	
Authors	21521
Authors of single-authored docs	675
AUTHORS COLLABORATION	

Single-authored docs	731
Co-Authors per Doc	4.98
International co-authorships %	15.19
DOCUMENT TYPES	
article	3254
article; book chapter	70
article; data paper	1
article; early access	41
article; proceedings paper	86
article; retracted publication	1
biographical-item	1
book review	22
correction	7
correction, addition	1
editorial material	102
editorial material; book chapter	2
letter	40
meeting abstract	82
news item	4
note	8
proceedings paper	187
reprint	3
review	703
review; book chapter	6
review; early access	8
review; retracted publication	5

3.1. Publications

Table 2 summarizes the publication volume, citation counts, and impact indicators (h and m indices) of the journals publishing in the field of touch therapy. The Journal of Alternative And Complementary Medicine, with 47 articles and 1,005 citations, reports an h-index of 20 and an m-index of 0.74, thereby

establishing itself as one of the leading journals in terms of both publication count and citation distribution. Similarly, the Journal of Holistic Nursing, with 42 articles and 411 citations, recorded an h-index of 12 and an m-index of 0.6. Although this indicates a relatively narrower impact in the literature, the journal demonstrates consistent performance within its field.

Other journals in the field show varied profiles. The American Journal of Occupational Therapy registered 1,600 citations from 38 articles, achieving an h-index of 21 and an m-index of 0.45. In addition, Alternative Therapies In Health And Medicine presented a moderate level of impact with 34 articles, 740 citations, an h-index of 16, and an m-index of 0.57. Plos One, with 33 articles, 457 citations, an h-index of 13, and an m-index of 0.68, exhibits a noteworthy publication performance. Notably, Infant Behavior & Development, despite comprising only 30 articles, accumulated 1,374 citations and recorded an h-index of 21 and an m-index of 0.7, emphasizing its substantial influence in the field despite the limited number of publications.

Table 2: Ranking of journals (top 10 journals)

Sources	Articles	Citations	h index	m index
Journal of Alternative And Complementary Medicine	47	1005	20	0,74
Journal of Holistic Nursing	42	411	12	0,6
American Journal of Occupatıonal Therapy	38	1600	21	0,45
Alternative Therapies In Health And Medicine	34	740	16	0,57
Plos One	33	457	13	0,68
Infant Behavior \& Development	30	1374	21	0,7
Journal of Bodywork And Movement Therapies	29	541	11	0,55
Cureus Journal of Medical Science	25	109	6	1
Complementary Therapies In Medicine	24	298	10	0,5
Experimental Brain Research	23	535	11	0,42

3.2. Countrys

Table 3 presents the production volume, total citation counts, and average citations per article for the top ten countries publishing within the field of alternative and holistic medicine. The United States leads the ranking with 1,615 articles and a cumulative 52,880 citations, which corresponds to an average of 32.7 citations per article. The United Kingdom follows in second place with 268 articles that have collectively received 7,741 citations, yielding approximately 28.9 citations per article. China is represented by 250 articles with 3,425 citations, resulting in an average of 13.7 citations per article.

In terms of geographic distribution, Canada stands out with 216 articles and 5,371 citations, amounting to an average of approximately 24.9 citations per article. Similarly, Germany's 212 articles garnered

4,328 citations, reflecting an average of 20.4 citations per article. Japan, with 203 articles and a total of 2,449 citations, shows a lower average of 12.1 citations per article, placing it among the less cited countries in this group.

Furthermore, Italy produced 165 articles and 3,264 citations, which translates to an average of 19.8 citations per article. In contrast, Australia, with 130 articles, accumulated 3,620 citations, corresponding to an average of 27.8 citations per article. Meanwhile, India published 122 articles that received 2,343 citations (averaging 19.2 citations per article), and Brazil, with 105 articles, recorded a total of 1,143 citations—yielding an average of just 10.9 citations per article.

Table 3: Ranking of countrys (top 10 countrys)

Region	Articles	Citations	Average Article Citations
USA	1615	52880	32,7
United Kingdom	268	7741	28,9
China	250	3425	13,7
Canada	216	5371	24,9
Germany	212	4328	20,4
Japan	203	2449	12,1
Italy	165	3264	19,8
Australia	130	3620	27,8
India	122	2343	19,2
Brazil	105	1143	10,9

3.3. Authors and Affiliations

When examining the publication performance of the authors, Field T achieved the highest productivity with 102 articles, garnering 6,582 citations and attaining an h-index of 52 alongside an m-index of 1.53, thereby establishing a leadership position in the field. Hernandez-Reif M, with 54 articles, amassed 3,381 citations, resulting in an h-index of 35 and an m-index of 1.21, indicative of a significant impact. In contrast, Diego M published 30 articles that received 2,176 citations, corresponding to an h-index of 23 and an m-index of 0.95, suggesting a moderate level of impact. Liu Y, despite contributing 18 articles, obtained 91 citations, yielding an h-index of 6 and an m-index of 0.43 and thus demonstrating a more limited influence. Similarly, Schanberg S, with 18 articles, accrued 1,476 citations and achieved an h-index of 16 and an m-index of 0.53, thereby producing noteworthy results. Additionally, Wang Y's 18 articles secured 187 citations with an h-index of 6 and an m-index of 0.21, reflecting a relatively low impact, whereas Wardell DW, with 17 articles, recorded 305 citations, an h-index of 8, and an m-index of 0.32. Finally, Zhang Y's 16 articles were associated with 287 citations, corresponding to an h-index of 7 and an m-index of 0.41, thus representing an average performance.

Furthermore, Aruin AS, with 15 articles, collected 188 citations, yielding an h-index of 9 and an m-index of 0.37, while Carey LM, also with 15 articles, received 585 citations and achieved an h-index of 11 with an m-index of 0.38, thereby demonstrating particularly strong citation performance (Table 4).

Table 4: Ranking of Authors (top 10 Authors)

Author	Articles	Citations	h index	m index
Field T	102	6582	52	1,53
Hernandez-Reif M	54	3381	35	1,21
Diego M	30	2176	23	0,95
Liu Y	18	91	6	0,43
Schanberg S	18	1476	16	0,53
Wang Y	18	187	6	0,21
Wardell DW	17	305	8	0,32
Zhang Y	16	287	7	0,41
Aruin AS	15	188	9	0,37
Carey LM	15	585	11	0,38

Regarding institutional contributions, the University of Miami leads the ranking with a total of 250 articles, thereby playing a decisive role in the field. The University of Toronto follows with 116 articles, while Duke University, with 98 articles, occupies the third position, drawing notable attention. The data further indicate that Ohio State University and the University of Washington achieved significant productivity with 86 and 85 articles, respectively. Moreover, Johns Hopkins University, contributing 84 articles, confirms its important standing in the field. In addition, Tel Aviv University, the University of Alberta, and the University of Pittsburgh each produced 78 articles, thereby making valuable contributions to institutional performance, whereas the University of Haifa, with 77 articles, is positioned at the lower end of the ranking (Table 5).

Table 5: Ranking of Affiliation (top 10 Affiliations)

Affiliation	Articles
Univ Miami	250
Univ Toronto	116
Duke Univ	98
Ohio State Univ	86
Univ Washington	85
Johns Hopkins Univ	84
Tel Aviv Univ	78
Univ Alberta	78

Univ Pıttsburgh	78
Univ Haifa	77

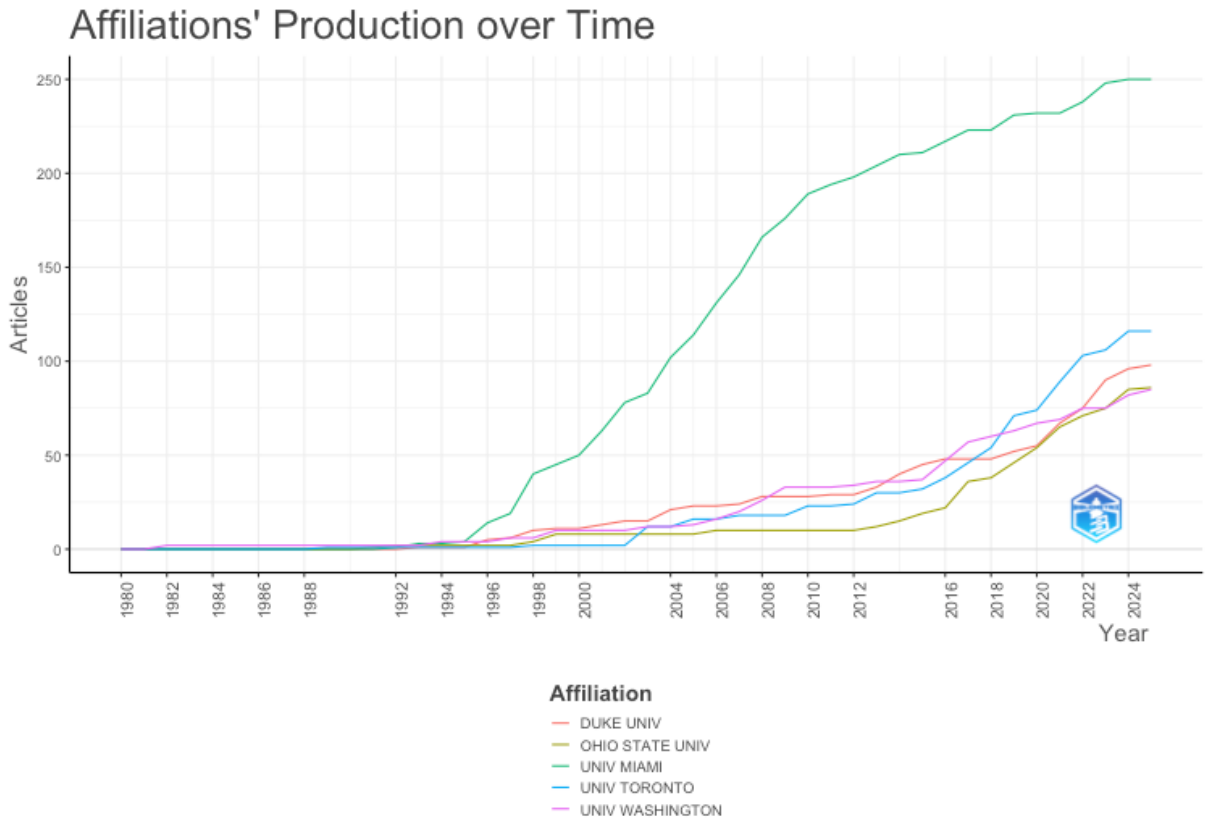


Figure 2: Affiliations'publication over time

Figure 2 illustrates the annual publication output from 1980 to 2024 of five different universities (Duke University, Ohio State University, University of Miami, University of Toronto, and University of Washington). Notably, the University of Miami (represented by the green line) has experienced a marked increase beginning in 2000, with its publication growth being considerably more pronounced compared to the other institutions. While Duke University, Ohio State University, University of Toronto, and University of Washington have also shown an upward trend, their increases are not as dramatic as that of the University of Miami. Overall, although all the institutions have seen growth in their publication outputs over time, the magnitude and rate of this growth vary significantly from one university to another.

3.4. Keywords

When examining the frequency of keywords used by the authors, the top 10 most frequently occurring terms were identified. The keyword with the highest frequency was "touch," which appeared 196 times. The subsequent keywords, in descending order, were: pain (n = 130), therapeutic touch (n = 118), therapy (n = 101), cancer (n = 94), massage (n = 92), rehabilitation (n = 92), anxiety (n = 87), stroke (n = 79), and massage therapy (n = 58) (Figure 3).

In Figure 4, under the heading "Trend Topics," the usage frequencies of keywords related to therapeutic applications and medical subjects, as determined from the period 1997–2023, are visually presented.

Terms such as "biofield therapies," "affective touch," "sensory processing," "COVID-19," "chronic pain," "therapy," "pain," "touch," "cancer," "healing touch," "therapeutic touch," "sensory," "complementary and alternative medicine," "posture," "sensory integration," "massage therapy," and "infants" represent a broad thematic spectrum that forms the core research focus of the field. In the figure, each term is depicted as a circle with a size proportional to its frequency during that period; an increase in the circle's size indicates a higher frequency of usage at that time.



Figure 3: Author's Keywords



Figure 4: Trend topics Keywords

4. DISCUSSION

In this study, the average document age was determined to be 11 years, and an annual growth rate of 8.72% was observed. The fact that each document received an average of 21.35 citations and that the total number of references reached 185,043 underscores the scientific impact and dissemination of the study.

An evaluation of the publication counts, h-indices, citation counts, and the ratio of citations to publications among journals focusing on Therapeutic Touch reveals that the h-index serves as a metric for assessing the impact of a journal's or author's published work. Briefly, the h-index is defined as the number of articles (h) that have each received at least h citations.[19] The m-index was introduced to eliminate the disadvantage faced by young researchers who may not yet have had sufficient time to garner high citation counts (20).

It was determined that the Journal of Alternative And Complementary Medicine is the most prolific outlet in the field of Therapeutic Touch, establishing itself as one of the leading journals in terms of both publication volume and citation distribution. Furthermore, Field T emerged as the most productive author with 102 articles, and the high values of the h-index and m-index associated with Field T confirm his/her role as a leading researcher in this domain. In addition, a study focusing on complementary and alternative medicine in cancer patients similarly identified the Journal of Alternative and Complementary Medicine as the most productive journal (21). Moreover, a bibliometric analysis of Reiki—one of the energy-based approaches—also reported the Journal of Alternative and Complementary Medicine as holding the top position (22).

The United States emerged as the country with the highest article count related to the topic, and it also leads the ranking in terms of total citation count. This indicates not only the high production capacity of the USA but also that its published studies have garnered widespread international attention. Similar

findings have been reported in other bibliometric studies on alternative and complementary medicine, which also identify the USA as the most productive country (21,22,23,24).

Among the top ten universities publishing in this field, the following institutions were ranked in descending order by publication count: University of Miami, University of Toronto, Duke University, Ohio State University, University of Washington, Johns Hopkins University, Tel Aviv University, University of Alberta, University of Pittsburgh, and University of Haifa. This ranking illustrates that institutions endowed with advanced research infrastructure tend to lead in productivity. Notably, while U.S.-based universities dominate the list, significant contributions also come from institutions in Canada and Israel.

An analysis of the most frequently used keywords by authors revealed the following top ten terms: touch, pain, therapeutic touch, therapy, cancer, massage, rehabilitation, anxiety, stroke, and massage therapy. The prominence of the term "pain" underscores the importance of pain management and the investigation of patients' symptomatic needs in clinical applications. Meanwhile, the keyword "therapeutic touch" highlights the effectiveness and diversity of touch-based therapies within the realm of alternative treatment methods. The broad inclusion of "therapy" reflects the wide spectrum of treatment approaches under consideration, and "cancer" reveals an active research interest in touch-based interventions for cancer patients.

Moreover, the thematic examination of these keywords over time demonstrates the evolving popularity of various topics related to therapeutic applications. Fundamental concepts such as "touch" and "therapy" have maintained a significant impact on studies within both clinical and alternative medicine domains. Additionally, the notable presence of contemporary topics including "COVID-19" suggests that the pandemic has had a discernible influence on research trends in the field.

5. CONCLUSION

In summary, our bibliometric analysis highlights a dynamic and growing field in Therapeutic Touch research from 1980 to 2025. With an average document age of 11 years, an annual growth rate of 8.72%, and robust citation metrics, the study underscores the significant scientific impact in this domain. The Journal of Alternative and Complementary Medicine emerged as a key publication outlet, while influential authors like Field T have been pivotal in advancing the field. The United States leads in production, and prominent institutions such as the University of Miami and University of Toronto highlight the role of well-equipped research infrastructures. Moreover, the prevalence of core keywords—such as "touch," "pain," and "therapeutic touch"—alongside emerging topics like "COVID-19" illustrates evolving research trends within both clinical and alternative medicine.

REFERENCES

1. Turan N. The importance of therapeutic touch in intensive care unit. Acıbadem Univ Health Sci J. 2015;6(3):134-139.
2. Mueller G, Palli C, Schumacher P. The effect of therapeutic touch on back pain in adults on a neurological unit: an experimental pilot study. Pain Manag Nurs. 2019;20(1):75-81. https://doi.org/10.1016/j.pmn.2018.09.002
3. Tabatabaee A, Zagheri Tafreshi M, Rassouli M, Aledavood SA, AlaviMajd H, Faramand SK. Effect of therapeutic touch on pain related parameters in patients with cancer: a randomized clinical trial. Mater Sociomed. 2016;28(3):220-223. https://doi.org/10.5455/msm.2016.28..
4. O'Mathúna DP. Therapeutic touch for healing acute wounds. Cochrane Database Syst Rev. 2016;5:CD002766. https://doi.org/10.1002/14651858.CD002766.pub4..
5. Bağcı H, Cinar Yucel S. A systematic review of the studies about therapeutic touch after the year of 2000. Int J Caring Sci. 2020;13:231-241.
6. Doğru BV, Utli H, Aykar FS. Effect of therapeutic touch on daytime sleepiness, stress and fatigue among students of nursing and midwifery: a randomized sham-controlled trial. Complement Ther Clin Pract. 2021;43:101322. https://doi.org/10.1016/j.ctcp.2021.101322..
7. Senderovich H, Ip ML, Berall A, et al. Therapeutic Touch® in a geriatric palliative care unit–a retrospective review. Compl Ther Clin Pract. 2016;24:134-138. https://doi.org/10.1016/j.ctcp.2016.06.002..
8. Ünal Aslan KS, Çetinkaya F. The effects of therapeutic touch on spiritual care and sleep quality in patients receiving palliative care. Perspect Psychiatr Care. 2022;58:374-382. https://doi.org/10.1111/ppc.12801
9. Alp FY, Yucel SC. The effect of therapeutic touch on the comfort and anxiety of nursing home residents. J Relig Health. 2021;60:2037-2050.
10. Çalışkan MA, Cerit B. Effect of therapeutic touch on sleep quality and anxiety in individuals with chronic obstructive pulmonary disease: a randomized controlled trial. Complement Ther Clin Pract. 2021;45:101481.
11. Pinar SE, Demirel G. The effect of therapeutic touch on labour pain, anxiety and childbirth attitude: a randomized controlled trial. Eur J Integr Med. 2021;41:101255.
12. Zafar Neya N, Kohan S, Miri S, Solimane L, Abbas Zadeh A, Abbaszadeh A, et al. The effect of the therapeutic touch on preoperative anxiety in women with elective surgeries. J Qualitative Res Health Sci. 2020;10(1):42-51.
13. Bonanno M, Papa GA, Calabrò RS. The neurophysiological impact of touch based therapy: insights and clinical benefits. J Integr Neurosci. 2024;23(12):214. https://doi.org/10.31083/j.jin2312214
14. Packheiser J, Hartmann H, Fredriksen K, Gazzola V, Keysers C, Michon F. A systematic review and multivariate meta-analysis of the physical and mental health benefits of touch interventions. Nat Hum Behav. 2024;8(6):1088-1107. https://doi.org/10.1038/s41562-024-01841-8
15. Golpinar M, Demir E. Global research output of the cerebellum: yesterday, today, and tomorrow. J Anat Soc India. 2020;69:155-165.
16. Golpinar M, Ekici M. Global research productivity and publication trends in vesicoureteral reflux: a bibliometric analysis. Minerva Pediatr. 2023;75(2):270-281. https://doi.org/10.23736/S2724-5276.21.06278-9
17. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JPA, Clarke M, Devereaux PJ, Kleijnen J, Moher D. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. PLOS Med. 2009;6:e10001000. https://doi.org/10.1371/journal.pmed.10001000

18. Aria M, Cuccurullo C. Bibliometrix: an R-tool for comprehensive science mapping analysis. J Informetr. 2017;11(4):959-975. https://doi.org/10.1016/j.joi.2017.08.007

19. Bornmann L, Daniel HD. What do we know about the h index? J Am Soc Inf Sci Technol. 2007;58(9):1381-1385.

20. Harzing A-W. Reflections on the h-index. Business&Leadership. 2012;1(9):101-106.

21. Yang W, Hao X, Qu J, Wang L, Zhang M, Jiang Y, Liu Y. Collaborative networks and thematic trends of research on the application of complementary and alternative medicine in cancer patients: a bibliometric analysis. Complement Ther Clin Pract. 2019;37:58-67. https://doi.org/10.1016/j.ctcp.2019.08.008

22. Demir Doğan M. Bibliometric analysis of the results of Reiki research. Eur J Integr Med. 2025;75:102442. https://doi.org/10.1016/j.eujim.2025.102442

23. Fu JY, Zhang X, Zhao YH, Huang MH, Chen DZ. Bibliometric analysis of complementary and alternative medicine research over three decades. Scientometrics. 2011;88:617-626.

24. Helha FN, Wang YP. Trends in complementary and alternative medicine for the treatment of common mental disorders: a bibliometric analysis of two decades. Complement Ther Clin Pract. 2022;46:101531. https://doi.org/10.1016/j.ctcp.2021.101531..

THE ROLE OF SHORT TANDEM REPEATS (STR) VARIATIONS IN NEUROBIOLOGICAL DISEASES

Elif Kürkçüoğlu

Istanbul University-Cerrahpasa, Institute of Forensic Sciences and Legal Medicine, Department of Science, İstanbul-Türkiye, ORCID: https://orcid.org/0009-0002-3752-0678

Ömer Karataş

Istanbul University-Cerrahpasa, Institute of Forensic Sciences and Legal Medicine, Department of Science, İstanbul-Türkiye, ORCID: https://orcid.org/0000-0002-1170-7509

Emel Hülya Yükseloğlu

Istanbul University-Cerrahpasa, Institute of Forensic Sciences and Legal Medicine, Department of Science, İstanbul-Türkiye, ORCID: https://orcid.org/0000-0003-2009-6065

SUMMARY

Short tandem repeats (STRs) are of significant importance in neurobiological diseases. Repetitive variations, in particular, contribute to the development of neurobiological diseases.In various disorders such as schizophrenia, depression, and Fragile X syndrome, analyses have been performed using methods such as Southern Blot, NGS, and GWAS, and the number of abnormal repeats in the relevant regions has been analyzed to identify associated gene regions.Repetitive variations occur in the genome through loss of gene function, RNA-mediated gain of function, gain of toxic function at the protein level, and RAN translation. While the mechanism may differ for each disease, some diseases may exhibit multiple of these mechanisms.This study aims to better understand the basis of repetitive variations, to examine disease-specific regions using new methods, to enable early diagnosis and treatment, and to develop treatment methods targeting these conditions.

KEYWORDS: STR, Repeat Variations, Neurobiology, Epigenetics.

1. INTRODUCTION

Our basic choices regarding daily life constitute our lifestyle [1].Factors such as dietary habits, behavior, stress, smoking and alcohol use, and physical activity are influential in lifestyle choices. The choices we make throughout our lives are influenced by both our genetic makeup and our environment [2]. However, researchers have found that genetic inheritance and environmental factors are insufficient when studying diseases and individual behaviors. In recent years, the term epigenetics has entered our lives, and some behaviors and diseases that cannot be explained by genetics have begun to be explained by epigenetics. Through epigenetic mechanisms, changes in gene expression that occur without altering the DNA sequence in the cell are passed on to the next generation [3]. Changes occurring in epigenetics have been associated with neurobiological diseases, respiratory system diseases, heart diseases, and cancer [4]. Epigenetic mechanisms are influenced by various environmental stimuli such as nutrition, family behavior, hormones, and drugs. These mechanisms include DNA methylation, histone modification, repression, changes in protein conformation, and RNA-induced silencing. All of these factors create a predisposition to disease by activating or suppressing gene expression during the developmental process [5]. Neurobiology investigates the structure, function, mechanism, genetics, and chemistry of the nervous system. All neuropsychological and neurodegenerative diseases are considered within the scope of neurobiological diseases. Studies show that epigenetic mechanisms play a role in the development of neurobiological diseases by causing changes in brain function. Stress, in particular, can negatively affect cognitive functions and initiate pathological processes in the brain. Abnormal DNA methylation that may occur will also lead to abnormal neuronal function [6]. While neuropsychology examines the relationship between brain function and behavior, neurodegenerative diseases examine diseases

affecting the brain and nervous system. Psychiatric disorders can seriously affect an individual's quality of life and cause disabilities. They are characterized by emotional, cognitive, and behavioral symptoms. Examples of psychiatric disorders include schizophrenia, bipolar disorder (BD), major depressive disorder (MDD), anxiety, fear-related disorders, obsessive-compulsive disorders, and personality disorders. Neurodegeneration, on the other hand, can be defined as the progressive loss of neurons, either structurally or functionally. This condition can occur due to damage at birth and be seen from infancy, or it can arise due to the effects of genetic factors and aging. The rarity of Alzheimer's and Parkinson's diseases in individuals under 40 years of age indicates that aging is a significant risk factor for these diseases. Huntington's disease is another neurodegenerative disease that appears at an early age [7].

1.1. Tandem Repeat Variations and Tandem Repeat Expansion Disorders (TRDs)

STR sequences, consisting of consecutive repeats of 2-6 nucleotide units, can expand beyond the normal range, leading to gene dysfunction and various clinical symptoms [8]. STRs, which can undergo expansion and contraction through replication slippage, play a critical role in neurobiological diseases. Replication slippage occurs when the template and synthesized strands are temporarily separated, misaligned, and form a hairpin structure during DNA replication. Abnormal expansion of these repeats disrupts cellular processes by altering the structure and function of encoded proteins or interfering with gene regulation and RNA processing. Generally, if these disruptions occur in the template strand, contraction is observed, and if they occur in the synthesized strand, expansion is observed. The chance of misalignment is higher in longer repeat sequences. Therefore, the slippage can be greater, and a higher mutation rate is observed. For example, spinal bulbar muscular atrophy (SBMA) is associated with the expansion of CAG trinucleotide repeats in the androgen receptor gene. CAGs are generally found in the genome in a maximum of 38 repeats; exceeding this value leads to the formation of misfolded polyglutamine protein aggregates, causing neurotoxicity [9–11].

1.2. Repeat Variations and Molecular Mechanism

Repeated variations disrupt gene function in various ways. As a result of these variations, abnormal expansion of the DNA sequence in a specific gene region leads to diseases associated with repeated variation [12]. Expansion can be observed in introns and exons in the genome, resulting in impaired protein function and abnormal gene expression [13]. It is usually caused by an abnormal number of trinucleotide repeats. When the repeat number exceeds the threshold value, it can lead to health problems in affected individuals. These diseases are caused by the influence of both genetic and environmental factors [14]. Pathogenic mechanisms are quite diverse and differ according to the location of the expanded STR within the gene (intron, exon, intergenic, non-translated). Mechanisms occurring in different regions contribute to the development of different diseases. Current research shows that repeat expansion diseases arise mainly through four molecular mechanisms [13,15].

1. Loss of function: Increased nucleotide repeats suppress gene transcription and inhibit gene expression [12].

2. RNA-mediated gain of function: Anomalous expansion of the repeating region results in the formation of RNA molecules, creating abnormal hairpin structures or circular RNA. These structures interact with RNA-binding proteins, disrupting RNA metabolism and gene expression [12].

3. Protein-level toxic gain of function: Repeat variations in exons lead to the production of proteins with abnormal amino acid repeat numbers [12].

4. Repeat-associated non-AUG translation: In this process, abnormal polypeptides are synthesized from repeating RNAs using non-AUG start codons. These polypeptides accumulate within the cell, disrupting protein homeostasis, organelle functions, and cellular signaling pathways; It leads to cell death in neurons [12].

Studies show that these mechanisms work together to contribute to disease development [13]. For example, in C9orf72-related ALS/FTD, GGGGCC repeat expansion both reduces gene expression and increases RNA accumulation, leading to the retention of RNA-binding proteins. Furthermore, this process activates multiple pathogenic pathways by increasing the production of toxic dipeptide repeats [16,17]. In Huntington's disease, abnormal CAG repeats both disrupt RNA processing and lead to the formation of

toxic abbreviated HTT proteins. In addition, RAN translation can also be observed in these repeat regions [18,19].

2. DETECTION OF STR VARIATIONS

Various methods are used to detect STR variations. With the advancement of technology, the preferred methods are also changing. These methods are shown in Figure 1. The first detection methods were Southern blot analysis and PCR-based methods [20,21]. The Southern blot method has been used for a long time to confirm repeat variations. In this method, DNA is cut with restriction enzymes and a labeled probe is attached to the repeat region. Thus, detailed information about the repeating regions can be obtained as a result of the analysis. Southern blot could detect >250 trinucleotide repeats, but it could not see the breaks within the repeat sequences themselves and was technically time-consuming [22]. In PCR-based methods, the relevant repeat region is amplified and cut, and discontinuous and continuous alleles are obtained by fragment length analysis. However, this method requires prior knowledge of the sequence and is limited when the repeat expansion is very large or when the GC is rich [23]. The limitations of these methods are overcome by technological advancements in PCR techniques and Sanger sequencing. Sanger sequencing can determine approximately 250-300 trinucleotide sequences by estimating repeat lengths [24]. Similarly, sequence variations can be extracted by creating heterogeneous amplified product mixtures with Repeat-Primed PCR (RP-PCR). It is widely used, especially in cases where the number of repeat variations is large and standard PCR results are unsuccessful. One of the primers is designed to bind to the repeat sequence, and the other to bind to the surrounding regions. When repeat expansion occurs, PCR amplifies repeats of different lengths to produce specific products. It indicates the breakpoints in repeat regions by detecting repeat expansions. However, its genotyping is limited to 200 trinucleotides. Therefore, it is generally used as a preliminary screening test; if the desired result is obtained, detailed methods such as Southern blot are used [25]. Optical Genome Mapping (OGM) is used in the analysis of variations larger than 500 base pairs. However, it cannot detect where the break occurs and the base-level location of the repeats [26]. Currently, NGS is used for short reads and LRS for long reads for more sensitive STR analysis [27]. NGS performs comprehensive genome analysis with high throughput. It sequences DNA in small fragments of 100–300 base pairs, and therefore has limitations in disease diagnosis. Because reads may not cover the entire repeat region, this leads to fragmented and incomplete data, making it difficult to accurately identify and size the expansions [28]. Nevertheless, NGS has the ability to read reference and non-reference tandem repeat variations using bioinformatics tools. Long-reading (LRS) technologies can utilize very long read sequences, such as tens of thousands of base pairs, while performing simultaneous methylation analysis and motif decoding. These technologies enable detailed characterization of repeat motifs [29]. Next-generation methods like LRS and NGS are costly and require extensive validation studies. If this is achieved, their use as a standard in STR variation analysis could be ensured [30]. Genome-wide association studies (GWAS) allow for the identification of at-risk loci by comparing STR frequency differences between control and case groups. The development of sequencing technologies has made it possible to directly trace the relationship between repeat variations and diseases [31]. LRS, by directly reading long repeat sequences, allows for the analysis of expansion and methylation in CAG repeats in Huntington's disease. Studies using GWAS have enabled researchers to identify 54 STRs associated with autism spectrum disorder (ASD) [32].

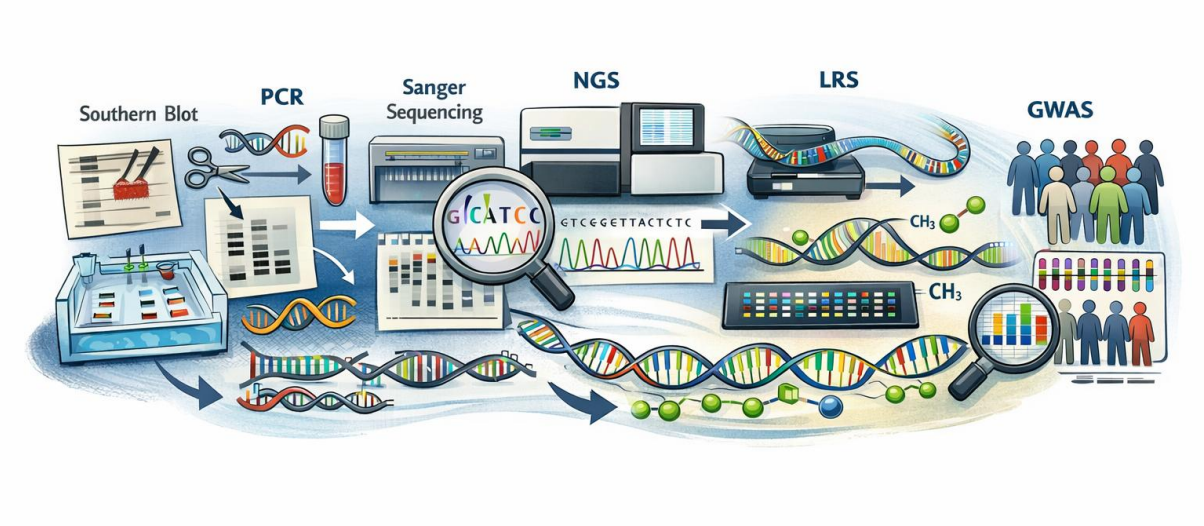


Figure 1. Different Methods Used in Detecting STR Variations.

3. GENETIC CHARACTERISTICS OF REPEAT VARIATIONS

The role of repeat variations in neurobiological diseases is examined below.

3.1. Fragile X Syndrome

The first described repeat expansion disorder is Fragile X Syndrome. This disease is inherited across generations and causes intellectual disability in children. In 1991, using cytogenetic and molecular techniques via Southern blotting, it was observed that the abnormal expansion of the CGG trinucleotide repeat sequence in the 5′ UTR region of the FMR1 gene leads to Fragile X Syndrome. Abnormal repeating regions suppress FMR1 gene transcription through promoter methylation, silencing the gene and leading to neuronal dysfunction [33,34].

3.2. Schizophrenia

A mental illness in which the person interprets reality abnormally and experiences hallucinations. A WGS study on schizophrenia found that repeat variation was significantly higher, particularly in brain expression and postsynaptic genes [35]. Abnormal repeat variations in the introns of the CACNA1C gene are associated with the disease.

3.3. Bipolar Disorder

A psychological illness characterized by abnormal mood, increased energy, accelerated cognitive activity, and increased motor movement. Similar to schizophrenia, it is associated with abnormal repeat variation in the introns of the CACNA1C gene [36].

3.4. Attention Deficit Hyperactivity Disorder (ADHD)

A disorder affecting brain development, characterized by difficulty focusing and excessive hyperactivity starting at a young age. It is associated with abnormal repeat variation in the DAT1 gene [12].

3.5. Depression

A mental illness characterized by low mood, appetite problems, sleep disturbances, fatigue, lack of concentration, and feelings of guilt and suicidal thoughts. It is influenced by genetic and environmental factors. It is particularly associated with abnormal repeat variations in the BDNF gene [12].

3.6. Autism Spectrum Disorder (ASD)

It is a neurodevelopmental disorder characterized by limited and repetitive movements, social and communication deficiencies seen from the first years of life. It is associated with abnormal repeat

variations in the DMPK, FXN, FGF14, and CACNB1 genes. It has also been shown that the CGG trinucleotide repeat may be a contributing factor [12,37].

3.7. Huntington's Disease

It is a mental illness resulting from the gradual breakdown of nerve cells in the brain; symptoms include eye movement abnormalities, involuntary and short-term muscle twitching, tics, and gait disturbances. In 1993, the HTT gene was isolated, and the pathogenicity of Huntington's disease was clarified using Southern blot and PCR techniques. Accordingly, the CAG trinucleotide sequence in the HTT gene is abnormally elongated, leading to a mutation in the huntingtin protein. This protein, with its misfolded conformation, aggregates in neurons, damaging neuronal function [38–40].

3.8. Myotonic Dystrophy Type 1

Myotonic dystrophy, a hereditary muscle disease, also brings with it serious mental disorders. In patients with myotonic dystrophy type 1 (DM1), CTG repeat expansion in the 3′ UTR region of the DMPK gene leads to the transcription of CUG repeat RNA, forming hairpin structures and abnormally binding to RNA-binding proteins. This interaction leads to multiple system dysfunction [41].

4. DISCUSSION-CONCLUSION

Epigenetic mechanisms have revealed the importance of environmental factors and our lifestyle in our genetics. STR regions, previously considered as junk DNA, now explain unknown aspects of DNA, and this explanation is made using next-generation technologies such as NGS and GWAS. Genome-wide studies and next-generation sequencing technologies have made detailed analysis of the entire genome possible. All these studies on STR variations have revealed that these variations cause tandem repeat expansion diseases. In other words, these are not just genome-wide variations, but fundamental structures that constitute the pathogenesis of neuropsychological diseases. This study examines neurobiological diseases caused by repetitive variations. The methods used in the analysis of these variations are constantly being improved with technological advancements. The limitations of the methods used are being overcome with technology. For example, NGS, used in short reads, did not provide sufficient success in longer read sequences. Therefore, long read technologies, which allow for comprehensive analysis in the analysis of complex repeat variations, have begun to be preferred. In analysis methods, the use of disease-specific regions will help to obtain more accurate results. In particular, innovations in sequencing technology and the expansion of STR research have enabled us to gain information about many neurobiological diseases. The importance of STRs and bioinformatics tools in understanding the pathogenesis of neurobiological diseases has thus been understood. Research in this area could contribute to the development of personalized therapeutic agents for the early diagnosis and treatment of related neurobiological diseases, thereby making disease treatment possible and helping to reduce symptoms. It is predicted that in the future, with the standardization of more sensitive and reliable technologies, analytical methods will improve, and studies on the importance of STR variations in neurobiological diseases will become more widespread through in-depth research.

REFERENCES

1. Baccarelli A, Bollati V. Epigenetics and environmental chemicals. *Curr Opin Pediatr*. 2009;21(2):243-251. doi:10.1097/MOP.0b013e32832925cc

2. Bollati V, Baccarelli A, Hou L, et al. Changes in DNA Methylation Patterns in Subjects Exposed to Low-Dose Benzene. *Cancer Res*. 2007;67(3):876-880. doi:10.1158/0008-5472.CAN-06-2995

3. Sarkies P. Molecular mechanisms of epigenetic inheritance: Possible evolutionary implications. *Semin Cell Dev Biol*. 2020;97:106-115. doi:10.1016/j.semcdb.2019.06.005

4. Alegría-Torres JA, Baccarelli A, Bollati V. Epigenetics and Lifestyle. *Epigenomics*. 2011;3(3):267-277. doi:10.2217/epi.11.22

5. Erol D, Elyas Z, Ünal S. Psikiyatrik Hastalıkların Gelişiminde Epigenetik Mekanizmalar. *Klinik Psikofarmakoloji Bülteni-Bulletin of Clinical Psychopharmacology*. 2010;20(1):109-114. doi:10.1080/10177833.2010.11790643

6. Tsankova N, Renthal W, Kumar A, Nestler EJ. Epigenetic regulation in psychiatric disorders. *Nat Rev Neurosci*. 2007;8(5):355-367. doi:10.1038/nrn2132

7. Tomruk C. The four horsemen of neurodegenerative diseases Alzheimer, Parkinson, Huntington and amyotrophic lateral skleroz; clinical definition and experimental models. *Istanbul Bilim University Florence Nightingale Journal of Medicine*. 2018;4(1):37-43. doi:10.5606/fng.btd.2018.006

8. Horton CA, Alexandari AM, Hayes MGB, et al. Short tandem repeats bind transcription factors to tune eukaryotic gene expression. *Science (1979)*. 2023;381(6664). doi:10.1126/science.add1250

9. Zoghbi HY, Orr HT. Glutamine Repeats and Neurodegeneration. *Annu Rev Neurosci*. 2000;23(1):217-247. doi:10.1146/annurev.neuro.23.1.217

10. Hannan AJ. Repeating themes of plastic genes and therapeutic schemes targeting the 'tandem repeatome.' *Brain Commun*. 2024;6(2). doi:10.1093/braincomms/fcae047

11. La Rosa P, Petrillo S, Bertini ES, Piemonte F. Oxidative Stress in DNA Repeat Expansion Disorders: A Focus on NRF2 Signaling Involvement. *Biomolecules*. 2020;10(5):702. doi:10.3390/biom10050702

12. Liu Y, Xia K. Aberrant Short Tandem Repeats: Pathogenicity, Mechanisms, Detection, and Roles in Neuropsychiatric Disorders. *Genes (Basel)*. 2025;16(4):406. doi:10.3390/genes16040406

13. Malik I, Kelley CP, Wang ET, Todd PK. Molecular mechanisms underlying nucleotide repeat expansion disorders. *Nat Rev Mol Cell Biol*. 2021;22(9):589-607. doi:10.1038/s41580-021-00382-6

14. Inserra A, De Gregorio D, Gobbi G. Psychedelics in Psychiatry: Neuroplastic, Immunomodulatory, and Neurotransmitter Mechanisms. *Pharmacol Rev*. 2021;73(1):202-277. doi:10.1124/pharmrev.120.000056

15. Annear DJ, Kooy RF. Unravelling the link between neurodevelopmental disorders and short tandem CGG-repeat expansions. *Emerg Top Life Sci*. 2023;7(3):265-275. doi:10.1042/ETLS20230021

16. Balendra R, Isaacs AM. C9orf72-mediated ALS and FTD: multiple pathways to disease. *Nat Rev Neurol*. 2018;14(9):544-558. doi:10.1038/s41582-018-0047-2

17. Yang S, Du H, Li Y, et al. Advances in the structure design of substrate materials for zinc anode of aqueous zinc ion batteries. *Green Energy & Environment*. 2023;8(6):1531-1552. doi:10.1016/j.gee.2022.08.009

18. Neueder A, Landles C, Ghosh R, et al. The pathogenic exon 1 HTT protein is produced by incomplete splicing in Huntington's disease patients. *Sci Rep*. 2017;7(1):1307. doi:10.1038/s41598-017-01510-z

19. Lieberman AP, Shakkottai VG, Albin RL. Polyglutamine Repeats in Neurodegenerative Diseases. *Annual Review of Pathology: Mechanisms of Disease*. 2019;14(1):1-27. doi:10.1146/annurev-pathmechdis-012418-012857

20. Spector E, Behlmann A, Kronquist K, Rose NC, Lyon E, Reddi H V. Laboratory testing for fragile X, 2021 revision: a technical standard of the American College of Medical Genetics and Genomics (ACMG). *Genetics in Medicine*. 2021;23(5):799-812. doi:10.1038/s41436-021-01115-y

21. Sequeiros J, Martindale J, Seneca S. EMQN Best Practice Guidelines for molecular genetic testing of SCAs. *European Journal of Human Genetics*. 2010;18(11):1173-1176. doi:10.1038/ejhg.2010.8

22. Buchman VL, Cooper-Knock J, Connor-Robson N, et al. Simultaneous and independent detection of C9ORF72 alleles with low and high number of GGGGCC repeats using an optimised protocol of Southern blot hybridisation. *Mol Neurodegener*. 2013;8(1):12. doi:10.1186/1750-1326-8-12

23. Tomé S, Gourdon G. Fast Assays to Detect Interruptions in CTG.CAG Repeat Expansions. In: 2020:11-23. doi:10.1007/978-1-4939-9784-8_2

24. Eren K, Taktakoğlu N, Pirim I. DNA Sequencing Methods: From Past to Present. *Eurasian J Med*. 2022;54(Suppl1):47-56. doi:10.5152/eurasianjmed.2022.22280

25. Chen L, Hadd A, Sah S, et al. An information-rich CGG repeat primed PCR that detects the full range of fragile X expanded alleles and minimizes the need for southern blot analysis. *J Mol Diagn*. 2010;12(5):589-600. doi:10.2353/jmoldx.2010.090227

26. Mantere T, Neveling K, Pebrel-Richard C, et al. Optical genome mapping enables constitutional chromosomal aberration detection. *The American Journal of Human Genetics*. 2021;108(8):1409-1422. doi:10.1016/j.ajhg.2021.05.012

27. Rajan-Babu IS, Dolzhenko E, Eberle MA, Friedman JM. Sequence composition changes in short tandem repeats: heterogeneity, detection, mechanisms and clinical implications. *Nat Rev Genet*. 2024;25(7):476-499. doi:10.1038/s41576-024-00696-z

28. Moon J. Tandem repeat disorders: from diagnosis to emerging therapeutic strategies. *encephalitis*. 2025;5(2):27-35. doi:10.47936/encephalitis.2024.00122

29. Stevanovski I, Chintalaphani SR, Gamaarachchi H, et al. Comprehensive genetic diagnosis of tandem repeat expansion disorders with programmable targeted nanopore sequencing. *Sci Adv*. 2022;8(9). doi:10.1126/sciadv.abm5386

30. Marx V. Method of the year: long-read sequencing. *Nat Methods*. 2023;20(1):6-11. doi:10.1038/s41592-022-01730-w

31. Liu Q, Zhang P, Wang D, Gu W, Wang K. Interrogating the “unsequenceable” genomic trinucleotide repeat disorders by long-read sequencing. *Genome Med*. 2017;9(1):65. doi:10.1186/s13073-017-0456-7

32. Sproviero W, Ghose U, Winchester LM, et al. The impact of Short Tandem Repeats on grey matter brain imaging derived phenotypes in UK Biobank. Preprint posted online March 1, 2023. doi:10.1101/2023.02.27.23286496

33. Hagerman PJ, Hagerman R. Fragile X syndrome. *Current Biology*. 2021;31(6):R273-R275. doi:10.1016/j.cub.2021.01.043

34. Richter JD, Zhao X. The molecular biology of FMRP: new insights into fragile X syndrome. *Nat Rev Neurosci*. 2021;22(4):209-222. doi:10.1038/s41583-021-00432-0

35. Halvorsen M, Huh R, Oskolkov N, et al. Increased burden of ultra-rare structural variants localizing to boundaries of topologically associated domains in schizophrenia. *Nat Commun*. 2020;11(1):1842. doi:10.1038/s41467-020-15707-w

36. Song JHT, Lowe CB, Kingsley DM. Characterization of a Human-Specific Tandem Repeat Associated with Bipolar Disorder and Schizophrenia. *The American Journal of Human Genetics*. 2018;103(3):421-430. doi:10.1016/j.ajhg.2018.07.011

37. Annear DJ, Vandeweyer G, Sanchis-Juan A, Raymond FL, Kooy RF. Non-Mendelian inheritance patterns and extreme deviation rates of CGG repeats in autism. *Genome Res*. 2022;32(11-12):1967-1980. doi:10.1101/gr.277011.122

38. Ross CA, Tabrizi SJ. Huntington's disease: from molecular pathogenesis to clinical treatment. *Lancet Neurol*. 2011;10(1):83-98. doi:10.1016/S1474-4422(10)70245-3

39. Harding RJ, Loppnau P, Ackloo S, et al. Design and characterization of mutant and wildtype huntingtin proteins produced from a toolkit of scalable eukaryotic expression systems. *Journal of Biological Chemistry*. 2019;294(17):6986-7001. doi:10.1074/jbc.RA118.007204

40. Zheng Z, Li A, Holmes BB, Marasa JC, Diamond MI. An N-terminal nuclear export signal regulates trafficking and aggregation of Huntingtin (Htt) protein exon 1. *J Biol Chem*. 2013;288(9):6063-6071. doi:10.1074/jbc.M112.413575

41. Mercuri E, Bönnemann CG, Muntoni F. Muscular dystrophies. *The Lancet*. 2019;394(10213):2025-2038. doi:10.1016/S0140-6736(19)32910-1

ARTIFICIAL INTELLIGENCE'S ADVANCES AND LIMITATIONS IN FORENSIC SCIENCE

Elif Kürkçüoğlu

Istanbul University-Cerrahpasa, Institute of Forensic Sciences and Legal Medicine, Department of Science, İstanbul-Türkiye, ORCID: https://orcid.org/0009-0002-3752-0678

Ömer Karataş

Istanbul University-Cerrahpasa, Institute of Forensic Sciences and Legal Medicine, Department of Science, İstanbul-Türkiye, ORCID: https://orcid.org/0000-0002-1170-7509

Emel Hülya Yükseloğlu

Istanbul University-Cerrahpasa, Institute of Forensic Sciences and Legal Medicine, Department of Science, İstanbul-Türkiye, ORCID: https://orcid.org/0000-0003-2009-6065

ABSTRACT: Crime is the violation of legal values that need to be protected for the maintenance of social order and the negligence shown toward the rules established for this purpose. Forensic science brings together different disciplines in solving crimes. Forensic sciences involve the collaborative work of various disciplines, including forensic medicine, toxicology, genetics, odontology, pathology, and document examination. Artificial intelligence is one of these disciplines; it rapidly analyzes complex data and plays a critical role in investigations. Artificial intelligence refers to systems capable of perceiving and processing environmental data, learning from it, and adapting to new situations. In solving crimes, the use of artificial intelligence helps prevent human error and accelerates the process in various areas such as crime scene investigation, DNA profiling, fingerprint analysis, image analysis, voice analysis, and the interpretation of statistical data. Large data sets are quickly analyzed in areas such profile analysis, kinship link identification, and genetic variation analysis using machine learning and deep learning techniques in DNA analysis, minimizing analyst errors and lowering effort. Nevertheless, it also brings with it ethical and legal responsibilities. This study aims to examine the role of artificial intelligence in evidence analysis and the ethical and legal limits of its use in forensic science.

KEYWORDS: Artificial Intelligence, Crime, Forensic Science, DNA.

1. INTRODUCTION

Forensic science actively participates in every step of the process by examining the crime scene and the suspect, collecting evidence, analyzing the evidence, establishing the relationship between the victim and the perpetrator, and solving the crime. In doing all this, forensic science draws assistance from various disciplines such as forensic informatics, forensic genetics, forensic odontology, and forensic toxicology. Today, the rise of artificial intelligence has also opened the door to many innovations by integrating AI into the field of forensic science.

Artificial intelligence (AI) refers to software systems that perceive and process environmental data, learn through experience, adapt to all possible situations, and have the ability to make decisions, modeling human intelligence [1]. Rather than simply performing programmed functions, it operates similarly to human intelligence and is constantly evolving. It perceives data and develops appropriate responses, possessing a goal-oriented decision-making mechanism. It mimics the thinking, learning, and decision-making abilities of humans. In this respect, it is a preferred interdisciplinary field of science [2,3]. It selects and processes the most efficient information, separating appropriate inputs and making decisions appropriate to the situation. With artificial intelligence, computer systems; Artificial intelligence has the ability to learn, make decisions, and solve problems. Today, artificial intelligence is used in various fields. Its impact is seen in diverse areas such as health, defense, security, education, law, and economics. In recent years, the use of artificial intelligence has also gained importance in the field of forensic science. In forensic science, artificial intelligence, which is involved in stages such as crime scene investigation, evidence analysis, and interpretation of DNA profiles, can be used in the judicial process

by using various algorithms. This allows tasks to be performed faster than by human hands and minimizes the margin of error by preventing human mistakes. The use of artificial intelligence is crucial in forensic science for faster and more accurate judgment. [4]. To understand how artificial intelligence works, it is necessary to understand machine learning, artificial neural networks, and deep learning, which examine data-driven learning processes.

1.1. Machine Learning: This is a system that models the problem based on the available data thanks to its learning ability. By experimenting with different variables in its existing algorithm, it updates the action parameters in a way that increases the efficiency of the model. As a result of the experiments, the optimal model is implemented, and the existing model is updated. This method will enable the use of the most efficient system in the algorithms prepared. [5]. It aims to perform functions such as object detection and natural language translation by automatically creating analytical models. Thus, the system creates models from complex data by programming itself without the need for programming. [6]. While providing ease in models containing large data sets, it enables reliable and repeatable decision-making thanks to what it learns from previous calculations and models. [7].

1.2. Artificial Neural Networks (ANN): It is a model developed by being inspired by the way brain neurons work. It mimics complex processes such as learning, decision-making, and problem-solving. This model, which processes and transmits information, consists of five components. These are; input, input weights, summing function, activation function, and output. The information given to the artificial neuron is defined as input. Input weight is the value that determines the effect on the data. Data weights determine the coefficient of the inputs to be used in the artificial neuron. [8,9]. The input of the artificial neuron is calculated using the summation function, and the result is passed to the activation function. The activation function processes the data from the summation function and creates the system output. This output can be given as input to other layers in the artificial neuron or transmitted to the outside world. Artificial neural networks can be retrained according to changes in the data and can produce solutions by adapting to the conditions. Thus, they can be used in fields such as data recognition, signal processing, and system identification [9,10].

1.3. Deep Learning: This is a system that can process large datasets. It allows for the creation of new datasets by analyzing datasets and obtaining new results. This structure enables understanding and learning from the complexity of data [11]. Data forms the basis of deep learning machine learning. The accessibility of data also contributes to the development of machine learning. The point to be considered in deep learning is that the primary data source must be accurate and reliable. Therefore, the accuracy of the data should always be confirmed and its suitability evaluated [5,12]. In image and sound analysis, which are subject to expertise, deep learning methods are used to enable faster and more accurate analysis of large datasets [9].

2. ARTIFICIAL INTELLIGENCE APPLICATIONS IN FORENSIC SCIENCE

In legal systems, the speed of decision-making and the shortening of the litigation process depend on the diligence and speed of the personnel working on the relevant case. Experts sometimes have a margin of error in their examinations. In today's technological developments, experts involved in forensic sciences can prevent human-induced errors by keeping up with technology and giving importance to the use of artificial intelligence. It is thought that the use of artificial intelligence will revolutionize the field in terms of achieving maximum efficiency in a short time [13]. The most commonly used artificial intelligence applications in forensic science, a multidisciplinary field, and their purposes are explained below.

2.1. Image Analysis: Image analysis allows for the analysis of people and objects by collecting data from video recordings and camera images. At the same time, the analysis of images such as crime scene photographs, video images, obtained radiological images, scars, sexual assault images, bloodstain patterns, and dental X-rays plays a critical role in cases. The fact that these image analyses yield similar results by different experts positively affects the judicial process. Therefore, the use of artificial intelligence should be included in the system to enable objective evaluation [14,15]. Thanks to artificial intelligence algorithms, standard and objective evaluations are made. The accuracy of the evidence

increases, and it emerges as reliable evidence in the judicial process. Thus, information about how the event occurred and the identity of the person can be obtained.

2.2. Voice Analysis: A voice is unique to each individual. It is impossible for different individuals to produce the same sound due to differences in larynx size, vocal tract shape, vocal production organs, and unique speaking styles [16]. Therefore, voice analysis is crucial in identifying the person's identity and the emotional state of the person when the voice was recorded. Voice data recorded at the crime scene or from another source can be used in courts. By comparing all available voice recordings, the identity of the voice, the content of the speech, and the emotional state of the person recording the voice are analyzed, and the number of suspects in the recordings is determined by the expert. An expert opinion is given on whether the recordings belong to the same person or whether different people are involved [17]. Although the subjective nature of the expert opinion helps in solving the case, it will only have a certain contribution. However, when used with artificial intelligence technologies, voice analysis becomes a significant piece of evidence in the judicial process. AI analyzes large files and identifies voices. In forensic science, AI-based voice analysis can be used to identify criminals through voice-based recognition, to understand how an event occurred by examining recorded voice data, and to shorten the process and classify large datasets simultaneously [18,19]. All of this increases the accuracy rate by performing the analysis in a shorter time compared to traditional methods and provides stronger evidence in court. However, the use of artificial intelligence must be regulated and controlled in accordance with ethical principles. Otherwise, instead of increasing the strength of the evidence, it may lead to the evidence being disregarded.

2.3. Text Analysis: By analyzing the words in hand written text, we can obtain information about the content of the text, the emotional state of the person, their identity, and character. In forensic cases, not only the texts written by the suspect but also documents such as autopsy reports, witness statements, and observation reports can be analyzed. Integrating artificial intelligence into this analysis allows for the automatic analysis of large datasets. Thus, by collecting all the data related to the case, it is possible to determine how the event occurred, information about all the evidence collected, and frequently used terms in the collected statements. This also contributes to solving the case [20,21].

2.4. DNA Analysis: DNA analysis enables the identification of biological samples (blood, saliva, semen, teeth, nails, etc.) obtained from the crime scene. DNA profiles are obtained using techniques such as DNA isolation, PCR, and electrophoresis [22]. In courts, DNA profiles are strong evidence. They can determine whether a suspect is convicted or acquitted. Integration of DNA analysis with artificial intelligence accelerates data analysis, shortens the trial process, and allows for more precise results, increasing the strength of the evidence. Electrophoresis showing DNA profiles added to the case file after expert interpretation uses AI-supported algorithms to prevent expert error. It allows for objective interpretation of graphs in a short time [4]. In cases involving mixed samples, forensic DNA analysis helps to understand how many individuals' DNA samples are present and to identify the samples, thus aiding in solving the case. In the electrophoresis obtained from the analysis, the presence of three or more alleles at two or more loci, or a peak greater than the heterozygous peak, indicates the presence of more than one participant in the profile, i.e., mixed DNA. Even with today's advanced technology, limitations can still arise in the analysis of mixed samples. DNA profiling of mixed samples, which relies on expert interpretation, is increasingly being replaced by artificial intelligence software [23,24].

There are several artificial intelligence applications used in DNA analysis. In particular, interpreting DNA profiles based on expert opinion can sometimes lead to errors. Since each expert interprets based on their own experience and expertise, incomplete conclusions can be reached. This is a factor that can mislead the judicial process. The use of artificial intelligence in the interpretation of forensic DNA analyses has facilitated this process. Developed software can reduce human workload, perform all possible interpretations, and complete the process in less time than human labor would. Thus, the interpretation of difficult-to-interpret electrograms will become more precise, and success in the field of identification will increase [25]. Therefore, a new perspective has been brought to forensic science in the interpretation of DNA profiles. Some artificial intelligence software applications used, STRmix and TrueAllele, are discussed.

-STRmix™: This is an STR-based software system developed in 2012 by analysts from Forensic Sciences South Australia (FSSA) and the Environmental Science and Research Institute (ESR). It collects quantitative data such as peak height when interpreting the profile. By examining all possible combinations, it identifies one genotype combination at each locus. It does this using the MCMC algorithm, which assigns an LR value to each possible genotype. For the program to function, parameters such as allele peak height, stutter peak ratio and height, and drop-in must be provided before the analysis[26].When interpreting the DNA profile, the number of participants is determined first based on the number of peaks at the loci. If a sample belonging to the suspect is available, it performs a comparison and calculates the LR. If the suspect is not available, comparisons can be made with samples in the database [27,28].

-TrueAllele: This is probabilistic genotyping software. It uses Bayes' theorem to identify all possible genotypes and calculates the LR. It has been used in forensic cases since 2009. It utilizes the MCMC model. A probability model describing STR data is available. Using the Bayesian model, the probability of the preferred genotype is found from the allele frequency of the population, and the likelihood function compares the combination of all genotypes with the STR model [29,30].

3. ETHICAL AND LEGAL ASPECTS OF USING ARTIFICIAL INTELLIGENCE IN FORENSIC SCIENCE

In forensic science, every analysis must be standardized so that the legal system can recognize the analysis and include the findings as an evidence in the file. Failure to do so compromises procedural compliance and jeopardizes the reliability of the investigation. Therefore, evidence must be verifiable, conform to standards, and have a predictable error rate. Similar criteria are sought in the application of artificial intelligence in forensic science. Studies related to DNA in forensic science, in particular, bring about ethical debates. The creation of a DNA database is paramount. Each country should organize its own DNA database in accordance with ethical and legal principles. The use of a DNA database is of great importance to countries. It facilitates the resolution of crimes and provides benefits in various forensic cases, such as the identification of missing persons. The use of artificial intelligence in forensic science, especially in DNA analysis, will also bring about similar debates.

When integrating the use of artificial intelligence into processes in any field, it should proceed in consultation with experts in the relevant field. In the field of forensic science, support from forensic science experts should be sought to incorporate the use of artificial intelligence in case processes. This is because artificial intelligence cannot make decisions on its own. It needs to be trained and introduced to the relevant program using machine learning. Therefore, there is always a margin of error. Even when the necessary program is created, expert knowledge is still required. Similarly, artificial intelligence can be used in the reporting phase. However, the principle of data confidentiality must be considered, and the basis on which it makes interpretations must be explained. Like an expert, all possible experiences should be recorded in the program, creating an infinite data bank, and the artificial intelligence should draw support from this data in reporting. When creating the data bank, the principle of confidentiality must be prioritized, and there should be no security vulnerabilities. External interference should not be allowed, and once the system is standardized, there should be no further intervention. The system can be updated with technological advancements and research, but this should not be left to the artificial intelligence alone; the system should be established through trials conducted under expert supervision.

There are ongoing debates regarding the ethical appropriateness of using artificial intelligence in forensic science. One of the points raised is the discussion of whether biological data obtained through artificial intelligence was obtained legally. Therefore, for data provided by artificial intelligence to be used in a legal case, it must be defined as legal evidence. Defining data as legally valid requires a detailed understanding of how the AI obtained this data and how it reached its conclusions. For this reason, it is important that AI data used in legal cases is standardized and reproducible. Otherwise, the suspect will have the right to object to the proceedings and invalidate the evidence [31]. In this process, the right to a fair trial must be protected, and the use of artificial intelligence must be done with the individual's knowledge. The individual's rights must be explained, and it must be considered that AI data is open to interpretation and expert opinion. In the legal process, the judge will not be able to find a point of contact

regarding who performed the data analysis and how it was carried out. Another important issue is that the information given to the AI is recorded. Although legal analyses are conducted without discrimination based on race, religion, or language, every sample, even any sample found at the crime scene unrelated to the crime, is recorded in the AI system. Personal rights must be protected in the judicial system, and the process must be explained transparently. For this reason, the data must be explained clearly and simply in a language that everyone can understand. Data analysis must be repeatable and standardized. Consistent results must be obtained in every analysis of the same sample. Only when these conditions are met can the accuracy of the data be trusted and the strength of the evidence be increased. Individuals involved in the forensic case (suspect, victim) should also be informed about how their DNA data was obtained, how and under what conditions it was analyzed, and how it was interpreted, and the process should be conducted transparently [32,33].

4. CONCLUSION

Artificial intelligence minimizes the margin of error by rapidly analyzing large amounts of data compared to traditional methods in evidence analysis and crime investigation. It shortens the crime investigation process and facilitates the investigation. However, there are points to consider in its use. Establishing and standardizing international systems regarding the use of artificial intelligence in forensic science is important for the reliability of evidence and the protection of personal rights. If it is not used in accordance with ethical and legal principles, the usability of evidence in the trial process is affected. If protective algorithms related to ethical regulations are not implemented, unauthorized and misuse of data and violation of personal data may occur, and the validity of the evidence may be questioned. This can lead to a violation of the right to a fair trial. Therefore, the judiciary needs to establish a standard for the use of artificial intelligence and contribute to experts taking a more effective role in the process by supporting the use of artificial intelligence. The use of artificial intelligence in forensic science with human supervision will support judicial processes and contribute to the achievement of justice if ethical rules are observed and the protection of personal data is complied with. This should be taken into account when developing systems to be used in investigations in the future.

5. REFERENCES

1. Russell SJ., Norvig Peter. *Artificial Intelligence*. 3rd ed. Pearson Education; 2009.

2. Kaplan A, Haenlein M. Siri, Siri, in my hand: Who's the fairest in the land? On the interpretations, illustrations, and implications of artificial intelligence. *Bus Horiz*. 2019;62(1):15-25. doi:10.1016/j.bushor.2018.08.004

3. Atalay M, Çelik E. BÜYÜK VERİ ANALİZİNDE YAPAY ZEKÂ VE MAKİNE ÖĞRENMESİ UYGULAMALARI - ARTIFICIAL INTELLIGENCE AND MACHINE LEARNING APPLICATIONS IN BIG DATA ANALYSIS. *Mehmet Akif Ersoy Üniversitesi Sosyal Bilimler Enstitüsü Dergisi*. Published online December 31, 2017:155-172. doi:10.20875/makusobed.309727

4. Görentaş MB, Uçkan T, Ayata F, Dizkırıcı A. Yapay Zeka ve Hukuk İlişkisine Adli Tıp Özelinde Bakış. *Euroasia Matematik, Mühendislik, Doğa Ve Tıp Bilimleri Dergisi Medical Sciences*. 2023;10(28):61-76.

5. Özgür SB. Algoritmalar, Yapay Zeka, Makine Öğrenmesi, Derin Öğrenme ve Uygulamaları: Beşeri Fayda Üretiminin Yazılımlar Tarafından Karşılanması. *Ekonomi ve Yönetim Araştırmaları Dergisi*. 2021;10(1):1-29.

6. Bishop CM. *Pattern Recognition and Machine Learning*. Springer Science + Business Media; 2009.

7. Goodfellow Ian, Bengio Yoshua, Courville Aaron. *Deep Learning*. The MIT Press; 2017.

8. Arıkan Kargı VSinem. *Yapay Sinir Ağ Modelleri ve Bir Tekstil Firmasında Uygulama*. Hiperlink; 2015.

9. İşcan H, Durgun A. Yapay Zekâ: Alt Dalları ve Uygulama Alanları. *Aksaray Üniversitesi İktisadi ve İdari Bilimler Fakültesi Dergisi*. 2024;16(4):201-234. doi:10.52791/aksarayiibd.1574207

10.Simpson PK. *Artificial Neural Systems : Foundations, Paradigms, Applications, and Implementations*. Pergamon Press; 1990.

11.Bengio Y. Learning Deep Architectures for AI. *Foundations and Trends® in Machine Learning*. 2009;2(1):1-127. doi:10.1561/2200000006

12.Ayyüce Kızrak M, Bolat B. Derin Öğrenme ile Kalabalık Analizi Üzerine Detaylı Bir Araştırma. *Bilişim Teknolojileri Dergisi*. 2018;11(3):263-286. doi:10.17671/gazibtd.419205

13.Chinnikatti SK. Artificial Intelligence in Forensic Science. *Forensic Sci Addict Res*. 2018;2(5). doi:10.31031/FSAR.2018.03.000554

14.Jain AK, Ross A. Bridging the gap: from biometrics to forensics. *Philos Trans R Soc Lond B Biol Sci*. 2015;370(1674). doi:10.1098/rstb.2014.0254

15.Mena J. *Machine Learning Forensics for Law Enforcement, Security, and Intelligence*. Auerbach Publications; 2016. doi:10.1201/b11026

16.Kinnunen T, Li H. An overview of text-independent speaker recognition: From features to supervectors. *Speech Commun*. 2010;52(1):12-40. doi:10.1016/j.specom.2009.08.009

17.Morrison GS, Zhang C. Forensic Voice Comparison: Overview. In: *Encyclopedia of Forensic Sciences, Third Edition*. Elsevier; 2023:737-750. doi:10.1016/B978-0-12-823677-2.00130-6

18.Suppa A, Asci F, Saggio G, et al. Voice Analysis with Machine Learning: One Step Closer to an Objective Diagnosis of Essential Tremor. *Movement Disorders*. 2021;36(6):1401-1410. doi:10.1002/mds.28508

19.Asci F, Costantini G, Di Leo P, et al. Machine-Learning Analysis of Voice Samples Recorded through Smartphones: The Combined Effect of Ageing and Gender. *Sensors*. 2020;20(18):5022. doi:10.3390/s20185022

20.Yu CH, Ward MW, Morabito M, Ding W. Crime Forecasting Using Data Mining Techniques. In: *2011 IEEE 11th International Conference on Data Mining Workshops*. IEEE; 2011:779-786. doi:10.1109/ICDMW.2011.56

21.Mujtaba G, Shuib L, Raj RG, Rajandram R, Shaikh K. Automatic Text Classification of ICD-10 Related CoD from Complex and Free Text Forensic Autopsy Reports. In: *2016 15th IEEE International Conference on Machine Learning and Applications (ICMLA)*. IEEE; 2016:1055-1058. doi:10.1109/ICMLA.2016.0191

22.Burns MA, Johnson BN, Brahmasandra SN, et al. An Integrated Nanoliter DNA Analysis Device. *Science (1979)*. 1998;282(5388):484-487. doi:10.1126/science.282.5388.484

23.Bieber FR, Buckleton JS, Budowle B, Butler JM, Coble MD. Evaluation of forensic DNA mixture evidence: protocol for evaluation, interpretation, and statistical calculations using the combined probability of inclusion. *BMC Genet*. 2016;17(1):125. doi:10.1186/s12863-016-0429-7

24.Tao R, Wang S, Zhang J, et al. Separation/extraction, detection, and interpretation of DNA mixtures in forensic science (review). *Int J Legal Med*. 2018;132(5):1247-1261. doi:10.1007/s00414-018-1862-0

25.Perlin MW, Legler MM, Spencer CE, et al. Validating TrueAllele DNA mixture interpretation. *J Forensic Sci*. 2011;56(6):1430-1447. doi:10.1111/j.1556-4029.2011.01859.x

26.Bright JA, Taylor D, McGovern C, et al. Developmental validation of STRmix™, expert software for the interpretation of forensic DNA profiles. *Forensic Sci Int Genet*. 2016;23:226-239. doi:10.1016/j.fsigen.2016.05.007

27.Bright JA, Taylor D, Curran J, Buckleton J. Searching mixed DNA profiles directly against profile databases. *Forensic Sci Int Genet*. 2014;9:102-110. doi:10.1016/j.fsigen.2013.12.001

28.Russell L, Cooper S, Wivell R, et al. A guide to results and diagnostics within a STRmix™ report. *WIREs Forensic Science*. 2019;1(6). doi:10.1002/wfs2.1354

29.Perlin MW. When Good DNA Goes Bad. *Journal of Forensic Research*. 2012;04(01). doi:10.4172/2157-7145.S11-003

30.Bauer DW, Butt N, Hornyak JM, Perlin MW. Validating TrueAllele Interpretation of DNA Mixtures Containing up to Ten Unknown Contributors. *J Forensic Sci*. 2020;65(2):380-398. doi:10.1111/1556-4029.14204

31.Thao NP. The Use of Artificial Intelligence in Criminal Investigation and Trials in Europe and Some Countries: Experience for Vietnam. *Vietnamese Journal of Legal Sciences*. 2023;8(1):55-77. doi:10.2478/vjls-2023-0003

32.Perlin MW. Forensic Sciences. In: *Forensic Sciences*. 2021.

33.Sapan Oğuzhan. *Ceza Muhakemesinde Yapay Zekâ Kullanımı*. Adalet Yayınevi; 2024.

A NURSING PRACTICE FRAMEWORK FOR SEPTIC SHOCK: FROM EARLY RECOGNITION TO CONTINUITY OF CARE BASED ON EVIDENCE-BASED GUIDELINES

Ali Hakan GÜNAYDIN

Giresun University, Faculty of Health Sciences, Department of Surgical Nursing, ORCID ID: 0009-0007-0479-1187

Öykü SARAYDEMİR

Giresun University, Şebinkarahisar Health Services Vocational School, Department of Emergency and First Aid, ORCID ID: 0009-0000-5463-2490

Yeşim YAMAN AKTAŞ

Giresun University, Faculty of Health Sciences, Department of Surgical Nursing, ORCID ID: 0000-0001-7403-4949

ABSTRACT

Objective: This review aims to evaluate nursing care in septic shock in light of current evidence-based guidelines and to present a nursing practice framework structured from early recognition to continuity of care.

Materials and Methods: This narrative review was structured through a targeted review of current adult sepsis and shock guidelines and nursing-focused literature. Core sources included the Surviving Sepsis Campaign 2021 and 2026 guidelines, the ESICM 2025 circulatory shock and hemodynamic monitoring guideline, and peer-reviewed publications mainly from 2021 to 2026, including systematic reviews, scoping reviews, narrative reviews, multicenter or cross-sectional studies, and nurse-led quality improvement reports. Sources were selected when they addressed adult sepsis or septic shock care, early recognition, screening tools, resuscitation and perfusion monitoring, antimicrobial therapy and source control, nursing competence, or continuity of care.

Findings: In septic shock, the nursing role extends beyond task execution and includes early recognition of clinical deterioration, initiation of rapid response processes, dynamic evaluation of resuscitation response, and escalation of care. Screening tools such as NEWS2, MEWS, and SIRS gain clinical relevance only when integrated with continuous bedside assessment. Fluid responsiveness and vasopressor therapy should be guided not only by hemodynamic targets but also by tissue perfusion indicators. Evidence indicates that nursing competence can be improved through education, simulation-based training, and decision-support systems, while continuity of care significantly influences patient outcomes.

Conclusion: Nursing care in septic shock represents a strategic process that translates guideline recommendations into bedside clinical decision-making. Nursing competence and system-level standardization play a critical role in improving patient safety and clinical outcomes.

Keywords: Septic shock; nursing care; early recognition; tissue perfusion; evidence-based practice

INTRODUCTION

Septic shock is one of the most severe clinical forms of sepsis and is characterized by persistent hypotension, the need for vasopressor support, elevated serum lactate levels, and marked tissue perfusion impairment.[1] According to Global Burden of Disease 2017 estimates, sepsis is a major public health problem associated with approximately 48.9 million cases and 11.0 million sepsis-related deaths worldwide; septic shock constitutes one of the subgroups with the highest mortality within this burden.[2] Defined by ongoing vasopressor requirement and elevated lactate despite adequate fluid resuscitation, septic shock is a time-critical condition involving profound circulatory, cellular, and metabolic

derangements and, when not recognized early, may progress to multiple organ dysfunction and high mortality.[1]

The pathophysiological basis of septic shock is the dysregulated host response to infection, which disrupts circulatory integrity and results in inadequate tissue perfusion.[1] Increased release of proinflammatory mediators and nitric oxide leads to systemic vasodilation and reduced vascular tone, while endothelial injury and increased capillary permeability cause intravascular fluid to shift into the extravascular compartment, reducing effective circulating volume.[1] Concurrent microcirculatory flow disturbances and dysregulation of the coagulation system further contribute to heterogeneous organ perfusion.[1] Consequently, even when macrocirculatory blood flow is not completely interrupted, the balance between oxygen delivery and cellular utilization is impaired, tissue hypoxia deepens, and organ dysfunction develops.[1] Clinically, this process may manifest as impaired peripheral perfusion, oliguria, elevated lactate, altered mental status, and multiple organ failure.[1]

This clinical and pathophysiological profile makes the nursing role critical in septic shock management.[3,4] Current sepsis literature and nursing-focused studies indicate that the nurse's role is not limited to implementing prescribed treatment; it also includes recognizing early clinical deterioration, accelerating first-hour interventions, safely monitoring resuscitation and perfusion response, coordinating infection control and organ function monitoring, and ensuring continuity of care.[3,4]

Rather than merely summarizing current guideline recommendations, this practice-oriented narrative review discusses how these recommendations are translated into bedside nursing decisions, prioritization processes, and interprofessional team coordination. The text is structured around four decision domains: early recognition and clinical assessment; first-hour management and perfusion-oriented resuscitation; infection control, organ monitoring, and supportive care; and standardization of care, nursing competence, and continuity of care.

Scope and source selection

This study was not designed as a systematic review; it was conducted as a narrative review based on targeted source selection. The literature framework was developed through searches of PubMed/MEDLINE, CINAHL, Google Scholar, and relevant guideline organization websites. The search terms included sepsis, septic shock, nursing care, early recognition, NEWS2, qSOFA, fluid responsiveness, vasopressor, antimicrobial stewardship, handoff, post-sepsis care, and continuity of care. Priority was given to publications from 2021 to 2026; however, the core epidemiological study defining the global sepsis burden was included despite falling outside this range. Pediatric sepsis studies, opinion papers not directly contributing to nursing care or bedside decision-making, and publications with limited relevance to adult septic shock management were excluded.

DEVELOPMENT

Conceptual model of the review

This review structures nursing care in septic shock around four interrelated decision domains: early recognition and clinical assessment; first-hour management and perfusion-oriented resuscitation; infection control and organ monitoring; and standardization and continuity of care. The proposed conceptual model aims to show not only the guideline recommendations themselves but also how these recommendations become integrated with bedside clinical reasoning, prioritization decisions, and interprofessional coordination. From this perspective, septic shock care is not a linear set of independent steps; it is a holistic care process in which each decision domain dynamically affects the others through continuous feedback mechanisms.

Figure 1. Nursing Practice Framework for Septic Shock

1. Early recognition and clinical assessment	2. First-hour management and perfusion-oriented resuscitation	3. Infection control, organ monitoring, and supportive care	4. Standardization, competence, and continuity of care

Recognizing deterioration, interpreting screening scores together with clinical signs, and escalating care	Lactate measurement, blood cultures, antimicrobial therapy, fluid and vasopressor safety, and dynamic response monitoring	Source control, antimicrobial safety, and early recognition of organ dysfunction	Protocol adherence, education and simulation, handoff, patient-family education, and follow-up planning

The model should be interpreted not as a linear task list but as a cyclic decision framework connected by serial reassessment, interprofessional communication, and escalation of care.

Early recognition and clinical assessment

Septic shock is often recognized not through a single monitor alarm but through the convergence of small yet meaningful changes in the patient's clinical condition.[5] Compared with previous observations, new tachypnea, agitation or lethargy, peripheral coldness, mottled skin, prolonged capillary refill time, reduced urine output, and deterioration in overall clinical appearance may indicate evolving tissue hypoperfusion.[1,5] Therefore, nursing assessment is not limited to recording body temperature, blood pressure, pulse rate, and respiratory rate.[4,5] It also involves identifying patterns of change relative to the patient's baseline condition, interpreting these changes in the context of infection, and reporting potential deterioration to the health care team without delay.[4,5] Current guidance considers sepsis and septic shock medical emergencies.[1] Careful assessment of peripheral perfusion, mental status, and overall clinical appearance therefore forms the basis for critical bedside decisions.[1,5]

To make clinical suspicion more systematic, assessment tools such as qSOFA, NEWS/NEWS2, MEWS, and SIRS are used.[6,7] These tools gather parameters such as respiratory rate, systolic blood pressure, level of consciousness, and body temperature within a standardized framework and support early recognition of high-risk patients and timely escalation of care.[7] However, according to current guidance, qSOFA should not be used as a standalone screening tool; rather, it should be considered a practical warning tool for rapidly identifying patients at risk of poor clinical outcomes.[1,6,7] The SOFA score is primarily used to determine the degree of infection-related organ dysfunction and illness severity.[6] The Surviving Sepsis Campaign (SSC) 2021 guideline did not recommend qSOFA as a single screening tool compared with SIRS, NEWS, or MEWS.[6] The SSC 2026 update strongly emphasizes that NEWS/NEWS2, MEWS, or SIRS should be preferred over qSOFA as a single tool for screening acutely ill in-hospital patients.[1] Because sepsis cannot be ruled in or ruled out by a single biomarker or test, screening scores gain meaning only when combined with clinical assessment.[1,7]

In this context, NEWS2 stands out as a practical and standardized assessment tool that supports early recognition of acute clinical deterioration.[8] By combining respiratory, circulatory, oxygenation, consciousness, and temperature parameters into a single scoring system, NEWS2 enables objective and comparable monitoring of patient change.[8] Nevertheless, the primary purpose of NEWS2 is not to establish a diagnosis; it is to identify high-risk patients early and accelerate clinical assessment and escalation of care.[8] Table 1 summarizes the core parameters and scoring system of NEWS2.[8]

This early assessment and screening process forms the basis for nurses' bedside decisions regarding monitoring, acceleration of care, and escalation of the clinical process.[4,5] Key decisions include not interpreting subtle clinical changes in high-risk patients as "expected," actively considering sepsis in the differential diagnosis, increasing monitoring frequency, reassessing hourly urine output and peripheral perfusion serially, interpreting new changes in mental status as potential indicators of clinical deterioration, and requesting higher-level clinical evaluation without delay in patients with positive screening findings.[1,4,5] Current guidelines and nursing literature show that screening tools such as NEWS/NEWS2, MEWS, or SIRS gain relevance only when accompanied by serial assessment of clinical status, including capillary refill, peripheral temperature, mental status, and overall clinical appearance.[1,6,7] In this respect, reduced urine output, prolonged capillary refill, and acute confusion are not merely data to be documented; they are clinical thresholds for accelerating care, activating rapid response systems, and transitioning to an appropriate level of care.[1,5] Scoping reviews examining nursing roles indicate that nurses' most prominent contribution in sepsis care is concentrated in recognizing early

clinical deterioration, translating it into clinical risk, and escalating the care process in a timely manner.[4,5,7]

Table 1. NEWS2 Score Parameters

Parameter	0 points	1 point	2 points	3 points
Respiratory rate (/min)	12-20	9-11	21-24	≤8 or ≥25
SpO_2 (%)	≥96	94-95	92-93	≤91
Supplemental oxygen use	Room air	—	Receiving oxygen	—
Systolic blood pressure (mmHg)	111-219	101-110	91-100	≤90 or ≥220
Pulse rate (/min)	51-90	41-50 or 91-110	111-130	≤40 or ≥131
Level of consciousness	Alert	—	—	Acute confusion / Voice / Pain / Unresponsive
Body temperature (°C)	36.1-38.0	35.1-36.0 or 38.1-39.0	≥39.1	≤35.0

The total NEWS2 score is obtained by summing parameter scores. Scores of 0-4 are associated with low risk, a score of 3 in a single parameter with low-to-medium risk, 5-6 with medium risk, and ≥7 with high risk.[8]

First-hour management and perfusion-oriented resuscitation

In septic shock, the first hour is a critical period during which timely and appropriate interventions directly influence clinical outcomes.[1] At this stage, the nurse's primary responsibility is to report suspected sepsis to the health care team without delay, ensure that initial interventions are carried out in a coordinated manner, and prevent delays in the care process.[3,9] The "code sepsis" and "sepsis huddle" approaches described in the SSC 2026 guideline serve this purpose by directing the multidisciplinary team toward rapid and shared evaluation when risk is recognized.[1] In the literature, standard operating procedures integrated with sepsis screening, accelerated team response after positive screening, and monitoring of these processes through quality improvement programs are described as effective institutional practices.[9,10] Therefore, first-hour management should be viewed as an integrated care domain that includes both the nurse's clinical awareness and institutional rapid response systems.[3,9,10] This process is not limited to initiating first interventions; it also includes moving the patient to a higher level of care according to clinical response.[1] Persistent hypotension, elevated serum lactate, worsening mental status, reduced urine output, and increasing oxygen requirement should suggest the need for closer monitoring, detailed evaluation, and, when necessary, ICU-level care.[1,5]

Nursing interventions within the first hour include organizing serum lactate measurement, blood culture collection, safe vascular access, preparation and administration of broad-spectrum antimicrobial therapy, initiation of crystalloid resuscitation, and hourly urine output monitoring.[1,3] The critical issue is not performing these tasks separately but carrying them out simultaneously, without delay, and with appropriate prioritization.[3] Current guidelines recommend early lactate measurement in possible sepsis and septic shock, collection of blood cultures as soon as possible and ideally before antimicrobial therapy, initiation of antimicrobial therapy within the first hour in septic shock, and avoidance of delay

in initial fluid resuscitation.[1] In this context, the timing between culture collection and antimicrobial initiation is directly related to the nurse's prioritization, organization, and team coordination skills.[3,9] Standard order sets, sepsis checklists, ready access to antimicrobials, rapid laboratory or point-of-care lactate measurement systems, and sepsis champions are also important structural components that support first-hour care and facilitate timely and safe execution of the process.[1,9] Nurse-driven rapid response protocols have been reported to shorten time to antimicrobial initiation, improve care standardization, and increase bundle compliance.[9] In this respect, first-hour management is not only a clinical decision domain but also an important indicator of health care organization and process quality. Time to antimicrobial initiation, time to initial lactate measurement, bundle compliance rate, and time to escalation of care are key monitoring outcomes of this process.[1,9]

The primary aim of resuscitation in septic shock is not merely to increase arterial pressure but to restore tissue perfusion.[1] The SSC 2026 guideline defines sepsis and septic shock as medical emergencies and emphasizes, as a good practice statement, that treatment and resuscitation should begin immediately.[1] Crystalloids are recommended as the first-line resuscitation fluid, and in sepsis-induced hypoperfusion or septic shock, initial fluid resuscitation should not be delayed; subsequent fluid management should be reassessed according to the patient's clinical response.[1,6] Therefore, the central focus in nursing care is not the amount of fluid administered alone but dynamic monitoring of the patient's response to resuscitation.[1,6,11]

Fluid responsiveness cannot be evaluated through a single parameter.[1,11] Capillary refill time, peripheral temperature, mottled skin, mental status, urine output, lactate trend, and lung auscultation findings should be interpreted together.[1,11] Even if arterial blood pressure reaches the normal range, resuscitation cannot be considered adequate when oliguria, confusion, or peripheral hypoperfusion persists.[1,11] Conversely, increased work of breathing, crackles, peripheral edema, and increasing oxygen requirement should raise concern for fluid overload.[11] Current guidance supports directing fluid therapy through dynamic assessment, using capillary refill time as an adjunctive perfusion indicator, and monitoring lactate trends through serial measurements.[1,6] Preference for balanced crystalloids and avoidance of starch-based solutions (hydroxyethyl starch solutions) are also important elements that directly affect nursing decisions in fluid management.[1,11]

The nursing role in vasopressor therapy is not limited to starting the infusion and adjusting infusion pump settings.[12] Although norepinephrine is the first-line agent, safe maintenance of titration, monitoring for dysrhythmias, assessment of peripheral perfusion, and holistic follow-up of organ response are central to care.[1,12] The current evidence-based approach recommends an initial mean arterial pressure (MAP) target of 65 mmHg for most patients and a 60-65 mmHg range for older adults and patients with comorbidities.[1,6] In nursing practice, this approach requires not only achieving the target pressure but also continuously evaluating its clinical correlates, including urine output, mental status, lactate trend, and peripheral perfusion findings.[3,12]

Starting vasopressors through a peripheral venous catheter without waiting for central venous access has become an important practice intended to prevent treatment delays.[1] However, this approach should be implemented together with appropriate vascular access selection, infusion line safety, frequent extravasation monitoring, and local protocols for managing complications.[1,3] Adding vasopressin when norepinephrine requirements increase is also among current recommendations.[1,6] The European Society of Intensive Care Medicine (ESICM) 2025 guideline on circulatory shock emphasizes the importance not only of arterial pressure targets but also of serial tissue perfusion assessment and advanced hemodynamic monitoring in patients with inadequate treatment response.[13] Hemodynamic monitoring should therefore be considered not merely as recording monitor data but as a holistic assessment of the patient's perfusion status together with clinical findings.[13]

Infection control, organ monitoring, and supportive care

After first-hour management, the focus of care shifts to evaluating whether the infection has been controlled and whether the initiated treatment is being maintained appropriately for the patient.[1] At this stage, the nurse's role includes not only administering antimicrobial therapy but also systematically monitoring clinical response, ensuring medication safety, and contributing to daily treatment reassessment.[3] Current guidelines recommend prolonged infusion of beta-lactam antibiotics after a

loading dose in eligible patients and antimicrobial de-escalation when microbiological data become available.[1] Therefore, the nurse's role in this process is not only to administer treatment but also to continuously evaluate its effectiveness and safety at the bedside.[3]

Source control is a key step that complements antimicrobial therapy.[1] When source control requires removal of an infected catheter, interventional procedures such as abscess drainage, or surgery, the nurse assumes critical responsibilities related to patient preparation, interprofessional coordination, pre- and post-procedure monitoring, and safe patient transfer.[3] When a clear anatomical source of infection is present, the need for source control should be evaluated rapidly and an appropriate intervention should be planned without delay.[1] Clinically, persistent fever, increasing vasopressor requirement, failure of lactate levels to decrease, or progression of organ dysfunction are important warning signs requiring reassessment for an ongoing infectious focus or inadequate source control.[1] Serial clinical observation data generated by nurses therefore constitute one of the main bases for decisions questioning the adequacy of treatment response.[3,4]

Nursing assessment becomes even more visible in maintaining organ function and delivering supportive care.[3] Reduced urine output, increased work of breathing and oxygen requirement, acute confusion or agitation, and glycemic instability are among the early clinical indicators of organ dysfunction in septic shock.[1] Therefore, the nurse's central responsibility is to recognize organ dysfunction early, systematically monitor responses to treatment, and report clinical deterioration to the health care team in a timely manner.[3,4] Current recommendations support initiating insulin therapy according to medical orders when blood glucose reaches ≥180 mg/dL, continuing venous thromboembolism prophylaxis when no contraindication exists, and assessing early enteral nutrition in appropriate patients.[1,6] Within this framework, hourly urine output monitoring, regular mental status assessment, close follow-up of respiratory parameters and oxygen requirement, glycemic monitoring, safety monitoring for medication adverse effects and bleeding risk, and clear communication with the patient and family constitute core nursing components of supportive care.[3,4] Nurses play a central role especially in recognizing clinical deterioration early, interpreting response to treatment, and communicating clinical information to the team to redirect care.[3,4,12]

Standardization of care, nursing competence, and continuity

The translation of guideline recommendations into patient outcomes in sepsis care depends not only on correct clinical decisions but also on their standard, timely, and consistent implementation within the institution.[1,14] Therefore, sustainability of sepsis care is closely related to accessible protocols, clear workflows, and regular quality improvement processes.[14] For the evidence-based practices presented in Table 2 to be implemented safely at the bedside, sepsis screening should be integrated into routine clinical workflow, care steps should be clearly defined, and implementation outcomes should be monitored regularly.[1,14] Current literature shows that audit-feedback cycles, performance monitoring, and institutional leadership support strengthen standardization and continuity in sepsis care.[14] In this context, a protocol-based approach should not be viewed as a bureaucratic structure replacing clinical judgment but as a core infrastructure that systematically transfers evidence-based care into daily clinical practice.[14]

The bedside counterpart of this infrastructure is nursing competence. In sepsis care, knowledge alone is not sufficient; the ability to recognize early clinical deterioration, determine clinical priorities, communicate effectively within the team, and make appropriate decisions under time pressure is at least as important as knowledge level.[15-17] Systematic reviews and multicenter studies indicate that nurses' sepsis knowledge, clinical confidence, and clinical reasoning can be improved through education, experience, simulation-based learning, and decision-support systems.[15-17] Therefore, education processes should not remain limited to in-service information sessions; they should become measurable clinical competence enabling the evidence-based recommendations summarized in Table 2 to be implemented safely, consistently, and promptly at the bedside.[3,15-17] Indicators such as knowledge level, clinical confidence, time to response after a sepsis alert, accuracy of critical decisions, and bundle compliance rate may be used to evaluate this competence.[15-17] Through this approach, education becomes not a periodic activity but a structural component that directly determines care quality.[15-17]

The sustainability of sepsis care does not end when the acute phase resolves; safe care transitions and monitoring of the post-sepsis period are integral to this approach.[1,6,12] Current guidelines identify structured handoff processes, medication reconciliation, written and verbal education for patients and families, systematic follow-up for physical, cognitive, and emotional problems, and referral to rehabilitation or mental health support when needed as core components of continuity of care.[1,6] From the nursing perspective, this process is not limited to providing information before discharge. It also means making visible the risks with which the patient moves to the next level of care, ensuring complete transfer of critical clinical information, and structuring information flow to reduce readmission risk.[1,6,12] Therefore, sepsis nursing should be considered not only as a role focused on managing acute deterioration but also as a holistic and continuity-oriented field of practice that supports recovery and safeguards care continuity.[3,4,12]

Table 2. Evidence-Based Nursing Interventions and Practice Recommendations in Septic Shock

Theme	Evidence-based practice	Strength of recommendation	Nursing implication
Early recognition	Performance improvement program including sepsis screening, standard operating procedures, and quality improvement strategies	Strong	Supports early recognition, standardized care flow, and bundle compliance.
Early recognition	Code sepsis or sepsis huddle protocol	Weak / conditional	Accelerates team coordination and escalation after a positive screen.
Early recognition	Prefer NEWS/NEWS2, MEWS, or SIRS over qSOFA for screening acutely ill patients	Strong	Makes high-risk patients visible earlier and supports early recognition of deterioration.
Early recognition	Collect blood cultures as soon as possible and ideally before antimicrobial therapy	Strong	Highlights the nurse's responsibility to balance culture collection and antimicrobial timing without delaying care.
Early recognition	Measure blood lactate	Weak / conditional	Makes hypoperfusion visible earlier and contributes to reassessment.
First hour	Start treatment and resuscitation immediately in sepsis and septic shock	Good practice statement	Reduces "wait-and-see" behavior and establishes a clinical threshold for accelerating care.
First hour	Initiate antimicrobial therapy ideally within 1 hour in septic shock and in probable or definite sepsis	Strong	Prioritizes time management and medication access in first-hour care.

Theme	Evidence-based practice	Strength of recommendation	Nursing implication
First hour	In possible sepsis without shock, initiate antimicrobial therapy within 3 hours if concern for infection persists after rapid assessment	Weak / conditional	Supports the balance between differential diagnosis and avoiding unnecessary delay.
Infection control	Rapidly evaluate anatomical foci requiring urgent source control	Good practice statement	Supports timely coordination of catheter removal, drainage, or surgical preparation.
Infection control	Administer beta-lactams as prolonged infusion after a loading dose	Strong	Emphasizes infusion safety, pump management, and vascular access monitoring.
Infection control	De-escalate antimicrobial therapy when microbiological diagnosis and susceptibility results are available	Strong	Reduces unnecessary broad-spectrum use and supports daily treatment review.
Infection control	Prefer shorter antimicrobial treatment durations when adequate source control has been achieved	Weak / conditional	Important for daily treatment reassessment and prevention of unnecessary prolongation.
Resuscitation	Use crystalloids as first-line fluid for resuscitation	Strong	Standardizes the initial nursing decision regarding fluid type.
Resuscitation	Prefer balanced crystalloids over 0.9% saline	Weak / conditional	Supports more deliberate fluid selection according to patient characteristics.
Resuscitation	Avoid starch-based solutions (hydroxyethyl starch solutions)	Strong	Clarifies products to avoid in safe fluid administration.
Resuscitation	Administer at least 30 mL/kg IV crystalloid within the first 3 hours in sepsis-induced hypoperfusion or septic shock	Weak / conditional	Prevents delay in initial fluid resuscitation but requires frequent reassessment.
Resuscitation	Guide fluid responsiveness using dynamic measures	Weak / conditional	Reduces reliance on static values alone through measures such as passive leg raise, SVV, or PPV.

Theme	Evidence-based practice	Strength of recommendation	Nursing implication
Resuscitation	Use serial lactate monitoring and capillary refill time as adjunctive perfusion indicators	Weak / conditional	Supports bedside reassessment of perfusion.
Hemodynamic monitoring	Use an initial MAP target of 65 mmHg	Strong	Provides a shared clinical target for vasopressor titration.
Hemodynamic monitoring	Individualize the initial MAP range as 60-65 mmHg in patients aged 65 years or older	Weak / conditional	Helps avoid excessive vasopressor exposure while maintaining adequate perfusion in older adults.
Hemodynamic monitoring	Start vasopressors peripherally rather than delaying until central access is secured	Weak / conditional	Reduces treatment delay and requires extravasation monitoring and vascular access safety.
Hemodynamic monitoring	Use norepinephrine as the first-line vasopressor; add vasopressin when requirements increase	Strong / conditional	Clarifies the nursing role in titration, rhythm monitoring, and multi-vasopressor management.
Organ support	Initiate insulin therapy when glucose is ≥180 mg/dL	Strong	Requires frequent glucose monitoring and hypoglycemia prevention.
Organ support	Use pharmacological VTE prophylaxis and prefer low-molecular-weight heparin over unfractionated heparin	Strong	Strengthens thromboembolism prevention together with bleeding-risk monitoring and mobilization.
Organ support	Initiate enteral nutrition within the first 72 hours in appropriate patients	Weak / conditional	Emphasizes nutrition tolerance, aspiration risk, and gastrointestinal monitoring.
Continuity of care	Use structured handoff to transfer critical information during care transitions	Weak / conditional	Reduces information loss during ICU-ward-discharge transitions.
Continuity of care	Provide written and verbal sepsis education to patients and families	Weak / conditional	Raises awareness of post-sepsis syndrome, symptoms requiring reassessment, and treatment continuity.

Theme	Evidence-based practice	Strength of recommendation	Nursing implication
Continuity of care	Plan post-critical illness follow-up, physical rehabilitation, and mental health support	Weak / conditional / good practice statement	Makes physical, cognitive, and emotional problems visible after discharge.

The strength of recommendation in Table 2 was summarized based on SSC 2026, SSC 2021, and ESICM 2025.[1,6,13] *Practice implications were supported by nursing-focused sepsis literature.*[3,4,14,15]

CONCLUSION

The value of nursing care in septic shock lies not merely in listing guideline recommendations but in the capacity to translate these recommendations into timely, safe, and holistic clinical decisions at the bedside.[1,3,4] The conceptual model presented in this review demonstrates that the nursing contribution is not limited to isolated interventions; rather, it constitutes a dynamic decision domain that extends across clinical vigilance in early recognition, coordinated first-hour care management, serial evaluation of perfusion and organ response, safe execution of infection control, and structured care transitions.[3,4,12] Therefore, the priority is not only to memorize guideline recommendations but to integrate them into standardized workflows, transform them into measurable nursing competencies, support them through safe team communication, and reflect them in patient outcomes through structured care transitions.[1,3,12]

From a clinical practice perspective, this framework shows that the nursing approach in septic shock is not merely a supportive role that implements treatment; it is a strategic clinical component that directly affects care quality and patient safety.[3,4,12] Future studies should examine more systematically the clinical outcome effects of nurse-initiated protocol-based practices, formal education and competence models, and post-sepsis continuity of care. Such work would strengthen both the visibility and measurability of nursing contributions in septic shock care.

REFERENCES

1. Prescott HC, Antonelli M, Alhazzani W, et al. Surviving Sepsis Campaign: international guidelines for management of sepsis and septic shock 2026. Crit Care Med. 2026;54(4):725-812. doi:10.1097/CCM.0000000000007075

2. Rudd KE, Johnson SC, Agesa KM, et al. Global, regional, and national sepsis incidence and mortality, 1990-2017: analysis for the Global Burden of Disease Study. Lancet. 2020;395(10219):200-211. doi:10.1016/S0140-6736(19)32989-7

3. Schorr CA, Seckel MA, Papathanassoglou E, Kleinpell R. Nursing implications of the updated 2021 Surviving Sepsis Campaign guidelines. Am J Crit Care. 2022;31(4):329-336. doi:10.4037/ajcc2022324

4. Lemoh AY, Rashidzada Z, Krishnasamy M, et al. Roles and responsibilities of registered nurses in the early recognition and management of sepsis in acute hospital settings: a scoping review. BMJ Open Qual. 2025;14(4):e003485. doi:10.1136/bmjoq-2025-003485

5. Hird C, Parker M. Suspected sepsis: patient assessment and management in the emergency department. Emerg Nurse. 2025;33(3):34-41. doi:10.7748/en.2025.e2221

6. Evans L, Rhodes A, Alhazzani W, et al. Surviving Sepsis Campaign: international guidelines for management of sepsis and septic shock 2021. Crit Care Med. 2021;49(11):e1063-e1143. doi:10.1097/CCM.0000000000005337

7. Seckel MA, Lejnieks JD. Sepsis identification tools: a narrative review. Crit Care Nurse. 2025;45(5):63-79. doi:10.4037/ccn2025240

8. Royal College of Physicians. National Early Warning Score (NEWS) 2: Standardising the Assessment of Acute-Illness Severity in the NHS. Updated report of a working party. Royal College of Physicians; 2017.

9. Semanco M, Wright S, Rich RL. Improving initial sepsis management through a nurse-driven rapid response team protocol. Crit Care Nurse. 2022;42(5):51-57. doi:10.4037/ccn2022608

10. Nunnally J, Ko SM, Ugale K, et al. A nursing-led sepsis response team guiding resuscitation with point-of-care ultrasound: a review and model for improving bundle compliance while individualizing sepsis care. SAGE Open Med. 2024;12:20503121241290378. doi:10.1177/20503121241290378

11. Haley M, Foroutan NK, Gronquist JM, Reddy R, Wusirika R, Khan A. Fluid resuscitation and sepsis management in patients with chronic kidney disease or end-stage renal disease: scoping review. Am J Crit Care. 2024;33(1):45-53. doi:10.4037/ajcc2024756

12. Cain C. Nurses as essential clinical leaders in sepsis care. Am J Crit Care. 2022;31(4):337. doi:10.4037/ajcc2022279

13. Monnet X, Messina A, Greco M, et al. ESICM guidelines on circulatory shock and hemodynamic monitoring 2025. Intensive Care Med. 2025;51(11):1971-2012. doi:10.1007/s00134-025-08137-z

14. Rababa M, Bani Hamad D, Hayajneh AA. Sepsis assessment and management in critically ill adults: a systematic review. PLoS One. 2022;17(7):e0270711. doi:10.1371/journal.pone.0270711

15. Abdalhafith O, Rababa M, Hayajneh AA, et al. Critical care nurses' knowledge, confidence, and clinical reasoning in sepsis management: a systematic review. BMC Nurs. 2025;24:424. doi:10.1186/s12912-025-02986-1

16. Bani Hamad D, Rababa M, Al-Rimawi R, et al. Barriers and facilitators affecting the implementation of the Sepsis Six protocol by nurses in acute care settings in Jordan: a cross-sectional study. SAGE Open Nurs. 2025;11:23779608251362276. doi:10.1177/23779608251362276

17. Chua WL, Teh CS, Basri MAB, et al. Nurses' knowledge and confidence in recognizing and managing patients with sepsis: a multi-site cross-sectional study. J Adv Nurs. 2023;79(2):616-629. doi:10.1111/jan.15435

DIGITAL HEALTH TECHNOLOGIES IN MONITORING SURGICAL PATIENTS

Öykü SARAYDEMİR

Giresun University, Şebinkarahisar Health Services Vocational School, Department of Emergency and First Aid, ORCID ID: 0009-0000-5463-2490

Ali Hakan GÜNAYDIN

Giresun University, Faculty of Health Sciences, Department of Surgical Nursing, ORCID ID: 0009-0007-0479-1187

Yeşim YAMAN AKTAŞ

Giresun University, Faculty of Health Sciences, Department of Surgical Nursing, ORCID ID: 0000-0001-7403-4949

ABSTRACT

Objective: This review aims to explore the use of digital health technologies in the postoperative follow-up of surgical patients.

Materials and Methods: Articles published between 2022 and 2026 were retrieved through systematic searches of PubMed, Google Scholar, and Nature digital databases.

Findings: Monitoring surgical patients is crucial for reducing preventable mortality and morbidity. Intermittent follow-ups within standardized care protocols may lead to delayed detection of clinical deterioration and do not enable continuous remote monitoring. In this context, digital health technologies have emerged as transformative tools in surgical care, contributing significantly to the management of both preoperative and postoperative processes through remote monitoring, virtual reality, telemedicine applications, and wearable devices. The most commonly used digital health technologies in surgical patient monitoring include wearable devices, mobile health applications, telemedicine and virtual visits, virtual reality tools, and artificial intelligence–supported decision-making systems. In the preoperative period, these technologies are primarily used to identify risk factors and support anesthesia planning. During surgery, technologies such as computer vision and virtual reality enhance surgical safety and improve decision-making accuracy. In the postoperative period, digital tools are utilized to detect complications, monitor the healing process, and assess wounds. Following discharge, wound monitoring and follow-up evaluations are predominantly conducted via telemedicine and mobile health applications. Despite their numerous advantages, digital health technologies have not yet been fully integrated into healthcare systems due to concerns such as cyber security risks and limited evidence regarding clinical effectiveness. Therefore, further high-quality clinical studies are needed.

Conclusion: Advancements in technology are continuously enhancing the monitoring of surgical patients. However, further clinical research and robust evidence on data security are required to facilitate the effective integration of these innovations into patient monitoring practices.

Keywords: Remote patient monitoring; digital health technologies; perioperative care; telehealth; telenursing

INTRODUCTION

Approximately 310 million major surgeries are performed worldwide each year[1]. In this context, there is a need for artificial intelligence tools that support every stage of surgical care: preoperative patient preparation and risk assessment; improving workflow and procedural performance during surgery; and reducing complications postoperatively[2].

The monitoring of surgical patients plays a significant role in reducing the incidence of preventable mortality and morbidity[3]. Therefore, continuous monitoring systems hold an important place in the care

of surgical patients, just as they do in intensive care units[1–4]. Intermittent monitoring intervals of 6–12 hours or 4–8 hours, as outlined in standardized care protocols, can lead to delayed detection of certain conditions where the clinical course deteriorates[4]. Ensuring continuity in patient monitoring is of great importance for the proper management of treatment protocols, the detection of complications, and achieving better clinical outcomes[1,5].

Digital health technologies that emerged in the 20th century have made significant contributions to the development of modern healthcare by enabling remote patient monitoring, telemedicine applications, and analyses through wearable devices[6].

DEVELOPMENT

1. Digital Monitoring Approaches for Surgical Patients

1.1. Digital Health Technologies in the Preoperative Period

Some of the digital technologies whose preoperative use has been tested in experimental studies in the literature include:

-The My PreHab Program (MPP) aims to optimize preoperative health by managing known and modifiable risk factors (such as smoking, anemia, nutrition, weight, blood glucose levels, activity, pain, etc.) that could lead to postoperative complications, with the assistance of physicians[7,8].

-Developed by the University of California, San Francisco (UCSF) for older adults, this program converts recommendations across six areas (nutrition, physical condition, home environment, care goals, advanced care processes, and anxiety) into digital content to facilitate preoperative rehabilitation[9].

-Pip was utilized as a digital health platform designed to improve overall preoperative health; it includes personalized care plans, sessions, appointments, unlimited communication with health advisors, and articles and resources to support the process, and is used both preoperatively and postoperatively[10].

-Fit4Surgery was used as a digital platform designed for both pre- and post-operative use, accessible via patients' personal devices, with the goal of improving physical function[11].

-The Be Prepared app has been used as a tool aimed at modifying health-risk behaviors, accessible via patients' phones, for those scheduled for major surgery[12].

-dHOPE is a home-based digital app designed specifically to assist patients scheduled for oncological surgery in their preoperative preparation[13].

-There are numerous studies on using virtual reality to reduce preoperative stress levels[14-16].

-The fitness tracker is an application that is controlled via a smartphone connection and aims to increase physical activity before surgery[17].

1.2. Digital Technologies Used During Surgery

Some of the digital technologies whose use during surgery has been tested in experimental studies in the literature include:

-In laparoscopic cholecystectomy, the Critical View of Safety (CVS) was used to prevent bile duct injuries[18].

-The use of augmented reality (AR) in fracture diagnosis and treatment in orthopedic surgery has been investigated[19,20].

-Perfusion assessment during laparoscopic cholecystectomy was performed using the Laser Speckle Contrast Imaging (LSCI) method[21].

-Arterial waveform data for the Hypotension Prediction Index (HPI) were obtained using the AcumenIQ sensor placed in an artery to facilitate the early detection of hemodynamic instability and acute kidney injury associated with major abdominal surgeries[22].

-Compliance of healthcare personnel with protocols aimed at preventing systemic toxicity from local anesthetics was evaluated using the Operating Room Black Box (ORBB), which provides precise data recording and features sensors in strategic locations[23].

-In colorectal surgery patients, the perfusion heat map method, which reflects tissue oxygen saturation, was used with hyperspectral imaging (HSI)[24].

1.3. Digital Technologies Used in the Postoperative Period

Some of the digital technologies whose postoperative use has been tested in experimental studies in the literature include:

-The effect of wearable sensors on the early detection of complications during postoperative monitoring has been investigated[25]. Within the context of the Ward Alert and Ambulatory Monitoring Study (WARD-AMS) for continuous monitoring following general surgery, a wearable device technology containing two sensors (on the wrist and chest) that continuously monitors vital signs was used[26]. In another study, patients who underwent surgery in various fields had a band called Biobeat attached to their chest to enable telehealth monitoring of vital sign data[27].

-Digital wound monitoring allows specialized nurses to evaluate patients' wound images and related information via smartphones[28].

-A digital home monitoring system (DHM) was used to facilitate home-based follow-up for patients who underwent thoracic surgery, monitor the recovery process, and manage complications[29].

-A digital health management approach based on the Information-Knowledge-Attitude-Practice (IKAP) theory was utilized to promote positive health behaviors in patients following mastectomy[30].

-In patients with esophageal cancer scheduled for surgery, an mHealth app was made available to patients from 2 weeks before hospital admission until 10 weeks after discharge to provide nutrition guidance, physical activity recommendations, and psychological support[31].

-The Hospi4Home app was used to identify emergencies by categorizing patients based on their postoperative responses[32].

-Virtual reality (VR) was used for stress management throughout the entire surgical process in orthopedic surgery[33]

2. Advantages of Digital Health Technologies

- Cost reduction,[34–36]
- Improving the standard of care and delivering effective treatment,[34,36]
- Easier access to professional information,[35,37]
- Clinical decision-making and support systems,[35–37]

3. Disadvantages of Digital Health Technologies

- Inequalities may arise due to low digital health literacy among older adults,[38]
- Insufficient technical infrastructure,[36, 39]
- Concerns regarding workload,[36]
- Data reliability issues,[39]
- Inadequate integration into clinical workflows,[36,39]

CONCLUSION

The primary goal of digital health technologies used before, during, and after surgery is to increase patient engagement in the care process and extend care beyond the clinical setting[40]. While digital health technologies offer advantages such as cost-effectiveness, improved care quality, easier access to professional information, and support for clinical decision-making, their effectiveness in the patient care process is limited by disadvantages including inadequate infrastructure, increased workload, security issues, and lack of integration into clinical workflows[34,35,36,37,39]. To ensure the continuity of digital health technologies in the patient care process, existing issues must be resolved, and these technologies must be integrated into a holistic care process.

REFERENCES

1. Fong Y. Importence of postoperative follow-up for patient outcome. *JAMA Surgery.* 2023;158(12):1301-1302. https://doi.org/10.1001/jamasurg.2023.4535?urlappend=%3Futm_source%3Dresearchgate.net%26utm_medium%3Darticle

2. Varghese C, Harrison EM, O'Grady G, Topol EJ. Artificial intelligence in surgical. *Nature Medicine. 2024;30*(5):1257-1268. https://doi.org/10.1038/s41591-024-02970-3

3. Jiva A, Cameron MM, Ademuyiwa AO, et al. Continuos physiological monitoring for the detection of postoperative deterioration: a protocol for a multistage, multicentre, international, prospective cohort study. *BMJ Open.* 2025;15:e104463. https://doi.org/10.1136/bmjopen-2025-104463

4. Larsen AT, Sopina L, Molgaard J, et al. Impact of postoperative in hospital continuous vital sign monitoring on healthcare cost, resource utilization and labor market outcomes. *The European Journal of Health Economics*. 2026;1-11. https://doi.org/10.1007/s10198-026-01919-2

5. Bonilla MAV, Bonilla CIS, Herrera MFDR, Palacios FJNH, Pineda MDR, Solano MV. The impact of surgical continuity of care on postoperative outcomes and hospital readmissions: a review. *Cureus.* 2025;17(8):e90207. https://doi.org/10.7759/cureus.90207

6. Hu S, Song D, Wan S, et al. Digital health: curent applications, challenges, and future direcitons for enhancing healthcare quatlity and safety. *Frontiers in Public Health*. 2023;13:1646802. https://doi.org/10.3389/fpubh.2025.1646802

7. Linedale EC, Bills E, Dimopoulos A, et al. Development of a feasible and acceptable digital prehabilitation pathway to improve elective surgical outcomes. *Frontiers in Digital Health.* 2023;5:1054894. https://doi.org/10.3389/fdgth.2023.1054894

8. Bills ER, Dimopoulos A, Burke ALJ, et al. Opportunities to optimise care and choice in joint replacement surgery using a digitally delivered, holistic PreHab pathway. *Journal of Orthopaedic Surgery.* 2024;32(2):10225536241234032. https://doi.org/10.1177/10225536241234032

9. Ogomori K, Broering J, Rogine C, Kin C, Chang GJ, Finlayson E. Evaluating a digital prehabilitation tool in patients with colorectal surgery: protocol for a multisite randomised controlled trial. *BMJ Open.* 2025;15:e088001. https://doi.org/10.1136/

10. Esper SA, Holder-Murray J, Meister KA, et al. A novel digital health platform with health coaches to optimize surgical patients: feasibility study at a large academic health system. *JMIR Perioperative Medicine.* 2024;7(1):e52125. https://periop.jmir.org/2024/1/e52125

11. ISRCTN Registry (2024). ISRCTN10633072: A study exploring a personalised digital prehabilitation programme, Fit 4 Surgery (F4S), for patients undergoing major surgery. Department of Health and Social Care. Published 2024. Accessed May 14, 2026. https://doi.org/10.1186/ISRCTN10633072

12. van der Velde M, van der Leeden M, Geleijn E, Veenhof C, Valkenet K, Be Prepared Group. The effectiveness of the be prepared mHealth app on recovery of physical functioning after majör elective surgery: multicenter randomized controlled trial. *JMIR mHealth and uHealth, 2025;13*: e58703. https://mhealth.jmir.org/2025/1/e58703

13. Kleve G, Santa CD, Kristiansen, F, et al. Digital home-based multimodal prehabilitation of colorectal cancer patients prior to surgery (the dHOPE study): a non-inferiority clinical trial protocol. *Frontiers in Digital Health.* 2025;7:1609678. https://doi.org/10.3389/fdgth.2025.1609678

14. Asiri S, Guilhermino M, Duff J. The effectiveness of using virtual reality technology for perioperative anxiety among adults undergoing elective surgery: a randomised controlled trail protocol. *Trials.* 2022;23:972. https://doi.org/10.1186/s13063-022-06908-3

15. Chiu PL, Li H, Yap, KYL. Virtual reality-based intervention to reduce preoperative anxiety in adults undergoing elective surgery. *JAMA Network Open.* 2023;6(10):e2340588. https://doi,org.10.1001/jamanetworkopen.2023.40588

16. Rizzo MG, Costello JP, Luxenburg D. Augmented reality for perioperative anxiety in patients undergoing surgery. *JAMA Network Open.* 2023;6(8):e2329310. https://jama.jamanetwork.com/article.aspx?doi=10.1001/jamanetworkopen.2023.29310&utm_campaign=articlePDF%26utm_medium=articlePDFlink%26utm_source=articlePDF%26utm_content=jamanetworkopen.2023.29310

17. Kilz JH, Abate MAS, Wieland VLS, et al. Preoperative physical activity improvement with the use of activity trackers in patients undergoing radical cystectomy-a bicentric, open-label, randomised, controlled trial: a clinical study protocol of the PreAct trial. *European Urology Open Science*. 2025;71,78-86. https://doi.org/10.1016/j.euros.2024.11.003

18. Leifman G, Golany T, Rivlin E, Khoury W, Assalia A, Reissman P. Real-time artificial intelligence validation of critical view of safety in laparoscopic cholecystectomy. *Intelligence-Based Medicine*. 2024;10:100153. https://doi.org/10.1016/j.ibmed.2024.100153

19. Canton SP, Austin CN, Steuer F, et al. Feasibility and usability of augmented reality technology in the orthopaedic operating room. *Current Reviews in Musculoskeletal Medicine*, 2024;17(5):117-128. https://doi.org/10.1007/s12178-024-09888-w

20. Dünki A, Polat Ö, Güney M. Artırılmış gerçeklik ile oluşturulan 3D modellerin tibia plato kırıklarının tanı ve ortopedi asistan eğitimi üzerindeki etkisi. *Namık Kemal Medical Journal*. 2025;13(3): 287-292. https://doi.org/10.4274/nkmj.galenos.2025.93041

21. Liu YZ, Shah SK, Sanders CM, et al. Utility and usability of laser speckle contrast imaging (LSCI) for displaying real-time tissue perfusion/blood flow in robot-assisted surgery (RAS): comparison to indocyanine green (ICG) and use in laparoscopic surgery. *Surgical Endoscopy*, 2023;37:4803-4811. https://doi.org/10.1007/s00464-022-09590-3

22. Ripolles-Melchor J, Sanchez LC, Tome-Roca JL, et al. Hypotension prediction index guided goal-directed therapy to reduce postoperative acute kidney injury during major abdominal surgery: study protocol for a multicenter randomized controlled clinical trial. *Trials.* 2024;25(1):288. https://doi.org/10.1186/s13063-024-08113-w

23. Lee G, Turner BS, Szydlowski JD, Simmons VC. Operating room black box technology to mitigate local anesthetic systemic toxicity risk associated with liposomal bupivacaine administration. *Journal of PeriAnesthesia Nursing.* 2025;40(6):1431-1437. https://doi.org/10.1016/j.jopan.2025.02.016

24. Barberio M, Lapergola A, Benedicenti S, et al. Intraoperative bowel perfusion quantification with hyperspectral imaging: a guidance tool for precision colorectal surgery. *Surgical Endoscopy*. 2022;36:8520-8532. https://doi.org/10.1007/s00464-022-09407-3

25. Mathias RJ, Govindarajan K, M NF. Prospective assessment of the efficacy of wearable technology in postoperative patient monitoring and early complication detection. *European Journal of Cardiovascular Medicine*, 2025;15:243-249. https://healthcare-bulletin.co.uk/article/prospective-assessment-of-the-efficacy-of-wearable-technology-in-postoperative-patient-monitoring-and-early-complication-detection-3986/

26. Syan J, Joshi M, Beard J, Attebery J, Ng FS, Khan S. Wearable continuous vital sign monitoring study (WARD-AMS) to detect clinical deterioration in postoperative general surgery patients: protocol for a randomized controlled trial. *JMIR Publications.* 2025;14(1):e81558. https://preprints.jmir.org/preprint/81558?__hstc=178719527.0ed434a4e2505bad978720b509a9849b.1779298695194.1779298695194.1779298695194.1&__hssc=178719527.1.1779298695195&__hsfp=0177881dd40451138a4a92b14a0d6815

27. Belliveau J, Pilote L, Grange E, Zaouter C, Roy M, Robin F. Continuous vital sign monitoring with Biobeat wearable devices for post-ambulatory surgery patients: a pilot feasibility study. *Journal of Clinical Monitoring and Computing.* 2025;39:523-531. https://doi.org/10.1007/s10877-025-01276-0

28. Rochon M, Tanner J, Cariaga K, et al. Post-discharge surgical site infection surveillance using patient smartphones: a single-centre experience in cardiac surgery. *British Journal of Healthcare*. 2024;30(7):1-11. https://doi.org/10.12968/bjhc.2024.0074

29. Nagappa M, Subramani Y, Yang H, et al. Enhancing quadruple health outcomes after thoracic surgery: feasibility pilot randomized controlled trial using digital home monitoring. *JMIR Perioperative Medicine*. 2025;8(1):e58998. https://periop.jmir.org/2025/1/e58998

30. Xu P, Zhang X, Lu L, et al. Digital health management via İKAP Theory improves upper limb function and psychological adaptation in postmastectomy patients: a randomized controlled trial. *Clinical Breast Cancer.* 2025;26(2):161-169. https://doi.org/10.1016/j.clbc.2025.08.017

31. Wu W, Yu CC, Ye W, Zhang X. Effectiveness of an mHealth-based multidomain interventions versus standard care on quality of life after esophagectomy for esophageal cancer: a randomized controlled trial. *Available at SSRN*, 2025;5781028. https://dx.doi.org/10.2139/ssrn.5781028

32. Bertoni S, MmK Magema JP, Van Geluwe B, Abbes Orabi N, Bislenghi G, D'Hoore A, Wolthuis A. Digital postoperative follow-up after colorectal resection: a multi-center preliminary qualitative study on a patient reporting and monitoring application. *Updates in Surgery.* 2024;76:139-146. https://doi.org/10.1007/s13304-023-01671-9

33. Moharam SA, ElSharkawy MS, Elkashef AM, et al. Effect of virtual reality on perioperative anxiety, stress and pain in total hip arthroplasty: a randomized controlled trial. *BMC Anesthesiology,* 2025*;*25:446. https://doi.org/10.1186/s12871-025-03316-3

34. Ardito V, Golubev G, Ciani O, Tarricone R. Evaluating barriers and facilitators to the uptake of mHealth apps in cancer care using the consolidated framework for implementation research: scoping literatüre review. *JMIR Cancer.* 2023;9:e42092. https://cancer.jmir.org/2023/1/e42092

35. Borges do Nascimento IJ, Abdulazeem HM, Vasanthan LT, et al. The global effect of digital health Technologies on health workers competencies and health workplace: an umbrella review of systematic reviews and lexical-based and sentence-based meta-analysis. *The Lancet Digital Health.* 2023;5(8):E534-E544. https://doi.org/10.1016/S2589-7500(23)00092-4

36. Wendel J, Hofmann AL, Widmann J, Wöckel A, Heuschmann P, Reese JP. Perceived benefits and disadvantages for healthcare professionals when implementing digital health technologies in breast cancer care: a systematic review. *Digital Health,* 2025;11:1-17. https://doi.org./ 10.1177/20552076251404497

37. Elmaleh Y, Guessous, K, Delvaux BV. Precision perioperative AI: from signals, images, and records to applications in anesthesia-a narrative mini-review proposing an operational framework. *Frontiers in Medicine*. 2026;23:1811197. https://doi.org/10.3389/fmed.2026.1811197

38. Valentim P, Arriaga M, Nogueira P, Costa A. Digital and navigational health literacy in surgical patients: vulnerabilities in the transitions to post-discharge care. *Healthcare.* 2025;13(24):3227. https://doi.org/10.3390/healthcare13243227

39. Brommeyer M, Whittaker M, Liang Z. Organizational factors driving the realization of digital health transformation benefits from health service managers: a qualitative study. *Journal of Healthcare Leadership*. 2024;16:455-472. https://doi.org/10.2147/JHL.S487589

40. Tanniru M, Kazziha S. Digital leadership and strategies to transform post-surgical transition of care (TOC). *Kosova Journal of Surgery.* 2025;9(1):9-23. https://kosovajournalofsurgery.net/kosova-journal-of-surgery-volume-9-issue-1-2/

EVALUATION OF VAN PROVINCE AIR QUALITY IN TERMS OF Co (COBALT), Zn (ZINC), Ni (NICKEL), Ag (SILVER), AND Se (SELENIUM)

VAN İLİ HAVA KALİTESİNİN Co (KOBALT), Zn (ÇİNKO), Ni (NİKEL), Ag (GÜMÜŞ), VE Se (SELENYUM) AÇISINDAN DEĞERLENDİRİLMESİ

Tülay GÜRSOY

Yüzüncü Yıl University, Faculty of Science, Department of Chemistry, Van, Campus, ORCID NO: 0000-0001-6166-6875

Necdet KARAKOYUN

Yüzüncü Yıl University, Muradiye Vocational High School, Van, Campus, ORCID NO: 0000-0002-6083-6921

ABSTRACT

Introduction: Air pollution is defined as the alteration of the natural composition of the air due to various causes, and the presence of foreign substances in the air in solid, liquid, and gaseous forms at concentrations and durations that may be harmful to human health, living organisms, ecological balance, and property.

According to 2023 statistical data from the https://ourworldindata.org/urbanization (WSI), 57.25% of the world's population lives in urban centers, while 42.75% lives in rural areas. According to the results of the Address-Based Population Registration System 2022 announced by TÜİK, 93.4% of our country's population lives in provincial and district centers.

Objective: In our research study, air pollution, which is a result of daily life and the technological age and threatens living health, was investigated in the vicinity of Van Province, which is located within the scope of a metropolitan city.

Methods: Air pollution that had formed over a period of at least three months was monitored in rainwater composition. Five different locations with different qualities were selected for the study and the concentrations of cobalt-zinc-nickel (heavy metal-toxic), silver (metal-toxic) and selenium (non-metal/metalloid-antitoxic) in the rainwater composition were measured using an ICP-MS device and evaluated based on the PM10 standard.

Results: Co, Zn, Ni concentrations were measured to be highest at L3 (Organized Industrial Zone) location with values of 0.010057, 16.9026, 0.10775 µg/ml, respectively, and Se concentration was measured to be highest at L1 (University Campus Area) location with 0.4097 µg/ml. The presence of Ag metal was not found in any location.

Conclusion: Striking findings were obtained regarding the relationship between industrial, transportation, heating, and human activities at the locations and air pollution. It has been determined that practices on the basis of state and private enterprises are necessary to reduce or even prevent air pollution.

Keywords: air pollution, rainwater, location, metal, heavy metal

1. INTRODUCTION

Air pollution refers to changes in the natural composition of the air due to various causes, as well as the presence of foreign substances in the air—in solid, liquid, or gaseous form—at concentrations and for durations that may be harmful to human health, living organisms, the ecological balance, and everything they come into contact with.

Metals and semimetals (metalloids) are elements that can exhibit toxic effects at both low and high concentrations and are generally associated with contamination and potential toxicity or ecotoxicity.

Through various forms of exposure, they accumulate in living organisms and cause metabolic disorders (Gürsoy, 2022; Özyiğit, 2021a).

While air pollutants are highly diverse, urban air pollution is generally determined by measuring concentrations of sulfur dioxide (SO_2), nitrogen oxides, carbon monoxide (CO), ozone (O_3), and particulate matter (PM) in the atmosphere. Ground-level ozone has become one of the key parameters monitored for urban air pollution, particularly in developed countries in recent years. Additionally, the EU Air Quality Standards legally mandate the monitoring of heavy metals such as lead (Pb), arsenic (As), cadmium (Cd), and nickel (Ni). Trace elements measured for industrial/urban pollution monitoring include copper (Cu), zinc (Zn), iron (Fe), manganese (Mn), vanadium (V), and mercury (Hg) (Gürsoy and Karakoyun Önal, 2025; Ali et al., 2013).

According to 2024 statistical data from the https://ourworldindata.org/urbanization, 61.6% of the world's population lives in urban centers, while 38.4% lives in rural areas. According to the results of the Address-Based Population Registration System 2025 announced by TÜİK, 93.6% of our country's population lives in provincial and district centers, while 6.4% lives in towns and villages.

In our research study, air pollution—a result of daily life and the technological age that threatens human health—was investigated in the vicinity of Van Province, Turkey, which is classified as a metropolitan area. Five distinct locations with varying characteristics were selected for the study, and the concentrations of cobalt, zinc, and nickel (heavy metals—toxic) and silver (metal—toxic) in rainwater, along with selenium (non-metal/metalloid—non-toxic), were evaluated in terms of environmental toxicity.

2. MATERIALS AND METHODS

Air pollution that had accumulated over a period of at least three months was monitored in the composition of rainwater. Five distinct locations with varying characteristics were selected for the study, and the concentrations of heavy metals (Co, Zn, Ni), metals (Ag), and nonmetals/metalloids (Se) in the rainwater composition were measured using an Agilent 7700 Inductively Coupled Plasma -Mass Spectrometry (ICP-MS) instrument, with ORS3 as the standard, and measured in He mode (Önder, 2012). The locations studied in the vicinity of Van Province were selected as L1 (University Campus Location), L2 (City Center Location), L3 (Organized Industrial Zone Location), L4 (Airport Area Location), and L5 (Automotive Industrial Site Location).

3. RESULTS

1. Co (COBALT):

Table 1. Concentrations (ppm) of the Co element measured in rainwater at different locations

	Co concentration (ppm)
L1 (Üniversite Yerleşkesi)	0,00155
L2 (City Center)	0,00002
L3(Organized Industrial Zone)	0,01006
L4 (Airport Campus)	0,00011
L5 (Automotive Indust. Site)	0,00018
WHO	**0,02000**

The element **cobalt (Co)**, an indispensable component of modern technology due to its heat resistance, corrosion resistance, magnetic properties, and critical applications ranging from electric vehicle batteries to superalloys, has not exceeded toxicity limits at any location. However, cobalt contamination is present at the L3 site (WHO/FAO, 2007; Okudan, 2009).

2. Zn (ZINC):

Table 2. Concentrations (ppm) of zinc measured in rainwater at different locations

	Zn concentration (ppm)
L1 (University Campus)	14,86061
L2 (City Center)	4,557520
L3(Organized Industrial Zone)	16,90265
L4 (Airport Campus)	2,090240
L5 (Automotive Indust. Site)	14,06999
WHO	**2,00000**

Zinc (Zn) is an essential element that plays a role in the immune system and metabolic processes in the human body, while also being a component of numerous everyday materials, including galvanizing, alloy production, organic compounds, automotive parts, the foundry industry, and battery manufacturing. Toxicity is present in all locations (WHO/FAO, 2007; Önder, 2012; Vardhan et al., 2019).

3. Ni (Nickel):

Table 3. Concentrations (ppm) of the Ni element measured in rainwater at different locations

	Ni concentration (ppm)
L1 (University Campus)	0,014830
L2 (City Center)	0,003381
L3(Organized Industrial Zone)	16,902650
L4 (Airport Campus)	0,005704
L5 (Automotive Indust. Site)	0,010323
WHO	**0,020000**

Nickel, a transition metal known for its corrosion resistance, stability even at high temperatures, and flexibility, is an essential trace element for living organisms. Its accumulation in the environment poses a toxicity risk. As a result of its widespread use in technology, it has caused toxicity at the L3 location (WHO/FAO, 2007; Özkan, 2009; Seven et al., 2018; Briffa et al., 2020).

4. Ag (SILVER)

Table 4. Concentration of the Ag element measured in rainwater at different locations (ppm)

	Ag concentration (ppm)
L1 (University Campus)	LOD
L2 (City Center)	LOD
L3(Organized Industrial Zone)	LOD
L4 (Airport Campus)	LOD
L5 (Automotive Indust. Site)	LOD
WHO	**0,1**

***LOD:** Below the limit of detection: Ag: 0.001 ppm

Silver, one of the trace elements found in small amounts in the Earth's crust, rarely causes toxicity (WHO/FAO, 2007; Eckelman and Graedel, 2007; Burrell, 2003).

5. Se (SELENIUM)

Table 5. Concentrations of the Se element measured in rainwater at various locations (ppm)

	Se concentration (ppm)
L1 (University Campus)	0,4097
L2 (City Center)	LOD
L3 (Organized Industrial Zone)	0,0963
L4 (Airport Campus)	0,0685
L5 (Automotive Indust. Site)	LOD
WHO	**0,1**

***LOD:** Below the limit of detection: Ag: 0.001 ppm

Selenium (Se) is a trace metalloid that possesses antitoxic properties against environmental toxicity and is vital for living organisms even in trace amounts. Selenium antitoxicity is present at the L1 locus, while selenium toxicity is present at the L3 and L4 loci. Environmental release occurs through both natural and anthropogenic pathways (WHO/FAO, 2007; Phadnis, 2021; Cao et al., 2015).

DISCUSSION

In our research study, heavy metal toxicity resulting from intensive industrial activity was observed only at the L3 (Organized Industrial Zone) location with regard to the cobalt element. Zn (zinc) heavy metal toxicity is present in all locations L1, L2, L3, L4, and L5 as a result of its widespread use in industrial, technological, construction, and consumer products. As expected, zinc heavy metal toxicity is higher at the L3 (Organized Industrial Zone) and L5 (Automotive Industrial Site) locations compared to other areas. Nickel (Ni) heavy metal toxicity has exceeded toxicity levels by dozens of times at the L3 (Organized Industrial Zone) location due to its widespread use in industrial and technological sectors. Since silver (Ag) is a trace element, no toxicity or contamination is present at any location. Selenium (Se), a non-metal/metalloid/non-toxic element, exhibits non-toxic accumulation at the L1 (University Campus) location due to ecological factors, while concentrations are present in the L3 (Organized

Industrial Zone) and L4 (Airport Campus) areas. The fact that all sites, except for the L2 city center location, are situated outside the city in areas with high wind speeds has contributed to the absence of pollution or toxicity regarding these elements.

Air pollution in Van Province is due to ecological factors. When compared to the PM10 standard, the highest level of air pollution in terms of the total of the aforementioned elements is found in L3 (Organized Industrial Zone).

REFERENCES

Ali, H., Khan, E., Ilahi, I., (2019). Environmental chemistry and ecotoxicology of hazardous heavy metals: environmental persistence, toxicity, and bioaccumulation. Journal of Chemistry, 1-14.

Briffa, J., Sinagra, E., Blundell, R. (2020). Heavy metal pollution in the environment and their toxicological effects on humans. Heliyon, 6(9), e04691.

Burrell, R. E., (2003). A scientific perspective on the use of topical silver preparations. Ostomy Wound Management, 49(5; SUPP), 19-24.

Cao, W., Wang, L., Xu, H., (2015). Selenium/tellurium containing polymer materials in nanobiotechnology. *Nano Today*, *10*(6), 717-736.

Eckelman, M.J., Graedel, T.E, (2007). Silver Emissions and their Environmental Impacts: A Multilevel Assessment, *Environ. Sci. Technol.* 41(17): 6283–6289.

Gürsoy, T., Ağır Metal Mazuriyetinin Genital Sistem Üzerine Etkileri, Mercan Yücel, U., Atasoy, N., Gürsoy, T., Eds., Ağır Metal Mazuriyetinin Doku ve Organlar Üzerine Etkileri, Bölüm 7, Duvar Yayınları, Kemeraltı-Konak / İZMİR, pp.147-158, Kasım 2022, ISBN: 978-625-8261-49-3, www.duvaryayinlari.com

Gürsoy, T., Karakoyun Önal G., "Grass Plant (Lolium L.) as a Bioindicator: Heavy Metal Content and Toxicity". ISPEC 9. International Conference on Medical&Health Sciences, Dubai, UAE. 15-19 May 2025. ISBN: 979-8-89695-085-1. P.12-13.

Okudan M., 2009, Kobalt ve Molibden İçeren Kullanılmış Hidrodesülfürizasyon (HDS) Katalizör Atıklarına Asidik Ve Alkali Liç Uygulaması, Yüksek Lisans Tezi, Süleyman Demirel Üniversitesi Fen Bilimleri Enstitüsü, Isparta, 6-9-13.

Önder S., 2012, Atıksular İle Sulanan Zirai Alanlardaki Ağır Metal Kirliliğinin Araştırılması, Yüksek Lisans Tezi, Selçuk Üniversitesi Fen Bilimleri Enstitüsü, Konya, 3-4-11-17-24-25.

Özkan G., 2009, Endüstriyel Bölge Komşuluğunda Kıyısal Kırsal Alandaki Hava Kalitesi; Muallimköy'de Partikül Madddede ve Topraktaki Ağır Metal Kirliliği, Yüksek Lisans Tezi, GYTE Fen Bilimleri Enstitüsüsü, Gebze, 9,12-22.

Özyiğit, İ.İ., (2021), Tarım Topraklarında Ağır Metaller; Kökenleri, Yayılışları ve Etkileri, Necmettin Erbakan Üniversitesi Ereğli Tarım Bilimleri Dergisi (Ereğli Journal of Agricultural Science), 1(1): 46-67.

Phadnis, P. P., 2021. Synthesis strategies for organoselenium compounds and their potential applications in human life. In Handbook on Synthesis Strategies for Advanced Materials: Volume-III: Materials Specific Synthesis Strategies (pp. 537-641). Singapore: Springer Singapore.

Seven, T., Can, B., Darende, B.N., Ocak, S., (2018). Hava ve Toprakta Ağır Metal Kirliliği, Ulusal Çevre Bilimleri Araştırma Dergisi, Sayı 1(2): 91-103.

Vardhan, K. H., Kumar, P. S., & Panda, R. C. (2019). A review on heavy metal pollution, toxicity and remedial measures: Current trends and future perspectives. Journal of Molecular Liquids, 290, 111197.

WHO, (2007). WHO-United Nations Environment Programme. Urban Air Pollution in Megacities of the World. Blackwell, UK, 1992:7-13.

İNVERTED PAPİLLOM ÖN TANISI İLE OPERE EDİLEN OLGUDA SKUAMÖZ HÜCRELİ KARSİNOM: KLİNİK VE PATOLOJİK KORELASYON

Ayşe Nur EVLEKSİZ

Kırıkkale Üniversitesi Tıp Fakültesi Tıbbi Patoloji Anabilim Dalı/ Araştırma Görevlisi Asistan Doktor

ORCID ID: 0009-0001-5582-8169

Şeyma ÖZTÜRK

Kırıkkale Üniversitesi Tıp Fakültesi Tıbbi Patoloji Anabilim Dalı/ Doktor Öğretim Üyesi, ORCID:0000-0002-2167-4253

Giriş: Sinonazal inverted papillomlar benign karakterli lezyonlar olmakla birlikte, rekürrens ve malign transformasyon potansiyelleri nedeniyle dikkatli değerlendirilmesi gereken oluşumlardır. Klinik ve radyolojik olarak benign izlenim verebilmelerine karşın, bazı olgularda eşlik eden ya da gelişen malignite saptanabilmektedir. Bu çalışmada, inverted papillom ön tanısı ile opere edilen ve histopatolojik inceleme sonucunda inverted papillom zemininde gelişen skuamöz hücreli karsinom tespit edilen olgu sunulmuştur.

Olgu Sunumu: Seksen dört yaşında erkek hasta, epistaksis ve sağ nazal pasajda kitle şikayetleri ile başvurdu. Radyolojik incelemelerde sinonazal sinüslerde yaygın mukozal kalınlaşma ve inflamatuar değişiklikler izlendi. Klinik ön tanı doğrultusunda hastaya fonksiyonel endoskopik sinüs cerrahisi ile birlikte sağ medial maksillektomi uygulandı. Makroskopik incelemede, en büyüğü 3 cm'ye ulaşan, düzensiz konturlu, yer yer kanamalı görünüme sahip multipl doku parçaları izlendi. Mikroskopik değerlendirmede, sinonazal mukozaya ait çok katlı yassı epitelin stroma içerisine doğru invajinasyonlar yaptığı ve epitelyal adacıklar oluşturduğu görüldü. Bu alanlarda yer yer belirgin hücresel pleomorfizm, nükleer atipi gösteren yüksek dereceli displazi karakterli alanlar dikkati çekti. Bazı bölgelerde bazal membran bütünlüğünün seçilemediği ve düzensiz sınırlı, infiltratif büyüme paterni sergileyen atipik skuamöz hücre adaları izlendi. Stromada yer yer inflamatuvar hücre infiltrasyonu eşlik etmekteydi. Tüm bu bulgular doğrultusunda lezyon invaziv özellikler gösteren skuamöz hücreli karsinom olarak değerlendirildi. Klinik ve radyolojik veriler ile birlikte değerlendirildiğinde olgunun inverted papillom zemininde gelişen veya eşlik eden maligniteyi temsil ettiği düşünüldü.

Sonuç: Bu olgu, inverted papillomların her zaman benign seyretmeyebileceğini ve klinik olarak öngörülemeyen malign odaklar içerebileceğini göstermektedir. Özellikle ileri yaş hastalarda epistaksis ve nazal kitle varlığında malignite olasılığı mutlaka göz önünde bulundurulmalıdır. Klinik, radyolojik ve histopatolojik bulguların birlikte değerlendirilmesi tanısal doğruluk ve tedavi planlaması açısından belirleyici rol oynamaktadır.

Giriş: Sinonazal inverted papillomlar, Schneiderian membran kökenli, nadir görülen benign epiteliyal neoplazmlardır [10]. Histolojik olarak epitelin stromaya doğru invajinasyonu ile karakterize olan bu lezyonlar, benign doğalarına rağmen lokal agresif büyüme potansiyeline sahiptir [1]. Ayrıca rekürrens eğilimleri ve özellikle skuamöz hücreli karsinom ile birliktelik göstermeleri ya da malign transformasyon riski nedeniyle klinik açıdan önem taşırlar [5, 9].

Literatürde inverted papillomların yaklaşık %5–15 oranında malignite ile ilişkili olabileceği bildirilmektedir [6]. Bu malignite, lezyon ile eş zamanlı bulunabileceği gibi, rekürren olgularda zaman içerisinde de gelişebilir [3]. Ancak klinik ve radyolojik bulguların çoğu zaman non-spesifik olması nedeniyle, malign komponentin preoperatif olarak saptanması güçtür.

Bu nedenle kesin tanı çoğunlukla cerrahi eksizyon materyalinin histopatolojik değerlendirilmesi ile konulmaktadır [8]. Bu çalışmada, inverted papillom ön tanısı ile opere edilen ve histopatolojik inceleme sonucunda skuamöz hücreli karsinom saptanan bir olgu sunulmuştur.

Olgu Sunumu: Seksen dört yaşında erkek hasta, tekrarlayan epistaksis ve sağ nazal pasajda dolgunluk hissi şikayetleri ile başvurdu. Bu şikayetlerinin son dönemde arttığı öğrenildi. Fizik muayene ve endoskopik değerlendirmede sağ nazal pasajda kitlesel oluşum izlendi.

Radyolojik incelemelerde sinonazal sinüslerde yaygın mukozal kalınlaşma, polipoid değişiklikler ve inflamatuvar bulgular saptandı . Görüntüleme bulguları spesifik olmamakla birlikte, lezyonun benign karakterli olabileceği yönünde değerlendirildi.

Fonksiyonel endoskopik sinüs cerrahisi ile birlikte sağ medial maksillektomi uygulandı. Operasyon sırasında sağ nazal pasajdan kaynaklanan kitle tamamen eksize edildi. Postoperatif dönemde hasta yakın izlem altında tutuldu. Operasyon sırasında gelişen anemi nedeniyle eritrosit süspansiyonu uygulanmış olup, takiplerinde hastanın genel durumu stabil seyretti ve ek komplikasyon gözlenmeden taburcu edildi. Makroskopik incelemede, en büyüğü 3 cm'ye ulaşan, düzensiz konturlu, yer yer hemorajik görünümde, kahverengi tonlarında multipl doku parçaları izlendi. Mikroskopik incelemede, sinonazal mukozaya ait çok katlı yassı epitelin stroma içerisine doğru belirgin invajinasyonlar yaptığı ve yer yer adacıklar oluşturduğu görüldü. (Resim 1) Bu yapı inverted papillom morfolojisi ile uyumlu olarak değerlendirildi.

Epitelde yer yer yüksek dereceli displazi alanları izlenirken, (Resim 2) bazı bölgelerde mitotik aktivitede artış gözlendi.

Fokal alanlarda yüzey epiteli ülserasyon göstermekteydi. Bazı alanlarda bazal membran bütünlüğünün seçilemediği ve düzensiz sınırlı, stroma içerisine doğru infiltratif büyüme paterni sergileyen atipik skuamöz hücre adacıkları izlendi. (Resim 3,4) Ayrıca stromada kronik inflamatuar hücre infiltrasyonu mevcuttu. (Resim 5)

Bu bulgular birlikte değerlendirildiğinde olgu, inverted papillom zemininde gelişen skuamöz hücreli karsinom olarak yorumlandı.

Tartışma: İnverted papillomlar her ne kadar benign neoplazmlar olarak sınıflandırılsa da, malignite ile olan ilişkileri nedeniyle dikkatli değerlendirilmelidir [5, 9]. Bu lezyonlarda skuamöz hücreli karsinom gelişimi eş zamanlı olarak mevcut olabilir ya da zaman içerisinde ortaya çıkabilir .

Klinik olarak epistaksis ve nazal obstrüksiyon gibi semptomlar hem benign hem de malign sinonazal lezyonlarda görülebileceğinden, ayırıcı tanıda sınırlı değer taşır [8]. Benzer şekilde radyolojik bulgular da çoğu zaman inflamatuar süreçler ile örtüşebilir [11]. Bu nedenle preoperatif dönemde malign komponentin atlanması olasıdır [4].

Histopatolojik inceleme bu noktada belirleyici rol oynar. İnverted papillomda tipik olarak görülen epitel invajinasyonuna ek olarak, belirgin hücresel atipi, yüksek dereceli displazi, artmış mitotik aktivite ve özellikle stromaya invazyon bulguları malignite lehine değerlendirilmelidir [2, 7]. Bazal membran bütünlüğünün kaybı ve infiltratif büyüme paterni, invaziv skuamöz hücreli karsinom tanısı için kritik öneme sahiptir.

Bu olgu, klinik olarak benign düşünülen bir lezyonda dahi malign odakların bulunabileceğini göstermektedir. Özellikle ileri yaş hastalarda ve epistaksis gibi alarm semptomlarının varlığında daha dikkatli bir yaklaşım gereklidir.

Cerrahi eksizyon sonrası elde edilen materyalin yeterli örnekleme ile detaylı histopatolojik incelemesi, doğru tanının konulmasında temel basamaktır. Bu yaklaşım, tedavi planlaması ve prognoz açısından doğrudan etkili olmaktadır.

Sonuç: Bu olgu, inverted papillomların her zaman benign seyretmeyebileceğini ve eşlik eden malignitenin klinik olarak öngörülemeyebileceğini göstermektedir. Klinik, radyolojik ve histopatolojik bulguların birlikte değerlendirilmesi, özellikle şüpheli olgularda tanısal doğruluğu artırmaktadır. Cerrahi materyalin dikkatli incelenmesi, malign transformasyonun erken saptanması açısından kritik öneme sahiptir. Özellikle ileri yaş hastalarda nazal kitle ve epistaksis varlığında malignite olasılığı mutlaka göz önünde bulundurulmalıdır.

Kaynaklar

1. Kim JS, Kwon SH (2017) Recurrence of sinonasal inverted papilloma following surgical approach: A meta-analysis. The Laryngoscope 127(1):52–58

2. Krouse JH (2000) Development of a staging system for inverted papilloma. The Laryngoscope 110(6):965–968

3. Lawson W, Schlecht NF, Brandwein-Gensler M (2008) The role of the human papillomavirus in the pathogenesis of Schneiderian inverted papillomas: an analytic overview of the evidence. Head Neck Pathol 2(2):49–59

4. Park MJ, Cho W, Kim JH, Chung Y-S, Jang YJ, Yu MS (2023) Preoperative Prediction of Sinonasal Inverted Papilloma-associated Squamous Cell Carcinoma (IP-SCC). The Laryngoscope 133(10):2502–2510

5. Re M, Gioacchini FM, Bajraktari A, Tomasetti M, Kaleci S, Rubini C, Bertini A, Magliulo G, Pasquini E (2017) Malignant transformation of sinonasal inverted papilloma and related genetic alterations: a systematic review. Eur Arch Oto-Rhino-Laryngol Off J Eur Fed Oto-Rhino-Laryngol Soc EUFOS Affil Ger Soc Oto-Rhino-Laryngol - Head Neck Surg 274(8):2991–3000

6. Sbrana MF, Borges RFR, Pinna F de R, Neto DB, Voegels RL (2021) Sinonasal inverted papilloma: rate of recurrence and malignant transformation in 44 operated patients. Braz J Otorhinolaryngol 87(1):80–84

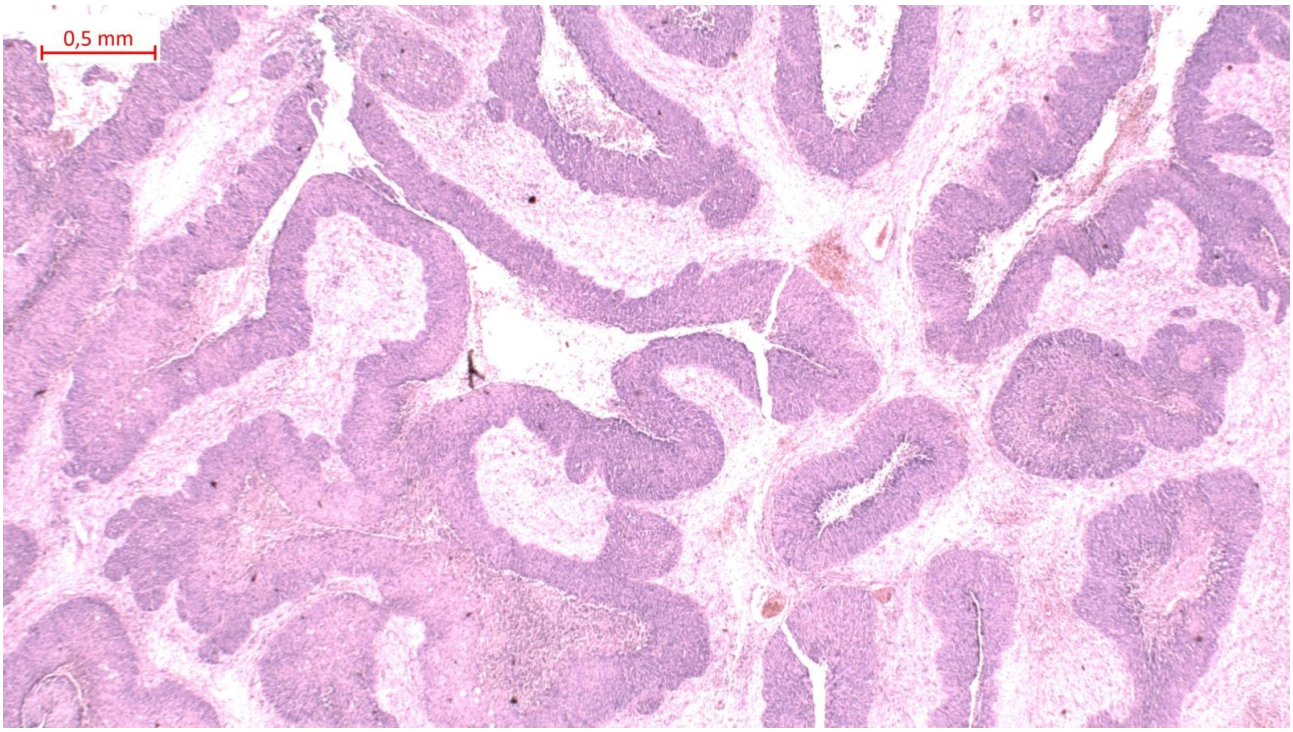
7. Speight PM, Takata T (2018) New tumour entities in the 4th edition of the World Health Organization Classification of Head and Neck tumours: odontogenic and maxillofacial bone tumours. Virchows Arch 472(3):331–339

8. Tuşaliu M, Mogoantă CA, Iancu C, Iovănescu D, Nițescu M, Bucur C, Perpelea A-C, Cîmpeanu OL, Palade OD (2024) Sinonasal inverted papilloma from diagnosis to treatment – a narrative review. Rom J Morphol Embryol 65(4):599–607

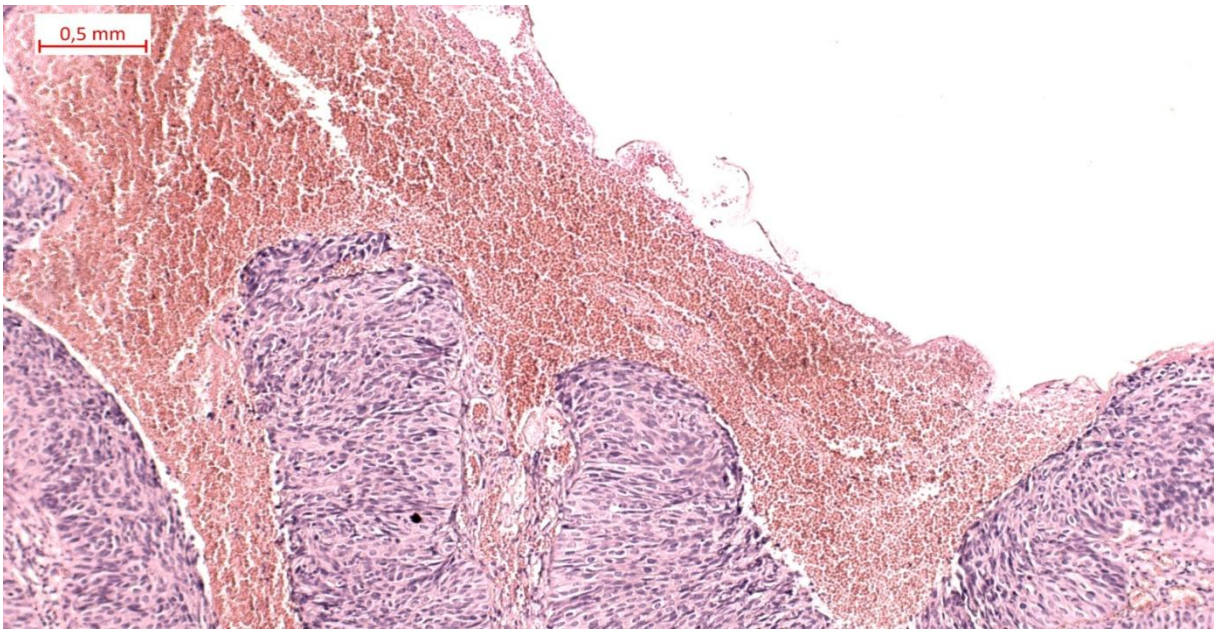
9. Viitasalo S, Ilmarinen T, Aaltonen L-M, et al (2023) Sinonasal inverted papilloma - malignant transformation and non-sinonasal malignancies. The Laryngoscope 133(3):506–511

10. Yeom S, Lee DH, Lim SC (2023) Clinical outcomes of sinonasal inverted papilloma: a retrospective analysis of 139 cases. J Laryngol Otol 137(10):1154–1157

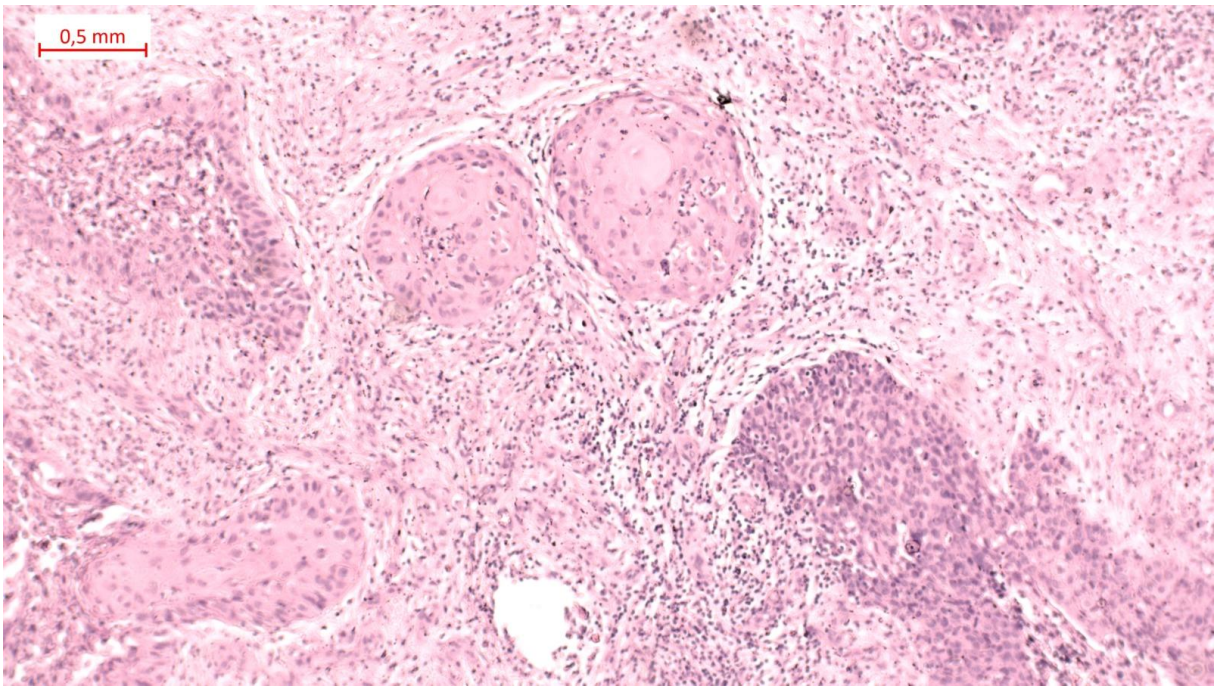
11. Yousem DM, Fellows DW, Kennedy DW, Bolger WE, Kashima H, Zinreich SJ (1992) Inverted papilloma: evaluation with MR imaging. Radiology 185(2):501–505



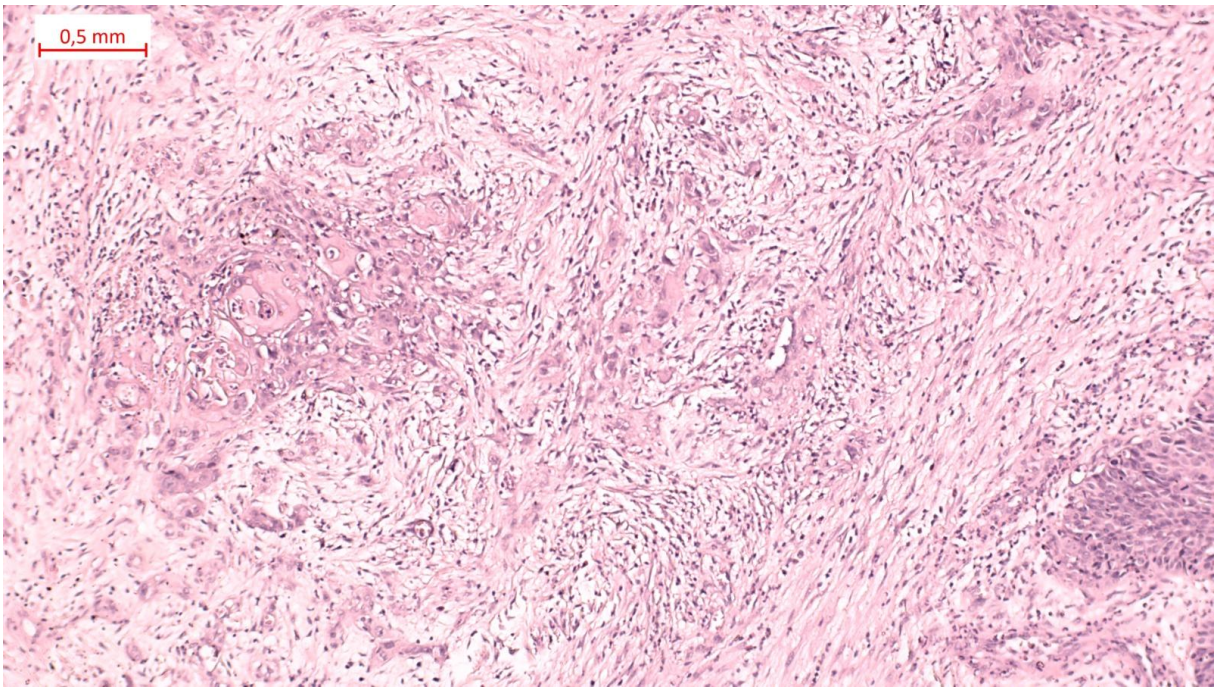
Resim 1: Yüzeyden stromaya doğru çok katkı yassı epitelin invajinasyonlar oluşturduğu görüldü. (H&E,x25)



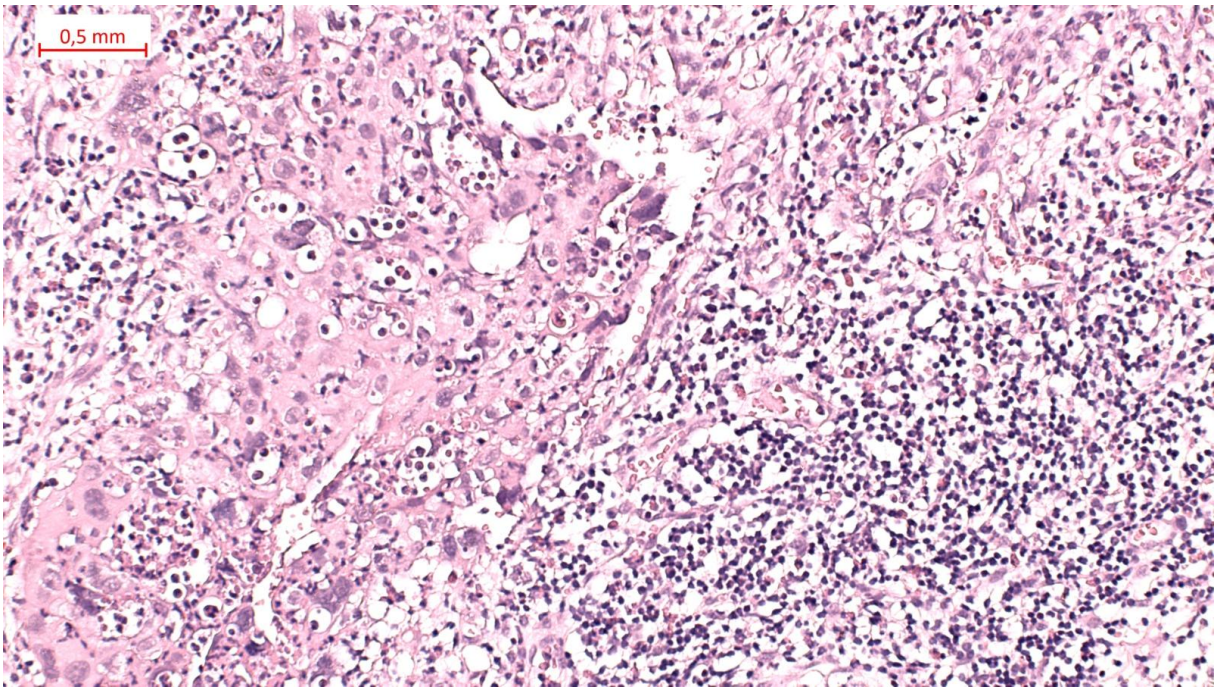
Resim 2: Epitelde yüksek dereceli displazi alanları izleniyor. (H&E, x100)



Resim 3: Stroma içerisinde skuamöz hücre adaları izlendi. (H&E,100)



Resim 4: Skuamöz hücre adaları düzensiz sınırlı olup hücresel atipi içermektedir. (H&E, x100)



Resim 5: Stroma içerisine infiltre olan skuamöz hücre adası çevresinde mononükleer iltihabi hücre infiltrasyonu görüldü. (H&E,x200)

KARACİĞER YETMEZLİĞİ İLE SEYREDEN SEPTİK ŞOK OLGUSUNDA TANI VE TEDAVİ SÜRECİ

Ergün Öztaş

Dr. Öğretim Üyesi, İç Hastalıkları AD., Özel Aritmi Hastanesi, ORCID ID: 0009-0007-5713-4404

Süleyman Bahar

Department of Infectious Diseases and Clinical Microbiology, Özel Aritmi Osmangazi Hastanesi, Bursa, Türkiye

Nazmi Demirel

Department of Gastroenterology, Özel Aritmi Osmangazi Hastanesi, Bursa, Türkiye

ÖZET

Karaciğer yetmezliği; metabolik, immünolojik ve hematolojik bozukluklara yol açan, enfeksiyonlara yatkınlığı artıran ve yüksek mortalite ile seyreden ciddi bir klinik tablodur. Bu hastalarda hepatik ensefalopati (HE), önemli komplikasyonlardan biridir. HE; ciddi karaciğer bozukluğu olan hastalarda, farklı nörolojik veya metabolik nedenler olmaksızın gelişen nöropsikiyatrik değişikliklerle karakterize bir sendromdur. Klinik tablo hafif mental bozukluklardan derin komaya kadar değişebilir. Özellikle akut karaciğer yetmezliğinde sık görülür. Septik şok ise enfeksiyona bağlı gelişen, doku perfüzyon bozukluğu, hipotansiyon ve çoklu organ yetmezliği ile seyreden hayatı tehdit eden acil bir durumdur.

Bu olgu sunumunda, karaciğer yetmezliği tanısıyla takip edilen ve hepatik ensefalopati bulguları eşliğinde septik şok gelişen bir hastanın tanı ve tedavi süreci değerlendirilmiştir. Hasta; bilinç bulanıklığı, halsizlik, ateş, hipotansiyon, sarılık, hiperventilasyon, flapping tremor ve mental durum değişiklikleri ile başvurmuştur. Fizik muayene ve laboratuvar incelemelerinde karaciğer fonksiyon testlerinde bozulma, INR yüksekliği, arteriyel amonyak artışı, laktat yüksekliği ve enfeksiyon belirteçlerinde belirgin yükselme saptanmıştır. Klinik değerlendirme sonucunda hepatik ensefalopati ile komplike septik şok ön tanısı konulmuştur.

Yoğun bakım koşullarında sıvı resüsitasyonu, geniş spektrumlu antibiyotik tedavisi, vazopressör desteği, laktuloz tedavisi, elektrolit düzenlenmesi, protein kısıtlı beslenme ve organ destek tedavileri uygulanmıştır. Enfeksiyon odağı araştırılarak uygun tedavi planlanmış, presipite edici faktörler kontrol altına alınmıştır.

Karaciğer yetmezliği bulunan hastalarda hepatik ensefalopati ve septik şokun erken tanınması, hızlı tedavi başlanması ve multidisipliner yoğun bakım yaklaşımı mortaliteyi azaltmada kritik öneme sahiptir. Bu olgu, erken müdahalenin prognoz üzerindeki belirleyici etkisini göstermektedir.

ANAHTAR KELİMELER: Karaciğer yetmezliği, hepatik ensefalopati, septik şok, sepsis, yoğun bakım

DIAGNOSTIC AND TREATMENT PROCESS IN A CASE OF SEPTIC SHOCK ASSOCIATED WITH LIVER FAILURE

A 71-Year-Old Woman with Decompensated Heart and Liver Failure, Colonic Bacterial Overgrowth, and Progressive Clinical Deterioration: A Case Report

ABSTRACT

Liver failure is a serious clinical condition characterized by metabolic, immunological, and hematological disorders, increased susceptibility to infections, and high mortality. Hepatic encephalopathy (HE) is one of the major complications observed in these patients. HE is a syndrome characterized by neuropsychiatric changes that develop in patients with severe liver dysfunction without any other neurological or metabolic cause. The clinical presentation may range from mild mental impairment to deep coma. It is particularly common in acute liver failure. Septic shock, on the other

hand, is a life-threatening emergency caused by infection and characterized by impaired tissue perfusion, hypotension, and multiple organ failure.

In this case report, the diagnostic and treatment process of a patient with liver failure who developed septic shock accompanied by hepatic encephalopathy findings was evaluated. The patient presented with confusion, fatigue, fever, hypotension, jaundice, hyperventilation, flapping tremor, and changes in mental status. Physical examination and laboratory findings revealed impaired liver function tests, elevated INR, increased arterial ammonia levels, elevated lactate levels, and significantly increased infection markers. As a result of clinical evaluation, a preliminary diagnosis of septic shock complicated by hepatic encephalopathy was established.

In intensive care conditions, fluid resuscitation, broad-spectrum antibiotic therapy, vasopressor support, lactulose treatment, electrolyte regulation, protein-restricted nutrition, and organ support therapies were administered. The source of infection was investigated, appropriate treatment was planned, and precipitating factors were brought under control.

Early recognition of hepatic encephalopathy and septic shock in patients with liver failure, rapid initiation of treatment, and a multidisciplinary intensive care approach are critically important in reducing mortality. This case highlights the decisive effect of early intervention on prognosis.

KEYWORDS: Liver failure, hepatic encephalopathy, septic shock, sepsis, intensive care

SUMMARY

A 71-year-old woman with a history of diabetes mellitus, hypertension, heart failure, and morbid obesity presented with progressive fatigue, unintentional weight loss, abdominal discomfort, and hematochezia. Her clinical course was complicated by the presence of a circumferential malignant-appearing rectal ulcer, ESBL-producing *Klebsiella pneumoniae* urinary tract infection, and profound metabolic derangements including hypokalemic metabolic alkalosis, hyperammonemia, and troponin elevation. Despite multidisciplinary management, the patient developed progressive hepatic and cardiac decompensation with colonic bacterial overgrowth and ultimately expired in the intensive care unit. This case highlights the complexities of managing multimorbidity in elderly patients and the critical importance of early recognition and aggressive management of organ failure in the setting of concurrent malignancy and infection.

CASE PRESENTATION

Dr. Ergün Öztaş (Internal Medicine): A 71-year-old woman presented to our clinic with a three-month history of progressive fatigue, unintentional weight loss (8 kg over two months), diffuse abdominal discomfort, and intermittent nausea. During the preceding one to two weeks, she reported episodes of hematochezia described as bright red blood per rectum. She denied fever, night sweats, or melena.

Her medical history was significant for diabetes mellitus, hypertension, chronic heart failure with reduced ejection fraction, and morbid obesity (body mass index 34 kg/m²). Her home medications included metformin, lisinopril, and furosemide. She reported no recent travel or animal contact.

Physical Examination: On admission, the patient appeared fatigued but was cooperative and oriented. Vital signs revealed: temperature 36.8°C, blood pressure 130/70 mmHg, heart rate 88 beats per minute, respiratory rate 16 breaths per minute, and oxygen saturation 86% on room air. Cardiopulmonary examination revealed an S3 gallop rhythm, a midsystolic murmur, and bilateral basilar crackles. Abdominal examination demonstrated diffuse tenderness in the suprapubic and left lower quadrants without guarding or rebound. Widespread ascites and anasarca were present. Rectal examination revealed no palpable mass; however, fecal occult blood testing was positive.

Initial Laboratory Findings: Laboratory evaluation revealed normocytic anemia (hemoglobin 10.2 g/dL; reference range 12.0-16.0), elevated erythrocyte sedimentation rate (48 mm/hour; reference <20), and progressive thrombocytopenia over preceding months.

Dr. Nazmi Demirel (Gastroenterology): Esophagogastroduodenoscopy performed on November 7, 2025, revealed hyperemic and edematous mucosa in the gastric fundus and corpus. Histopathological

examination of biopsy specimens demonstrated chronic gastritis with marked inflammation and moderate activity, negative for *Helicobacter pylori.* No atrophy, intestinal metaplasia, or dysplasia was reported.

Colonoscopy on November 11, 2025, identified a patchy ulceration approximately 1 cm in diameter with hyperemic borders in the sigmoid colon at 20 cm. In the rectum, at 8-10 cm from the anal verge, a circumferential, friable ulcer with an irregular base was observed, highly suspicious for malignancy (Figure 1). Multiple biopsies were obtained from both lesions.

Dr. Nazmi Demirel: The endoscopic findings strongly suggested a primary rectal malignancy. However, on November 22, 2025, the patient's clinical status deteriorated acutely. She developed fever (38.5°C), tachycardia (102 beats per minute), and tachypnea (22 breaths per minute). Laboratory evaluation revealed leukocytosis (14.2 K/μL; reference range 4.5-11.0) and markedly elevated C-reactive protein (92 mg/L; reference <5).

Dr. Süleyman Bahar (Infectious Diseases): Blood and urine cultures were obtained to identify the source of fever. On November 24, 2025, urine culture demonstrated growth of extended-spectrum beta-lactamase (ESBL)-producing *Klebsiella pneumoniae*, with accompanying leukocyte esterase and nitrite positivity. Antimicrobial susceptibility testing revealed resistance to penicillins (ampicillin), penicillin-beta-lactamase inhibitor combinations (amoxicillin-clavulanate), and all tested cephalosporins (cefazolin, ceftriaxone). The isolate remained susceptible to carbapenems (meropenem), aminoglycosides (amikacin, gentamicin), and fluoroquinolones (ciprofloxacin). Blood cultures showed no growth.

Dr. Süleyman Bahar:Intravenous meropenem (3×1 g daily) was initiated for treatment of the complicated urinary tract infection. Despite appropriate antibiotic therapy, the patient's clinical condition continued to deteriorate. Serial laboratory investigations over subsequent days revealed a cascade of metabolic and hematologic abnormalities (Table 1).

Table 1. Selected Laboratory Parameters Over Time

Date	Parameter (Unit)	Result	Reference Range
Nov 22, 2025	Erythrocyte Sedimentation Rate (mm/h)	**112**	0–20
Nov 24, 2025	Arterial Blood Gas – Potassium (mmol/L)	**2.5**	3.5–5.0
	Arterial Blood Gas – Bicarbonate (mmol/L)	**31.8**	24–28
Nov 27, 2025	Hemoglobin (g/dL)	**8.9**	12.0–16.0
	Mean Corpuscular Volume (fL)	101	80–100
	C-Reactive Protein (mg/L)	**92.8**	<5.0
	Serum Albumin (g/L)	**24.7**	35–50
	International Normalized Ratio	**1.67**	0.9–1.2
Nov 28, 2025	Serum Ammonia (μmol/L)	**149**	11–35
Nov 29, 2025	High-Sensitivity Troponin I (ng/L)	**20.3**	<14

Notable abnormalities included: macrocytic anemia (MCV 101 fL) with progressive hemoglobin decline; hypoalbuminemia indicating malnutrition and chronic disease; persistent severe systemic inflammation (elevated CRP and ESR); hypokalemia with compensated metabolic alkalosis; marked hyperammonemia despite normal liver enzyme levels; and elevated troponin suggesting myocardial injury.

(Radiology): Contrast-enhanced thoracoabdominal computed tomography performed on November 29, 2025, to evaluate for metastatic disease and abdominal complications revealed: bilateral pleural effusions; moderate ascites in the hepatorenal and splenorenal spaces; colonic distension extending to the cecum; and rectal wall thickening. A 30 mm well-circumscribed, homogeneous, fat-density lesion (-10 to -20 Hounsfield units) was identified in the pancreatic tail, consistent with either a pancreatic pseudocyst or intrapancreatic lipoma. No focal liver lesions suspicious for metastases were identified.

Dr. Ergün Öztaş: On December 9, 2025, the patient developed progressive dyspnea and tachypnea. Arterial blood gas analysis demonstrated persistent metabolic alkalosis (HCO3- 31.6 mmol/L) with worsening hypoxemia (PaO2 67 mmHg, oxygen saturation 90.7% on room air). Despite intensive care unit admission and aggressive supportive measures, the patient's clinical status continued to decline with progressive hepatic and cardiac decompensation. She developed overt hepatic encephalopathy, worsening coagulopathy, and refractory hypotension requiring vasopressor support. The patient expired on December 15, 2025.

CLINICAL REASONING

This complex case illustrates the challenge of managing multiple interacting pathophysiological processes in an elderly patient with significant baseline comorbidities. We can conceptualize the clinical picture through three interconnected domains:

1. Primary Gastrointestinal Pathology: The circumferential, friable rectal ulcer observed on colonoscopy is highly suspicious for primary rectal adenocarcinoma . The sigmoid colon ulceration may represent a synchronous lesion, an inflammatory change, or a separate pathological process. The presence of ascites on CT imaging raises concern for peritoneal carcinomatosis; however, the differential diagnosis must also include transudative ascites secondary to hypoalbuminemia and heart failure. Paracentesis would have been essential for definitive differentiation.

2. Infectious Complications: The development of urosepsis due to ESBL-producing *K. pneumoniae*significantly contributed to the systemic inflammatory response syndrome (SIRS), explaining the elevated acute-phase reactants (CRP, ESR, leukocytosis) and likely exacerbating metabolic instability. ESBL-producing organisms represent a growing therapeutic challenge, particularly in elderly patients with multiple comorbidities .

3. Metabolic, Nutritional, and Cardiac Decompensation:

- Hypokalemia and Metabolic Alkalosis: The etiology of this acid-base disturbance is likely multifactorial, potentially including gastrointestinal losses from nausea/vomiting related to the underlying malignancy or gastritis, poor nutritional intake, and diuretic therapy for heart failure.

- Hyperammonemia: The development of significant hyperammonemia in the setting of normal liver enzymes and absence of radiographic liver metastases is particularly noteworthy. Potential mechanisms include: a) occult hepatic dysfunction secondary to micrometastatic disease; b) portosystemic shunting due to tumor involvement of the portal venous system; c) systemic ammonia loading from the urease-positive K. Pneumoniae urinary tract infection; and d) small intestinal bacterial overgrowth (SIBO) secondary to colonic distension and dysmotility, which may have contributed to increased ammonia production .

- Hematologic Abnormalities: The combination of macrocytic anemia and thrombocytopenia raises consideration of nutritional deficiencies (B12, folate), anemia of chronic disease, or bone marrow infiltration (myelophthisis) from metastatic malignancy.

- Troponin Elevation: The elevated troponin level in this clinical context most likely represents Type 2 myocardial infarction (demand ischemia) resulting from increased myocardial oxygen demand in the setting of severe anemia, infection, and tachycardia. This finding underscores the limited cardiac reserve in this patient with pre-existing heart failure and the importance of multidisciplinary management .

MANAGEMENT AND FOLLOW-UP

The patient was managed concurrently by a multidisciplinary team:

- Infectious Diseases: Intravenous meropenem (3×1 g daily) was continued based on susceptibility testing, with a planned 14-day course.

- Nephrology/Internal Medicine: Severe hypokalemia was aggressively corrected with intravenous potassium chloride infusion under close monitoring. The etiology of hyperammonemia was investigated with portal vein Doppler ultrasonography, which revealed no evidence of overt portosystemic shunting. Lactulose was initiated for symptomatic management of hyperammonemia.

- Cardiology: Cardiology consultation confirmed Type 2 myocardial infarction on the basis of echocardiography demonstrating preserved left ventricular function. The patient was maintained on close hemodynamic monitoring.

- Nutritional Support: Clinical nutrition services initiated high-protein enteral nutrition support for hypoalbuminemia and malnutrition.

- Medical Oncology/Gastroenterology: Rectal biopsy results were pending at the time of clinical deterioration. Definitive oncologic management (including staging with pelvic MRI and PET-CT, and consideration of neoadjuvant chemoradiotherapy or surgery) could not be pursued due to the patient's rapidly declining clinical status.

- Intensive Care: The patient was transferred to the intensive care unit on December 10, 2025, for management of progressive hepatic encephalopathy, refractory hypotension requiring vasopressor support, and worsening respiratory failure. Despite maximal supportive care, including continuous renal replacement therapy for ammonia control and mechanical ventilation, the patient expired on December 15, 2025.

DISCUSSION

This case represents a perfect storm of geriatric medical complexity, illustrating the challenges inherent in managing elderly patients with multimorbidity . Several critical considerations emerge from this case:

Delayed Diagnosis and Treatment Initiation: The presence of multiple comorbidities (heart failure, diabetes, obesity) may have masked or delayed recognition of the underlying rectal malignancy. Elderly patients with colorectal cancer often present with more advanced disease and experience delayed diagnoses compared to younger populations . In this case, the biopsy results confirming malignancy were pending at the time of clinical deterioration, precluding timely oncologic intervention.

Infection with Multidrug-Resistant Organisms: The isolation of ESBL-producing K. pneumoniae in this patient is consistent with the increasing global prevalence of multidrug-resistant organisms . As illustrated by patient stories from the European Centre for Disease Prevention and Control, such infections can have devastating consequences, particularly in vulnerable populations . The presence of an indwelling urinary catheter (for management of diuresis in heart failure) may have increased the risk of healthcare-associated infection.

Progressive Liver Failure and Hyperammonemia: The development of hyperammonemia and subsequent hepatic encephalopathy in this patient was likely multifactorial. Recent guidelines emphasize the importance of identifying and treating precipitants of hepatic encephalopathy, including infection, gastrointestinal bleeding, and metabolic disturbances . In this case, potential contributors included sepsis, possible small intestinal bacterial overgrowth secondary to colonic dysmotility, and occult liver dysfunction. Continuous renal replacement therapy, recommended for ammonia control in acute liver failure, was employed but ultimately insufficient to reverse the clinical trajectory .

Cardiac Complications:The elevated troponin level and subsequent hemodynamic instability reflect the vulnerability of the failing heart to systemic stressors. Elderly patients with pre-existing cardiac disease are at particular risk for Type 2 myocardial infarction during acute illness .

Critical Analysis of Clinical Management: In retrospect, several questions arise regarding potential missed opportunities in this patient's management:

1. Earlier comprehensive geriatric assessment: Comprehensive Geriatric Assessment (CGA) has been shown to improve outcomes in elderly cancer patients by identifying frailty, predicting treatment

tolerance, and guiding individualized care plans . In this case, earlier CGA might have identified the patient's high-risk status and prompted more aggressive upfront intervention.

2. Proactive nutritional support: Despite initiation of nutritional support, the patient's profound hypoalbuminemia and malnutrition may have been addressed more aggressively earlier in the clinical course.

3. Aggressive ammonia management:While lactulose was initiated and continuous renal replacement therapy ultimately employed, earlier consideration of these interventions might have altered the trajectory of hepatic encephalopathy.

4. Multidisciplinary tumor board review: Earlier discussion of this case in a multidisciplinary tumor board (including medical oncology, radiation oncology, surgery, and geriatrics) might have facilitated more rapid diagnostic confirmation and treatment planning.

Limitations:This case report has several limitations. The absence of final histopathological confirmation of rectal malignancy represents a significant gap. Additionally, the lack of paracentesis for ascites analysis limits definitive characterization of the ascites etiology. Finally, the retrospective nature of this analysis precludes definitive conclusions about causal relationships.

FINAL DIAGNOSIS

(Based on clinical findings and available data; pending final histopathological confirmation)

1. Suspected primary rectal adenocarcinoma (circumferential ulcer with malignant appearance on colonoscopy)

2. ESBL-producing Klebsiella pneumoniae complicated urinary tract infection** with urosepsis

3. Decompensated heart failure with Type 2 myocardial infarction (demand ischemia)

4. Progressive liver failure with hyperammonemia and hepatic encephalopathy, likely multifactorial (sepsis, possible small intestinal bacterial overgrowth, occult hepatic dysfunction)

5. Hypokalemic metabolic alkalosis

6. Malnutrition (hypoalbuminemia, macrocytic anemia, thrombocytopenia)

7. Chronic active gastritis, H. pylori negative

8. Morbid obesity

9. Type 2 diabetes mellitus

10. Hypertension

CONCLUSIONS AND CLINICAL PEARLS

This case illustrates the formidable challenges of managing concurrent malignancy, multidrug-resistant infection, and progressive organ failure in an elderly patient with significant baseline comorbidities. Key lessons include:

1. Multidisciplinary management is essential for elderly patients with complex multimorbidity. Early involvement of geriatrics, infectious diseases, cardiology, nephrology, and oncology is critical .

2. Comprehensive Geriatric Assessment should be considered in all elderly cancer patients to identify frailty, guide treatment decisions, and optimize outcomes .

3. Multidrug-resistant infections represent an increasing threat in vulnerable populations and require prompt recognition and appropriate antibiotic selection based on susceptibility testing

4. Hyperammonemia in the setting of normal liver enzymes should prompt consideration of multiple potential etiologies, including infection with urease-positive organisms, portosystemic shunting, and small intestinal bacterial overgrowth .

5. Early recognition of clinical deterioration and timely transfer to intensive care are essential for optimizing outcomes in critically ill patients with multiorgan dysfunction.

6. Advance care planning and goals of care discussions should be initiated early in the course of serious illness, particularly in elderly patients with multiple comorbidities and suspected malignancy.

The death of this patient underscores the devastating consequences that can ensue when multiple disease processes converge in a vulnerable host. Future efforts should focus on early identification of high-risk elderly patients, aggressive management of modifiable risk factors, and development of integrated care pathways that address the unique needs of this growing population.

PATIENT PERSPECTIVE

The patient's family expressed gratitude for the efforts of the medical team and noted that the patient had been experiencing significant fatigue and discomfort in the months preceding admission. They appreciated the team's communication throughout the hospitalization and were present at the time of death.

DECLARATION

- Ethics Approval and Consent to Participate: Written informed consent was obtained from the patient's next of kin for publication of this case report and any accompanying images.

- Conflict of Interest: The authors declare no conflicts of interest.

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REFERENCES

1. Sung H, Ferlay J, Siegel RL, et al. (2021). Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA*: A Cancer Journal for Clinicians*, 71(3), 209-249. https://doi.org/10.3322/caac.21660

2. Papamichael D, Audisio RA, Glimelius B, et al. (2015). Treatment of colorectal cancer in olderpatients:InternationalSocietyofGeriatricOncology(SIOG)consensus recommendations2013. *Annals of Oncology,* 26(3), 463-476. https://doi.org/10.1093/annonc/mdu

3. Boccaccino A, et al. (2025). Management of Elderly Colorectal Cancer Patients: A Comprehensive Review Encompassing Geriatric Assessment. *Cancers*, 17(20), 3336. https://doi.org/10.3390/cancers17203336

4. European Centre for Disease Prevention and Control. (2024). Patient story: Yira. *European Antibiotic Awareness Day*. https://antibiotic.ecdc.europa.eu/en/patient-story-yira

5. Kronsten VT, Kibble H, Elliott J, et al. (2025). Hepatic encephalopathy: Part 2, inpatient management. *Frontline Gastroenterology*. https://doi.org/10.1136/flgastro-2025-103330

6. Extermann M, Aapro M, Bernabei R, et al. (2005). Use of comprehensive geriatric assessment in older cancer patients: Recommendations from the task force on CGA of the International Society of Geriatric Oncology (SIOG). *Critical Reviews in Oncology/Hematology,* 55(3), 241-252. https://doi.org/10.1016/j.critrevonc.2005.06.003

7. Balducci L, Extermann M. (2000). Management of cancer in the older person: A practical approach. *The Oncologist,* 5(3), 224-237. https://doi.org/10.1634/theoncologist.5-3-224

8. Price TJ, Zannino D, Wilson K, et al. (2012). Bevacizumab is equally effective and no more toxic in elderly patients with advanced colorectal cancer: A subgroup analysis from the AGITG MAX trial. *Annals of Oncology*, 23(6), 1531-1536. https://doi.org/10.1093/annonc/mdr488

9. Rostkowska OM, Międzybrodzki R, Miszewska-Szyszkowska D, et al. (2021). Treatment of recurrent urinary tract infections in a 60-year-old kidney transplant recipient: The use of phage therapy. Transplant Infectious Disease, 23(1), e13391. https://doi.org/10.1111/tid.13391

10. Podschun R, Ullmann U. (1998). Klebsiella spp. as nosocomial pathogens: Epidemiology, taxonomy, typing methods, and pathogenicity factors. *Clinical Microbiology Reviews*, 11(4), 589-603. https://doi.org/10.1128/CMR.11.4.589

-Figure Legends

Figure 1.Colonoscopic image demonstrating a circumferential, friable ulcer with irregular borders in the rectum at 8-10 cm from the anal verge, highly suspicious for malignancy.

Figure 2. Contrast-enhanced computed tomography image showing: (A) bilateral pleural effusions; (B) moderate ascites; (C) fat-density lesion in the pancreatic tail; (D) rectal wall thickening.

AUTOMATED SYSTEMS USED IN BACTERIAL IDENTIFICATION AND THEIR WORKING PRINCIPLES

Husameddin ASIDE

Inonu University, Faculty of Pharmacy, Malatya, TURKIYE, ORCID ID:0009-0002-9646-846X

Tuba UNVER

Inonu University, Faculty of Pharmacy, Department of Pharmaceutical Microbiology, Malatya, TURKIYE, ORCID ID:0000-0002-8655-2716

ABSTRACT

Aim: This study aims to evaluate the main conventional and modern methods used in bacterial identification, particularly by comparing the working principles, advantages, and limitations of automated biochemical systems, Matrix-Assisted Laser Desorption/Ionization - Time-of-Flight (MALDI-TOF MS), Rapid Evaporative Ionization Mass Spectrometry (REIMS), molecular methods, and artificial intelligence-supported approaches.

Material and Method: In this study, current and fundamental sources in the literature were examined; culture-based methods, Gram staining, biochemical tests, automated biochemical systems, mass spectrometry-based methods, and molecular approaches were evaluated. Priority was given to current sources, but fundamental sources that explain the development process and the subject's basic working principles were also used.

Results: The data examined showed that while conventional methods allow the isolation of live pathogens, they are time-consuming; automated biochemical systems offer significant advantages for routine laboratory applications and for integrating antibiotic susceptibility testing. MALDI-TOF MS has been shown to offer significant advantages in speed and accuracy, whereas REIMS, although promising for rapid, direct analysis, is still under development. Molecular methods offer high sensitivity and specificity but are often considered complementary to other methods due to their cost and technical infrastructure requirements.

Conclusion: The most appropriate approach in clinical microbiology laboratories should be determined based on the laboratory's technical infrastructure, sample volume, personnel experience, and clinical requirements.

Keywords: Bacterial identification, Clinical microbiology, MALDI-TOF MS, Molecular methods, Automated systems

1. INTRODUCTION

Bacterial infections pose a significant threat to global public health due to the prevalence of both hospital-acquired and community-acquired pathogens.[1] In critical clinical situations, particularly bacteremia and sepsis, rapid identification of the causative microorganism and early initiation of appropriate antimicrobial treatment are crucial for preventing serious complications.[2,3] Since delays in effective antibiotic treatment in septic shock have been shown to increase mortality, shortening the diagnostic time is considered a clinically important requirement.[4]

The increasing global burden of antibiotic resistance has made the need for rapid, reliable diagnostic approaches that detect the causative agent and resistance patterns more apparent.[5,6] The limited use of rapid diagnostic tests can make it difficult to obtain early data on the causative microorganism and susceptibility to guide appropriate treatment; This situation can particularly increase the tendency towards empirical broad-spectrum antibiotic use in severe infections.[3,7,8]

Clinical microbiology laboratories have for many years relied on traditional approaches based on culture, Gram staining, microscopic examination, and biochemical/phenotypic tests for bacterial identification.[9,10] While these methods form the basis of classical microbiology, the time required for

results can be prolonged due to the need for culture and phenotypic evaluation, and interpretation by experienced personnel may be required at some stages. In addition, most traditional methods do not directly detect genetic markers of antibiotic resistance; additional culture and time are required to obtain phenotypic results.[11] These limitations have increased the need for faster, standardized, and automated systems in bacterial identification.[8]

In line with this need, automation-based approaches have become increasingly important in clinical microbiology laboratories. Automated biochemical systems such as VITEK 2, BD Phoenix, and MicroScan WalkAway offer bacterial identification and, in many cases, antimicrobial susceptibility assessment via standardized panel or card structures.[12–16] MALDI-TOF MS is an important technology that provides rapid, highly accurate identification by analyzing the protein profiles of microorganisms.[17,18] In addition, REIMS, molecular diagnostic approaches, and artificial intelligence-supported applications are considered as complementary or emerging technologies in the bacterial identification process.[19–22]

The aim of this review is to examine the main automated systems used for bacterial identification and their basic operating principles. In this context, mass spectrometry-based approaches such as automated biochemical systems, MALDI-TOF MS, and REIMS are discussed, and traditional, molecular, and artificial intelligence-supported methods are addressed in a comparative and complementary framework with automated systems.

2. METHODS

2.1. A Brief Overview of Traditional Methods and the Need for Automation

Clinical microbiology laboratories play a fundamental role in the identification of bacterial agents and in guiding antimicrobial therapy. The traditional diagnostic process includes obtaining an appropriate clinical sample, inoculating it onto suitable culture media, evaluating microbial growth after incubation, and identifying the microorganism by microscopic examination and biochemical or other phenotypic characteristics.[9,10] In this context, blood culture, Gram staining, microscopic examination, biochemical identification tests, and antibiotic susceptibility testing have been used as the basic steps in bacterial diagnosis for many years. Blood culture, in particular, enables detection of the causative microorganism in bloodstream infections, while Gram staining provides rapid preliminary information, contributing to early guidance for empirical treatment. Biochemical tests enable phenotypic identification based on the metabolic and enzymatic characteristics of bacteria. Antibiotic susceptibility testing is also important for determining the susceptibility of isolated bacteria to antimicrobial agents, thereby facilitating the selection of appropriate treatment and the monitoring of resistance patterns.[23,24]

However, since most conventional methods rely on the growth of live microorganisms, obtaining pure cultures, and incubation processes, the diagnostic process can be lengthy.[8,20] The completion of culture-based identification and susceptibility testing often takes 24–72 hours, which can delay targeted therapy, especially in conditions requiring rapid clinical decisions, such as bacteremia, sepsis, and septic shock. Since it has been shown that delays in effective antibiotic treatment in septic shock can increase the risk of mortality, shortening the diagnostic time is considered a clinically important requirement.[4] In addition, the diagnostic yield of conventional methods may be limited in microorganisms that grow slowly, are difficult to culture, or do not have distinct phenotypic characteristics; interpreting some results may require experienced personnel. These limitations have increased the need for faster, standardized, traceable, and automated systems for bacterial identification.[8,20]

2.2. Automatic Identification Systems and Working Principles

2.2.1. The Role of Automation in Clinical Microbiology Laboratories

Automation in clinical microbiology laboratories is considered a significant development that strengthens the standardization of culture-based workflows and increases laboratory efficiency. Automated systems contribute to a more organized, traceable, and repeatable workflow by reducing reliance on manual processes, especially in laboratories with high sample volumes.[12–14] However, because implementing these systems requires significant initial investment, workflow restructuring, and personnel training, the benefits should be evaluated in light of each laboratory's technical infrastructure and clinical requirements.[12,13]

2.2.2. Automated Biochemical Systems

Automated biochemical systems can perform bacterial identification and, on some platforms, antimicrobial susceptibility testing on the same device. In these systems, after inoculating a standardized bacterial suspension prepared from a pure culture onto reaction cards or panels, the biochemical, optical, fluorogenic, chromogenic, or redox-based signals generated during incubation are automatically recorded and analyzed by the device. Species-level identification can be performed using the obtained reaction patterns; antimicrobial susceptibility assessment can be carried out by determining the MIC and interpreting it based on growth kinetics or broth microdilution.[15,16,25,26]

VITEK 2, BD Phoenix, and MicroScan WalkAway are among the leading automated biochemical systems widely used in this field. VITEK 2 evaluates biochemical reactions and growth responses to certain antimicrobial agents using miniaturized cards, while BD Phoenix can perform identification and susceptibility testing using panels containing dried reagents. MicroScan WalkAway is one of the systems that enable bacterial identification and antimicrobial susceptibility assessment, with a panel-based structure and device options suitable for laboratories of different scales.[15,16,25–28] Although various studies have reported that these systems can generally provide reliable results in frequently encountered clinical isolates, additional validation may be required in some problematic isolates, species showing similar phenotypic characteristics, and clinically critical resistance phenotypes.[26,27]

2.2.3. Matrix-Assisted Laser Desorption/Ionization - Time-of-Flight (MALDI-TOF MS)

Matrix-Assisted Laser Desorption/Ionization - Time-of-Flight (MALDI-TOF MS) is a proteomic method widely used in clinical microbiology laboratories today, enabling rapid and accurate identification of bacteria and yeasts isolated from culture.[17,18,29] The basic principle of the method is to analyze the mass-to-charge ratios of the microorganism's proteins and compare the resulting spectral profile with reference spectra in the database.[18,29] While direct colony spreading is sufficient for many bacteria, additional extraction steps may be required to obtain higher quality spectra for some Gram-positive bacteria, yeasts, and problematic isolates.[29]

The main advantages of MALDI-TOF MS in routine use are its ability to deliver results within minutes, its high sample-processing capacity, and its low cost per isolate after the initial equipment investment.[17,18,30] However, because identification success is closely related to the database's scope and spectral quality, additional steps may be required for species underrepresented in the database or for closely related microorganisms. Verification may be required. Furthermore, because the method does not provide detailed antimicrobial susceptibility data for routine use, it should be evaluated alongside conventional susceptibility testing or, when necessary, complementary molecular analyses.[18,29]

2.2.4. Rapid Evaporative Ionization Mass Spectrometry (REIMS)

Rapid Evaporative Ionization Mass Spectrometry (REIMS) is a mass spectrometry method based on medium ionization that allows the analysis of microorganisms growing in culture without requiring detailed pre-processing. The method relies on evaluating the spectral profiles of ionized molecules in an aerosol formed by local heating. These profiles, which are particularly lipid-weighted, are evaluated in microorganism identification using statistical classification models and reference datasets.[19,31] Minimal sample preparation, direct analysis from culture plates, and quick results are among the main advantages of the method.[19]

However, REIMS performance can be affected by the classification model used, the scope of the reference dataset, culture conditions, and equipment infrastructure. In addition, requirements for data analysis, laboratory integration, and clinical standardization may limit the method's transition to routine clinical use. Therefore, although REIMS is a promising approach in clinical microbiology, it is considered a technology that requires additional validation and standardization studies for widespread routine application.[19,31]

2.3. Comparative Molecular Diagnostic Approaches with Automated Systems

Molecular and nucleic acid-based diagnostic methods are gaining increasing importance in clinical situations where rapid pathogen detection is necessary. These methods can target specific bacterial DNA or RNA sequences, enabling culture-independent detection of pathogens or faster identification of pathogens from positive cultures.[20,32] PCR-based tests and multiplex molecular panels can support

targeted treatment decisions by quickly detecting multiple microorganisms and selected resistance markers.[32,33] However, the clinical use of these methods is affected by factors such as cost, technical infrastructure, expertise requirements, and the accurate interpretation of results in a clinical context. Furthermore, the fact that the diagnostic scope of panel-based tests is limited to targeted pathogens and resistance markers, that non-panel agents cannot be detected, and that genotypic results do not always fully correspond with phenotypic resistance constitute significant limitations.[11,33,34] Therefore, molecular methods are considered complementary tools that support rapid and sensitive diagnosis in clinical microbiology, but they often need to be evaluated alongside culture-based and automated systems.[20,32]

NGS is an advanced molecular method that provides comprehensive analysis of the genetic material of microorganisms. This approach can provide information on species identification, resistance genes, virulence markers, and phylogenetic relationships.[35] In clinical microbiology, it can contribute particularly to the evaluation of resistance mechanisms, outbreak relationships, and some infections that cannot be explained by culture. However, due to high cost, technical infrastructure requirements, the need for bioinformatic analysis, and difficulty in clinical interpretation, its routine use remains limited; currently, it seems more suitable for advanced diagnostic investigations and referral centers.[35]

Table 1. Comparative summary of the main diagnostic approaches.

Method	Main principle	Advantage	Disadvantage
Traditional culture and biochemistry	Reproduction, colony morphology, and phenotypic reactions	Obtaining live isolates; workflow compatible with AST	Long result time; dependence on experience
Automated biochemical systems	Optical or biochemical analysis of card/panel reactions	Standardization, high sample capacity, AST integration	Panel/database scope, validation requirement
MALDI-TOF MS	Comparison of protein spectra with the database	Fast and accurate identification in minutes	Dependence on database coverage and spectrum quality
REIMS	Lipid-weighted spectral profile and statistical classification	Minimal sample preparation and the potential for direct analysis	Standardization requirement for routine use
Molecular methods	Amplification or sequencing of DNA/RNA targets	High sensitivity, early detection of resistance genes	Cost, panel scope, and difficulty in clinical interpretation

2.4. New Technologies and Artificial Intelligence in the Development of Automated Systems

The increasing digitalization of clinical microbiology laboratories has enabled the systematic processing of large, multivariate datasets; this has made artificial intelligence and machine learning-based approaches more visible in laboratory applications.[21,36] Machine learning algorithms can classify new samples or predict specific outcomes by learning patterns from labeled data. Therefore, they have significant potential in image analysis, spectral data evaluation, and decision support processes.[21,36]

AI-supported approaches are showing promising results, particularly in the automated interpretation of Gram-stained preparations and advanced processing of MALDI-TOF MS data. Deep learning models can contribute to the differentiation of basic bacterial groups by analyzing morphological features in microscopic images; machine learning models can generate additional predictions regarding the probability of antimicrobial resistance from peak patterns in MALDI-TOF MS spectra.[22,36] However, model performance can vary depending on laboratories, instrument platforms, and time; Data quality, standardization, external validation, and adaptation to local workflows are highlighted. Therefore, at the

current stage, it seems more appropriate to consider AI-based systems as auxiliary systems supporting expert evaluation rather than independent decision-making tools.[21,22,36]

2.5. Clinical and Economic Evaluation of Automated Identification Systems

In evaluating bacterial identification systems, not only analytical accuracy but also the contribution of the results to the clinical decision-making process, their impact on laboratory workflow, and economic outcomes should be considered.[7,8,37] While traditional culture-based methods have some advantages, such as low technology requirements, they can make it difficult to arrange appropriate antimicrobial treatment in a timely manner due to long turnaround times and labor-intensive workflows.[8] The fact that delayed initiation of effective treatment in severe infections has been shown to be associated with more negative clinical outcomes further highlights the clinical importance of diagnostic time.[4]

In contrast, the integrated use of rapid diagnostic approaches with antimicrobial stewardship programs has been associated with shorter time to access appropriate treatment, reduced hospital stays, and, in some studies, better clinical outcomes.[3,7,37] Automated biochemical systems and MALDI-TOF MS offer significant operational advantages over conventional methods, including shorter identification times and improved laboratory workflows. The economic value of MALDI-TOF MS is not limited solely to the device investment cost; its ability to shorten identification time, enable more efficient use of laboratory resources, and contribute to the treatment process through appropriate clinical integration should also be considered.[18,30,38] Therefore, the true value of rapid diagnostic technologies should be evaluated not only in terms of device cost but also in terms of their overall impact on diagnosis time, antibiotic use, hospital stay, and patient outcomes.[3,7,37]

3. CONCLUSION

Methods used in bacterial identification play a significant role in clinical microbiology laboratories by accelerating the diagnostic process, increasing standardization, and guiding appropriate antimicrobial treatment. The data examined in this review show that no single system constitutes an ideal solution in terms of all criteria; method selection should be evaluated not only on the basis of analytical accuracy, but also within a multi-dimensional framework including speed, clinical benefit, cost, technical infrastructure requirements, database dependence, personnel experience, contribution to laboratory workflow, and integration of antibiotic susceptibility testing. While traditional methods remain important for isolating live pathogens and enabling further investigation, the need for culture and incubation prolongs the diagnostic process and is a significant limitation, especially in situations requiring rapid clinical decisions, such as bacteremia, sepsis, and septic shock. Automated biochemical systems offer significant advantages, particularly in routine laboratory applications, by providing both identification and antibiotic susceptibility testing; however, additional validation may be required for problematic isolates, species exhibiting similar phenotypic characteristics, and critical resistance phenotypes. MALDI-TOF MS stands out in terms of speed and accuracy due to its ability to provide results within minutes, high sample capacity, and accurate identification of numerous microorganisms with its suitable database; however, it needs to be evaluated in conjunction with complementary methods because it does not provide detailed antibiotic susceptibility information, and its discriminatory power may be limited in some closely related species. REIMS attracts attention for its potential for rapid, direct analysis, but it is currently considered a developing technology due to the need for standardization, data analysis, a reference database, and clinical validation. Molecular methods enable rapid detection of pathogens and selected resistance markers through PCR-based tests and multiplex panels; however, their target dependence, inability to detect off-panel agents, and the fact that genotypic results do not always fully reflect phenotypic counterparts constitute significant limitations. Although NGS provides more comprehensive data, it currently seems better suited to advanced diagnostic investigations and reference centers due to its high cost and the need for bioinformatics infrastructure. While AI-powered approaches are promising, particularly in image analysis and advanced processing of MALDI-TOF MS data, their reliable use in routine laboratory applications requires external validation, standardization, and reproducibility studies across different centers. Consequently, it is considered that the most appropriate approach for bacterial identification should be determined by the laboratory's technical infrastructure, sample volume, economic resources, personnel qualifications, and clinical requirements, and that complementary technologies should be used together when necessary. Therefore, it is recommended that

studies aimed at developing more integrated, accessible, standardized, and clinically beneficial systems in the future be supported.

REFERENCES

1. Ikuta KS, Swetschinski LR, Robles Aguilar G, et al. Global mortality associated with 33 bacterial pathogens in 2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet*. 2022;400(10369):2221-2248. doi:10.1016/S0140-6736(22)02185-7
2. Evans L, Rhodes A, Alhazzani W, et al. Surviving Sepsis Campaign: international guidelines for management of sepsis and septic shock 2021. *Intensive Care Med*. 2021;47(11):1181-1247. doi:10.1007/s00134-021-06506-y
3. Perez KK, Olsen RJ, Musick WL, Cernoch PL, Davis JR, Peterson LE, Musser JM. Integrating rapid diagnostics and antimicrobial stewardship improves outcomes in patients with antibiotic-resistant Gram-negative bacteremia. *J Infect*. 2014;69(3):216-225. doi:10.1016/j.jinf.2014.05.005
4. Kumar A, Roberts D, Wood KE, et al. Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. *Crit Care Med*. 2006;34(6):1589-1596. doi:10.1097/01.CCM.0000217961.75225.E9
5. GBD 2021 Antimicrobial Resistance Collaborators. Global burden of bacterial antimicrobial resistance 1990–2021: a systematic analysis with forecasts to 2050. *Lancet*. 2024;404(10459):1199-1226. doi:10.1016/S0140-6736(24)01867-1
6. World Health Organization. *2023 Antibacterial Agents in Clinical and Preclinical Development: An Overview and Analysis*. World Health Organization; 2024.
7. Timbrook TT, Morton JB, McConeghy KW, Caffrey AR, Mylonakis E, LaPlante KL. The effect of molecular rapid diagnostic testing on clinical outcomes in bloodstream infections: a systematic review and meta-analysis. *Clin Infect Dis*. 2017;64(1):15-23. doi:10.1093/cid/ciw649
8. Caliendo AM, Gilbert DN, Ginocchio CC, et al. Better tests, better care: improved diagnostics for infectious diseases. *Clin Infect Dis*. 2013;57(Suppl 3):S139-S170. doi:10.1093/cid/cit578
9. Jorgensen JH, Carroll KC, Funke G, Pfaller MA, Landry ML, Richter SS, Warnock DW, eds. *Manual of Clinical Microbiology*. 11th ed. ASM Press; 2015. doi:10.1128/9781555817381
10. Leber AL, ed. *Clinical Microbiology Procedures Handbook*. 4th ed. ASM Press; 2016. doi:10.1128/9781555818814
11. Banerjee R, Humphries R. Rapid antimicrobial susceptibility testing methods for blood cultures and their clinical impact. *Front Med*. 2021;8:635831. doi:10.3389/fmed.2021.635831
12. Antonios K, Croxatto A, Culbreath K. Current state of laboratory automation in clinical microbiology laboratory. *Clin Chem*. 2022;68(1):99-114. doi:10.1093/clinchem/hvab242
13. Burckhardt I. Laboratory automation in clinical microbiology. *Bioengineering*. 2018;5(4):102. doi:10.3390/bioengineering5040102
14. Croxatto A, Prod'hom G, Faverjon F, Rochais Y, Greub G. Laboratory automation in clinical bacteriology: what system to choose? *Clin Microbiol Infect*. 2016;22(3):217-235. doi:10.1016/j.cmi.2015.09.030
15. Beckman Coulter. *MicroScan WalkAway Plus System*. Beckman Coulter; 2025.
16. bioMérieux. *VITEK 2*. bioMérieux; 2025.
17. Seng P, Drancourt M, Gouriet F, et al. Ongoing revolution in bacteriology: routine identification of bacteria by matrix-assisted laser desorption ionization time-of-flight mass spectrometry. *Clin Infect Dis*. 2009;49(4):543-551. doi:10.1086/600885
18. Patel R. MALDI-TOF MS for the diagnosis of infectious diseases. *Clin Chem*. 2015;61(1):100-111. doi:10.1373/clinchem.2014.221770

19. Bolt F, Cameron SJS, Karancsi T, et al. Automated high-throughput identification and characterization of clinically important bacteria and fungi using rapid evaporative ionization mass spectrometry. *Anal Chem*. 2016;88(19):9419-9426. doi:10.1021/acs.analchem.6b01016

20. Mancini N, Carletti S, Ghidoli N, Cichero P, Burioni R, Clementi M. The era of molecular and other non-culture-based methods in diagnosis of sepsis. *Clin Microbiol Rev*. 2010;23(1):235-251. doi:10.1128/CMR.00043-09

21. Egli A, Schrenzel J, Greub G. Digital microbiology. *Clin Microbiol Infect*. 2020;26(10):1324-1331. doi:10.1016/j.cmi.2020.06.023

22. Weis C, Cuénod A, Rieck B, et al. Direct antimicrobial resistance prediction from clinical MALDI-TOF mass spectra using machine learning. *Nat Med*. 2022;28(1):164-174. doi:10.1038/s41591-021-01619-9

23. Clinical and Laboratory Standards Institute. *Performance Standards for Antimicrobial Susceptibility Testing*. 36th ed. CLSI supplement M100. Clinical and Laboratory Standards Institute; 2026.

24. European Committee on Antimicrobial Susceptibility Testing. *Breakpoint Tables for Interpretation of MICs and Zone Diameters*. Version 16.0. European Committee on Antimicrobial Susceptibility Testing; 2026.

25. Pincus DH. Microbial identification using the bioMérieux VITEK 2 system. In: Miller MJ, ed. *Encyclopedia of Rapid Microbiological Methods*. PDA/DHI; 2006:1-32.

26. Ligozzi M, Bernini C, Bonora MG, De Fatima M, Zuliani J, Fontana R. Evaluation of the VITEK 2 system for identification and antimicrobial susceptibility testing of medically relevant Gram-positive cocci. *J Clin Microbiol*. 2002;40(5):1681-1686. doi:10.1128/JCM.40.5.1681-1686.2002

27. Carroll KC, Glanz BD, Borek AP, Burger C, Bhally HS, Henciak S, Flayhart D. Evaluation of the BD Phoenix automated microbiology system for identification and antimicrobial susceptibility testing of Enterobacteriaceae. *J Clin Microbiol*. 2006;44(10):3506-3509. doi:10.1128/JCM.00994-06

28. McGregor A, Schio F, Beaton S, Boulton V, Perman M, Gilbert G. The MicroScan WalkAway diagnostic microbiology system: an evaluation. *Pathology*. 1995;27(2):172-176. doi:10.1080/00313029500169552

29. Clark AE, Kaleta EJ, Arora A, Wolk DM. Matrix-assisted laser desorption ionization-time of flight mass spectrometry: a fundamental shift in the routine practice of clinical microbiology. *Clin Microbiol Rev*. 2013;26(3):547-603. doi:10.1128/CMR.00072-12

30. Tran A, Alby K, Kerr A, Jones M, Gilligan PH. Cost savings realized by implementation of routine microbiological identification by matrix-assisted laser desorption ionization-time of flight mass spectrometry. *J Clin Microbiol*. 2015;53(8):2473-2479. doi:10.1128/JCM.00833-15

31. Strittmatter N, Rebec M, Jones EA, et al. Characterization and identification of clinically relevant microorganisms using rapid evaporative ionization mass spectrometry. *Anal Chem*. 2014;86(13):6555-6562. doi:10.1021/ac501075f

32. van Belkum A, Durand G, Peyret M, et al. Rapid clinical bacteriology and its future impact. *Ann Lab Med*. 2013;33(1):14-27. doi:10.3343/alm.2013.33.1.14

33. Messacar K, Parker SK, Todd JK, Dominguez SR. Implementation of rapid molecular infectious disease diagnostics: the role of diagnostic and antimicrobial stewardship. *J Clin Microbiol*. 2017;55(3):715-723. doi:10.1128/JCM.02264-16

34. BioFire Diagnostics LLC. *BIOFIRE Blood Culture Identification 2 Panel Instructions for Use*. BioFire Diagnostics LLC; 2022.

35. Gu W, Miller S, Chiu CY. Clinical metagenomic next-generation sequencing for pathogen detection. *Nat Rev Genet*. 2019;20(6):341-355. doi:10.1038/s41576-019-0113-7

36. Peiffer-Smadja N, Dellière S, Rodriguez C, et al. Machine learning in the clinical microbiology laboratory: has the time come for routine practice? *Clin Microbiol Infect*. 2020;26(10):1300-1309. doi:10.1016/j.cmi.2020.02.006

37. Goff DA, Jankowski C, Tenover FC. Using rapid diagnostic tests to optimize antimicrobial selection in antimicrobial stewardship programs. *Pharmacotherapy*. 2012;32(8):677-687. doi:10.1002/j.1875-9114.2012.01137.x

38. Tan KE, Ellis BC, Lee R, Stamper PD, Zhang SX, Carroll KC. Prospective evaluation of a matrix-assisted laser desorption ionization-time of flight mass spectrometry system in a hospital clinical microbiology laboratory for identification of bacteria and yeasts: a bench-by-bench study for assessing the impact on time to identification and cost-effectiveness. *J Clin Microbiol*. 2012;50(10):3301-3308. doi:10.1128/JCM.01405-12

ÖĞRETMENLERİN NÖROGELİŞİMSEL BOZUKLUKLAR KONUSUNDAKİ BİLGİ VE FARKINDALIKLARI: TÜRKİYE'DEKİ ÇALIŞMALARIN İNCELENMESİ

Cansu YATMAZ

Ankara Üniversitesi, Sağlık Bilimleri Enstitüsü, Çocuk Gelişimi ABD Doktora Öğrencisi, Ankara, Türkiye, ORCID: 0000-0003-2291-5546

Neriman ARAL

Ankara Üniversitesi, Sağlık Bilimleri Fakültesi, Çocuk Gelişimi Bölümü Öğretim Üyesi, Ankara, Türkiye, ORCID: 0000-0002-9266-938X

ÖZET

Çalışmada, Türkiye'deki öğretmenlerin nörogelişimsel bozukluklara (dikkat eksikliği ve hiperaktivite bozukluğu, otizm spektrum bozukluğu, zihinsel yetersizlikler, öğrenme güçlüğü) ilişkin bilgi ve farkındalık düzeyleri sistematik bir şekilde incelenmiştir. Sonuç olarak, Türkiye'de öğretmenlerin nörogelişimsel bozukluklara dair bilgi ve farkındalıklarını inceleyen 2025 yılına kadar olan araştırmaların bulguları, öğretmenlerin bu bozukluklara ilişkin bilgi düzeylerinin genelde düşük olduğunu, kavram yanılgılarının yaygın şekilde görüldüğünü ve hizmet içi eğitimlerin farkındalık ile bilgi düzeyinin artırılmasında etkili bir araç olduğunu ortaya koymaktadır. Özellikle formal eğitim eksiklikleri, erken tanı ve bireyselleştirilmiş eğitim süreçlerinde yetersizliklere yol açmaktadır. Öğrenim düzeyi, mesleki deneyim ve alınan eğitimler bilgi düzeyini olumlu etkilerken, sınıf kapasitelerinin yüksekliği ve destek mekanizmalarının sınırlılığı bu gelişimi kısıtlamaktadır. Bu doğrultuda, nörogelişimsel bozukluklara yönelik lisans programlarının içeriklerinin güçlendirilmesi, hizmet içi eğitimlerin kapsam ve niteliğinin artırılması, uygulamaya dayalı eğitim fırsatlarının yaygınlaştırılması, bireyselleştirilmiş öğretim süreçlerinin etkin biçimde desteklenmesi ve farkındalık artırıcı eğitim materyalleri ile kaynakların erişilebilirliğinin artırılması önerilmektedir.

Anahtar Kelimeler: Nörogelişim, Nörogelişimsel bozukluklar, öğretmen bilgi düzeyi, öğretmen farkındalığı

ABSTRACT

The study systematically examined the levels of knowledge and awareness among teachers in Turkey regarding neurodevelopmental disorders (attention-deficit/hyperactivity disorder, autism spectrum disorder, intellectual disabilities, and specific learning disorders). As a result, the findings of studies conducted through 2025 that examined teachers' knowledge and awareness of neurodevelopmental disorders in Turkey indicate that teachers' knowledge levels regarding these disorders are generally low, misconceptions are widespread, and in-service training is an effective tool for increasing both awareness and knowledge levels. In particular, deficiencies in formal education lead to inadequacies in early diagnosis and individualized educational processes. While educational level, professional experience, and training received positively influence knowledge levels, high class sizes and limited support mechanisms constrain this development. In this regard, it is recommended to strengthen the content of undergraduate programs focused on neurodevelopmental disorders, expand the scope and quality of in-service training, increase opportunities for practice-based education, effectively support individualized teaching processes, and enhance the accessibility of awareness-raising educational materials and resources.

Keywords: Neurodevelopment, Neurodevelopmental disorders, teacher knowledge level, teacher awareness

GİRİŞ

Nörogelişim, merkezi sinir sisteminin (özellikle beynin) doğum öncesinden başlayıp yetişkinliğe kadar uzanan süreçte büyüme, olgunlaşma ve organize olma sürecidir. Nörogelişimsel bozukluklar ise beyin gelişiminin çeşitli faktörlerin etkisiyle farklılaştığı ve farklı nörolojik ile psikiyatrik belirtilerle kendini gösteren gelişimsel bozukluklardır. DSM-5'te nörogelişimsel bozukluklar, anlıksal (entelektüel) yetersizlik, iletişim bozuklukları, otizm açılımı kapsamında bozukluk, dikkat eksikliği/aşırı hareketlilik bozukluğu, öğrenme güçlüğü, devinsel (motor) bozukluklar ve diğer nörogelişimsel bozukluklar olarak sınıflandırılmaktadır.[1] Nörogelişimsel bozukluklar, çocukların resmi eğitime başlamadan önceki erken gelişim döneminde ortaya çıkan bir durumdur. Bu bozukluklara sahip çocuklar, hafıza sorunları yaşar ve davranış, motor beceriler ve konuşma gibi alanlarda zorluklarla karşılaşırlar. Erken dönemde ortaya çıkan gelişimsel sorunların, kişisel, sosyal, akademik ve mesleki alanlarda işlev bozukluklarına yol açtığı bilinmektedir.[2] Çocukluk döneminde en sık rastlanan bozukluklar arasında zihinsel yetersizlik (ZY), otizm spektrum bozukluğu (OSB) ve dikkat eksikliği/hiperaktivite bozukluğu (DEHB) gibi nörogelişimsel bozukluklardır. Ancak, erken çocukluk döneminde bu bozuklukların tespit edilmesi, fiziksel engellerden daha zor olabilmektedir.[3] Bu süreçte öğretmenler, sadece bilgi aktaran birer eğitmen değil; çocuğun beynindeki dinamik bağları şekillendiren, potansiyeli açığa çıkaran ve kapsayıcı bir çevre sunan en kritik aktörlerdir.

Öğretmenlerin nörogelişimsel bozukluklara ilişkin farkındalık düzeyleri ve erken dönemde gerçekleştirdikleri doğru yönlendirmeler, çocukların gelişimsel, akademik ve sosyal süreçleri üzerinde önemli etkiler yaratabilmektedir. Özellikle okul öncesi, sınıf ve özel eğitim öğretmenleri, özel gereksinimli çocukların eğitim yaşamlarında karşılaştıkları ilk profesyoneller arasında yer almaları nedeniyle kritik bir role sahiptir. Bu bağlamda, öğretmenlerin kapsayıcı eğitim anlayışını benimsemeleri, olumlu tutum ve davranışlar sergilemeleri ve etkili uygulamalarla öğrencilere rehberlik etmeleri, çocukların eğitim süreçlerinin niteliğini artırmada ve potansiyellerini en üst düzeyde gerçekleştirmelerinde büyük önem taşımaktadır.[4]

Öğretmenler, sınıf dinamiklerini günlük olarak gözlemlemeleri ve bu süreçte edindikleri sezgisel anlayışları sayesinde, çocuklarda ortaya çıkabilecek sorunları erken fark etme ve çözüm bulma konusunda en öncelikli rolü üstlenmektedir. Bu yönleriyle, erken dönemde tanıma ve gerekli müdahaleleri başlatma noktasında ilk savunma hattı olarak görev yaparlar. Öğretmenler, çocuklarla her gün kurdukları etkileşimler ve yaptıkları gözlemler sayesinde, genellikle gözden kaçabilecek ince belirtileri fark etme konusunda özel bir avantaja sahiptir.[5] Bu bağlamda, öğretmenlerin DEHB'li çocuklara yönelik algılarının genellikle DEHB hakkındaki bilgi düzeylerinden etkilendiği belirtilmektedir. Öğretmenlerin DEHB hakkında yeterli bilgiye sahip olmaları ve olumlu tutum geliştirmeleri, bu çocukların doğru şekilde desteklenmesi ve yönlendirilmesi açısından hayati öneme sahiptir. Dolayısıyla, öğretmenlerin DEHB konusundaki bilgi düzeyi ve tutumları, çocuk-öğretmen ilişkisi kalitesini ve dolaylı olarak çocukların genel gelişimini etkileyen temel unsurlar arasında yer almaktadır.[6] Benzer şekilde, Otizm Spektrum Bozukluğu (OSB) belirtilerinin sınıf ortamında sıkça gözlemlenebildiği ve erken müdahalenin OSB'li çocukların yönetiminde kritik önem taşıdığı bilinmektedir. Bu nedenle, öğretmenlerin OSB hakkında bilgi sahibi olması, bu belirtileri tanıyabilmeleri açısından son derece önemlidir.[7] Ayrıca öğrenme güçlükleri (ÖG) öğretmenlerin bilgi ve farkındalık düzeylerinin önem taşıdığı diğer bir alan olarak öne çıkmaktadır.[8] Zihinsel engelli çocuklara yönelik bilgi ve farkındalık düzeyi de öğretmenler için hayati bir öneme sahiptir.[9]

Nörogelişimsel bozukluklar içinde yer alan kategoriler üzerine ayrı ayrı çalışmalar yapılmış olsa da bu çalışmaları bir araya getiren bir yayın bulunmamaktadır. Bu nedenle, bu derleme çalışması, sistematik bir alan yazını tarayarak Türkiye'de nörogelişimsel bozukluklar hakkında öğretmenlerin bilgi ve farkındalıklarıyla ilgili yayınlanmış çalışmaların yıllara göre dağılımını incelemeyi, bu çalışmaların hangi bakış açılarından ele alındığını ve hangi değişkenler çerçevesinde değerlendirildiğini belirlemeyi amaçlamaktadır.

MATERYAL VE YÖNTEM

Bu bölümde araştırmanın yöntemi, veri tarama ve toplama süreci ile araştırmaya dahil edilen çalışmaların belirlenmesinde kullanılan dahil etme ve dışlama kriterlerine ilişkin bilgiler sunulmaktadır.

Araştırmanın Yöntemi: Bu çalışmada, Türkiye'de öğretmenlerin nörogelişimsel bozukluklar konusundaki bilgi ve farkındalıklarına ilişkin yapılan araştırmaların incelenmesinde sistematik derleme yöntemi kullanılmıştır. Bu çalışmanın hazırlanmasında yalnızca ulusal kaynaklı araştırmalardan faydalanılmıştır.

Veri Tarama ve Toplama Süreci: Bu çalışmada, Türkiye'de öğretmenlerin nörogelişimsel bozukluklara dair bilgi ve farkındalıklarını inceleyen 2025 yılına kadar olan araştırmaların sistematik olarak derlenmesi amaçlanmıştır. Bu doğrultuda, herhangi bir başlangıç tarihi belirtilmeden, 2025 yılına kadar yapılmış tüm ilgili araştırmalar taranmıştır.

Araştırmanın Dahil Etme ve Dışlama Kriterleri: Çalışmaya Türkçe yayımlanmış araştırmalar veya YÖK Tez Merkezi'nde yer alan lisansüstü tez çalışmalar ile nörogelişimsel bozukluklar kapsamında öğretmenlerle yürütülmüş çalışmalar dahil edilmiştir. Ölçek uyarlama çalışmaları, etkililiği belirlemeye yönelik deneysel araştırmalar, Türkçe dışında yayımlanan tez ve makaleler, kaynaştırma eğitimi ve iki farklı engel gibi konulara odaklanan çalışmalar, nörogelişimsel bozukluklar dışında farklı engel gruplarını ele alan araştırmalar ile yalnızca pedagojik beceriler veya genel eğitim süreçlerine odaklanan çalışmalar kapsam dışında bırakılmıştır. Tarama sürecinde toplam 340 çalışmaya ulaşılmıştır. Dahil edilme ve dışlama kriterleri doğrultusunda yapılan değerlendirmeler sonucunda 178 çalışma incelemeye alınmıştır. Bu çalışmalar içerik açısından ayrıntılı olarak değerlendirilmiş, araştırmanın amacıyla doğrudan ilişkili olan ve öğretmenlerin nörogelişimsel bozukluklara ilişkin bilgi ve farkındalıklarını ele alan 65 çalışma araştırmanın veri kaynağını oluşturmuştur. Çalışmaların seçimi PRISMA akış şeması temel alınarak gerçekleştirilmiş; tarama, eleme, uygunluk değerlendirmesi ve dahil etme aşamaları sistematik bir şekilde yürütülmüştür.

BULGULAR

Türkiye'de nörogelişimsel bozukluklar hakkında öğretmenlerin bilgi ve farkındalıklarıyla ilgili yayınlanmış çalışmaların incelenmesi amacıyla yürütülen çalışmaların bulguları aşağıda sunulmuştur.

Dikkat Eksikliği ve Hiperaktivite Bozukluğu (DEHB) konusunda öğretmenlerle yapılan çalışmaların 2007, 2013, 2015, 2019, 2021 ve 2024 yıllarında gerçekleştirildiği belirlenmiştir. Bu çalışmaların konusu, yöntem/deseni, yayın türü ile öğretmenlerin bilgi ve farkındalıkları Tablo 1 ve Tablo 2'de; örneklem grubu Şekil 1'de sunulmuştur.

Tablo 1. Araştırmaya dahil edilen DEHB konusundaki çalışmaların konusu, yöntem/desen, yayın türü

Yazar(lar) ve Yılı	Çalışma Konusu	Yöntem/ Desen	Yayın Türü
Almacıoğlu (2007)[10]	Sınıf öğretmenleri ve PDR öğretmenlerinin DEHB tanıma yeterlilikleri	Betimsel/ Nicel	Yüksek Lisans Tezi
Göl ve Bayık (2013)[11]	İlköğretim sınıf öğretmenlerinin DEHB tanıma yeterlilikleri	Kesitsel Ve Tanımlayıcı Araştırma/ Nicel	Araştırma Makalesi
Şimşek vd., (2015)[31]	PDR öğretmenlerinin DEHB hakkındaki bilgi ve inançlarının incelenmesi	Yarı Yapılandırılmış Anket / Nicel	Araştırma Makalesi
Kıranşal (2019)[32]	DEHB hakkında öğretmenlerin damgalama algıları ve bununla ilişkili faktörler	Kesitsel Desen/ Nicel	Yüksek Lisans Tezi
Küçük vd., (2021)[13]	Öğretmenlerin bilişsel gelişim ve DEHB konularındaki bilgi düzeyleri	Tanımlayıcı Araştırma/ Nicel	Araştırma Makalesi

Biçer ve Çetin (2024)[14]	Öğretmenlerin DEHB tanıma yeterlilikleri	Nedensel Karşılaştırma Araştırması/ Nicel	Araştırma Makalesi

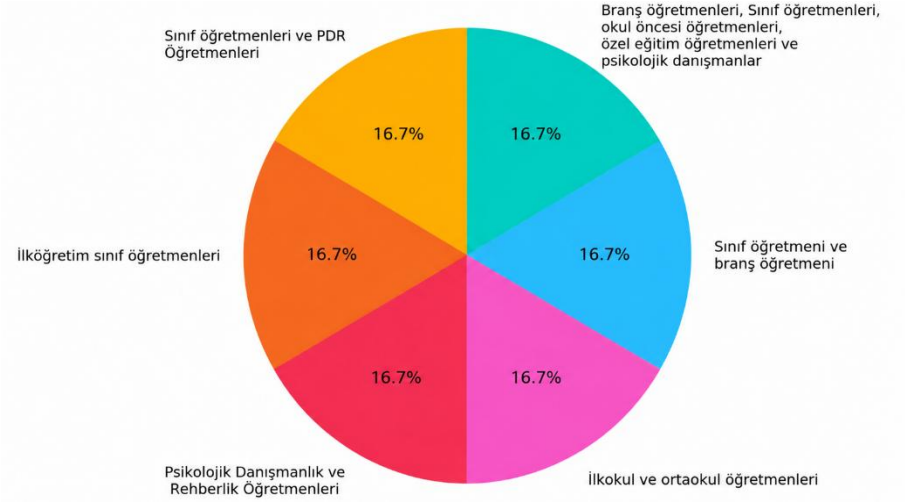
Tablo 1 incelendiğinde, DEHB konusunda öğretmenlerle yürütülen çalışmaların ağırlıklı olarak öğretmenlerin DEHB'yi tanıma yeterlilikleri, bilgi düzeyleri, inançları ve damgalama algıları üzerine odaklandığı görülmektedir. Araştırmaların tamamı nicel yöntemlerle gerçekleştirilmiş olup betimsel, tanımlayıcı, kesitsel ve nedensel karşılaştırma desenleri kullanılmıştır. Çalışmaların büyük çoğunluğu araştırma makalesi olarak yayımlanırken, iki çalışma yüksek lisans tezi niteliğindedir.

Tablo 2. Araştırmaya dahil edilen DEHB konusundaki çalışmalarda öğretmenlerin DEHB hakkındaki bilgi ve farkındalıkları

Yazar(lar) ve Yılı	**Katılımcı Grubu**	**Ölçüm Aracı**	**Bilgi Durumu**	**Farkındalık Seviyesi**	**Sonuç ve Öneriler**
Almacıoğlu (2007)[10]	Sınıf Öğretmenleri ve PDR	DEHB Tanıma Yeterlilik Ölçeği	Sınıf ve rehberlik öğretmenlerinin DEHB bilgi düzeyleri oldukça düşük bulunmuştur.	Farkındalık seviyesi sınıf öğretmenlerinde düşüktür; rehberlik öğretmenlerinde kısmi farkındalık gözlenmiştir.	DEHB'nin yönetsel bir sorun olarak ele alınması ve öğretmenlerin DEHB konusunda ciddi bir hizmet içi eğitimden geçirilmesi önerilmiştir.
Göl ve Bayık (2013)[11]	İlköğretim Sınıf Öğretmenleri	DEHB Tanıma Yeterlilik Ölçeği	Hizmet içi eğitim alan öğretmenlerin bilgi düzeyleri diğerlerinden daha yüksek bulunmuştur.	Farkındalık seviyeleri orta düzeydedir; hizmet içi eğitim alan öğretmenlerde farkındalık daha belirgindir.	DEHB konusunda öğretmen yetiştirme programlarına içerik eklenmesi, hizmet içi eğitim verilmesi ve okullarda sağlık hemşiresi bulundurulması önerilmiştir.
Şimşek vd., (2015)[31]	Psikolojik Danışmanlık ve Rehberlik öğretmenleri	DEHB Hakkında Hazırlanmış Yarı Yapılandırılmış Anket	DEHB'nin sıklığı, nedenleri, alt tipleri, tanısı, tedavisi ve bilgi kaynakları sorgulanmıştır. Bazı konularda bilimsel bilgilerle çelişen bilgi ve inançlar belirlenmiştir.	Farkındalık düzeyi kısmen yeterli bulunmuş; ancak DEHB'nin tedavisi, zekâ düzeyi ve etiketleme konusunda yanlış/eksik inanışlar olduğu görülmüştür.	PDR öğretmenlerinin DEHB tedavisi, zekâ düzeyi ve etiketleme gibi konularda doğru bilgilendirilmesi önerilmiştir.
Kıranşal (2019)[32]	İlkokul ve Ortaokul Öğretmenleri,	DEHB Damgalama (Stigma) Ölçeği	Bilgi düzeyi, DEHB hakkında eğitim veya deneyim sahibi olan öğretmenlerde daha yüksektir.	Farkındalık seviyeleri düşük, damgalama algısı farkındalığı olumsuz etkilemektedir.	DEHB damgalama algısının azaltılması için öğretmenler arası iş birliği, stigma azaltıcı eğitimler ve farkındalık çalışmaları önerilmiştir.

Küçük vd., (2021)[13]	Sınıf Öğretmenleri ve Branş Öğretmenleri	DEHB Tanıma Yeterlilik Ölçeği	Sınıf öğretmenlerinin DEHB tanıma yeterlilikleri düşük bulunmuş, branşa göre fark görülmemiştir.	Farkındalık seviyeleri genel olarak düşüktür; özel eğitim öğretmenlerinde kısmi farkındalık gözlenmiştir	DEHB farkındalığı artırmak için daha geniş çaplı eğitimler düzenlenmesi önerilmiştir.
Biçer ve Çetin (2024)[14]	Branş Öğretmenleri, Sınıf Öğretmenleri, Okul Öncesi Öğretmenleri, Özel Eğitim Öğretmenleri ve PDR	DEHB Tanıma Yeterlilik Ölçeği	Eğitim, deneyim ve materyal kullanımı gibi değişkenlere bağlı olarak bilgi düzeyi değişkenlik gösteriyor. Eğitim alan öğretmenlerin, özellikle psikolojik danışman ve özel eğitim branşında bilgi düzeyleri yüksektir.	Özel Eğitim Öğretmenleri ve PDR, DEHB konusunda daha yüksek farkındalık gösterirken, genel Sınıf Öğretmenleri veya Okul Öncesi Öğretmenlerinde farkındalık seviyeleri daha sınırlıdır.	DEHB konusunda daha fazla materyal geliştirme ve öğretmenlere sürekli mesleki gelişim eğitimleri verilmesi önerilmiştir.

Tablo 2'de öğretmenlerin DEHB konusundaki bilgi ve farkındalıklarına ait bulgular incelendiğinde, öğretmenlerin genel olarak DEHB'e ilişkin bilgi düzeylerinin sınırlı olduğu görülmektedir. Özellikle sınıf öğretmenlerinde farkındalık düzeyinin düşük olduğu, buna karşılık özel eğitim ve PDR alanında çalışan öğretmenlerin daha yüksek farkındalığa sahip olduğu anlaşılmaktadır.



Şekil 1. Araştırmaya dahil edilen DEHB konusundaki çalışmaların örneklem grubu

Şekil 1'e göre, DEHB konusunda yapılan çalışmalar farklı öğretmen gruplarıyla yürütülmüştür. En sık incelenen gruplar sınıf öğretmenleri ve PDR öğretmenleri olup, bazı araştırmalarda farklı branş ve kademelerden öğretmenler birlikte değerlendirilmiştir.

Otizm Spektrum Bozukluğu (OSB) konusunda öğretmenlerle yapılan çalışmaların 2009, 2016, 2019, 2020, 2022, 2023, 2024 ve 2025 yıllarında gerçekleştirildiği belirlenmiştir. Bu çalışmaların konusu, yöntem/deseni, yayın türü ile öğretmenlerin bilgi ve farkındalıkları Tablo 3 ve Tablo 4'te; örneklem

grubu Şekil 2'de sunulmuştur. İncelenen çalışmaların çalışma sayısının en yüksek olduğu yıllar 2019, 2022 ve 2025 olup bu yıllarda ikişer araştırma yer almaktadır. Diğer yıllarda ise birer çalışma bulunmaktadır.

Tablo 3. Araştırmaya dahil edilen OSB konusundaki çalışmaların konusu yöntem/desen, yayın türü

Yazar(lar) ve Yılı	Çalışma Konusu	Yöntem/Desen	Yayın Türü
Yumak (2009)[15]	İlköğretimde öğretmen ve yöneticilerin otistik çocuklara bakış açısı.	Karma/ Karma	Yüksek Lisans Tezi
Er-Sabuncuoğlu (2016)[16]	Okul öncesi öğretmenlerin otizm bilgisi	Betimsel/ Nicel	Araştırma Makalesi
Hacıibrahimoğlu ve Ustaoğlu (2019)[17]	Okul öncesi öğretmen adaylarının otizm spektrum bozukluğu (OSB) hakkındaki bilgi ve tutumları	Betimsel/ Nicel	Araştırma Makalesi
Batum (2019)[33]	Otizm spektrum bozukluğuna yönelik toplumsal tutumlar	Betimsel Ve İlişkisel Tarama Modeli/ Nicel	Yüksek Lisans Tezi
Akgül ve Mertoğlu (2020)[34]	Öğretmen eğitim programlarında otizm farkındalığı	Tarama Modeli Ve Anket Çalışması/ Karma	Araştırma Makalesi
Burak vd., (2022)[35]	Okul öncesi öğretmenlerin otizm bilgisi ve problem davranışlarla ilişkisi.	İlişkisel Tarama/ Nicel	Araştırma Makalesi
Aral vd., (2022)[18]	Öğretmenlerin otizm spektrum bozukluğuna yönelik tutumları	Tarama Modeli/ Nicel	Konferans Bildirisi
Asma (2023)[19]	Öğretmenlerin otizm hakkındaki bilgi ve tutumları	Kesitsel Ve Tanımlayıcı Araştırma/ Nicel	Tıpta Uzmanlık Tezi
Efe (2024)[36]	Sınıf öğretmenlerinin Otizm Spektrum Bozukluğu konusundaki bilgi düzeyleri	Yarı Yapılandırılmış Görüşme/ Nitel	Yüksek Lisans Tezi
Baş (2025)[37]	Okul öncesi ve sınıf öğretmeni adaylarının Otizm Spektrum Bozukluğu farkındalık düzeyleri	Betimsel/ Nicel	Yüksek Lisans Tezi
Uz (2025)[38]	Farklı branşlardaki öğretmen adaylarının otizm farkındalık düzeyleri	Tarama Modeli/ Nicel	Yüksek Lisans Tezi

Tablo 3 incelendiğinde, OSB konusunda öğretmenlerle yapılan çalışmaların ağırlıklı olarak öğretmenlerin bilgi, tutum ve farkındalık düzeylerine odaklandığı görülmektedir. Araştırmalarda çoğunlukla nicel yöntemler kullanılmış, yalnızca bir çalışmada karma yöntem tercih edilmiştir. Çalışmaların önemli bir kısmı araştırma makalesi ve yüksek lisans tezi olarak yayımlanmıştır.

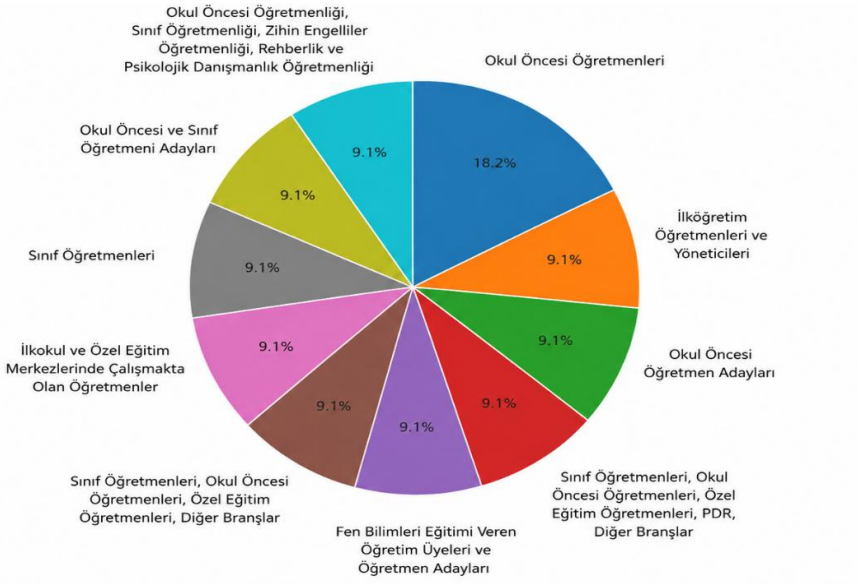
Tablo 4. Araştırmaya dahil edilen OSB konusundaki çalışmalarda öğretmenlerin OSB hakkındaki bilgi ve farkındalıkları

Yazar(lar) ve Yılı	Katılımcı Grubu	Ölçüm Aracı	Bilgi Durumu	Farkındalık Seviyesi	Sonuç ve Öneriler
Yumak (2009)[15]	İlköğretim Öğretmenleri ve Yöneticileri	Anket, Görüşme	Otizm bilgisi genelde yetersiz, öğretmenler kendilerini eksik hissediyor.	Düşük, otistik çocuklara karşı nasıl yaklaşacaklarını bilmiyorlar.	Otizm ile ilgili hizmet içi eğitimlerin yaygınlaştırılması önerilmiştir. Öğretmenler daha fazla destek ve kaynak istemektedir.
Er-Sabuncuoğlu (2016)[16]	Okul Öncesi Öğretmenleri	OSB Bilgi Formu	Bilgi seviyeleri beklenenin altında; otizmin nedenleri, belirtileri ve eğitimi konusunda eksik bilgiler yaygın.	Farkındalık düzeyleri sınırlı; otizm konusunda temel bilgi eksiklikleri nedeniyle yeterli bilinç oluşmamış.	OSB hakkında güncel bilgilerle hizmet içi eğitim verilmesi gerektiği belirtilmiştir. Öğretmen eğitiminin güçlendirilmesi önerilmiştir.
Hacıibrahimoğlu ve Ustaoğlu (2019)[17]	Okul Öncesi Öğretmen Adayları	Otizm Dahil Etme Anketi	Temel konularda bilgi eksiklikleri mevcut; özellikle tanı ve tedavi süreçleri konusunda yanlış bilgiler sıkça görülmüştür.	Bilgi düzeyinin artışıyla farkındalık seviyeleri de yükselmektedir; bilgi eksikliği olan adaylar otizmi yeterince anlamamaktadır.	Eğitim programlarının otizm bilgilerini daha kapsamlı şekilde kapsaması gerektiği önerilmiştir.
Batum (2019)[33]	Sınıf Öğretmenleri, Okul Öncesi Öğretmenleri, Özel Eğitim Öğretmenleri, PDR, Diğer Branşlar	Otizm Spektrum Bozukluğuna Yönelik Toplumsal Tutumlar Ölçeği (OYTTÖ) ve Kişisel Bilgi Formu	Öğretmenlerin genel olarak otizm spektrum bozukluğu (OSB) konusundaki bilgi düzeylerinin düşük olduğu görülmüştür.	Katılımcıların farkındalık düzeyi, özellikle otizmli bireylerin toplumsal yaşam ve kişisel mesafeye ilişkin tutumlarında belirgin farklılık göstermiştir.	OSB'li bireylere yönelik tutumların geliştirilmesi için hizmet içi eğitim programlarının artırılması önerilmektedir. Ayrıca, farkındalık eksikliği, etiketleme ve sosyal mesafe oluşturma gibi nedenlerin ele alınması gerektiği vurgulanmıştır

Akgül ve Mertoğlu (2020)[34]	Fen Bilimleri Eğitimi Veren Öğretim Üyeleri ve Öğretmen Adayları	Belge Analizi, Anket	Çoğunluk, özel gereksinimli öğrencilerle çalışmamış; bilgi seviyeleri genelde düşük.	Bilinçlenme düşük; programlar eksik görülmüş.	Lisans düzeyinde daha fazla otizm dersi verilmesi gerektiği ve öğretim elemanlarının farkındalığının artırılması gerektiği belirtilmiştir.
Burak vd., (2022)[35]	Okul Öncesi Öğretmenleri	Otizm Bilgi Ölçeği, Sınıf İçi Rahatsızlık Ölçeği	Özel eğitim merkezinde çalışanların bilgisi daha yüksek, genel eğitimdeki öğretmenler eksik hissetmekte.	Özel eğitimde çalışanlar daha yüksek farkındalık göstermiştir.	Özel eğitim merkezlerindeki stratejilerin genel eğitim ortamlarına taşınması gerektiği belirtilmiştir. Strateji ve yöntemlere odaklanılması gerektiğine değinilmiştir.
Aral vd., (2022)[18]	Sınıf Öğretmenleri, Okul Öncesi Öğretmenleri, Özel Eğitim Öğretmenleri, Diğer Branşlar	Kişisel Bilgi Formu ve Otizm Spektrum Bozukluğuna Yönelik Toplumsal Tutum Ölçeği	Kadın, Lisans mezunu, kamu sektöründe çalışan ve OSB eğitimi almış öğretmenlerde bilgi düzeyi yüksek.	Kadın öğretmenler ve OSB eğitimi alanlar daha yüksek farkındalık seviyesine sahip.	Kadın, lisans mezunu, kamu sektöründe çalışan ve OSB eğitimi almış öğretmenler daha olumlu tutumlara sahiptir. OSB farkındalığını artırmak için eğitim programları düzenlenmesi ve özel okul öğretmenlerinin düşük farkındalık nedenlerinin incelenmesi önerilmiştir.
Asma (2023)[19]	İlkokul ve Özel Eğitim Merkezlerinde Çalışmakta Olan Öğretmenler	OSB Bilgi Düzeyi Anketi	Kadın öğretmenler erkeklere göre daha yüksek bilgi seviyesine sahip.	Eğitime katılan öğretmenlerin farkındalık seviyesi daha yüksektir; eğitim almayanlar yeterli farkındalık gösterememektedir.	Otizm eğitimi almayan öğretmenlere yönelik programlar geliştirilmesi gerektiği vurgulanmıştır. Kaynaştırma eğitiminin yaygınlaştırılma

					sı gerektiği ifade edilmiştir.
Efe (2024)[36]	Sınıf Öğretmenleri	Demografik Bilgi Formu ve yarı yapılandırılmış görüşme soruları	Öğretmenler OSB'yi gelişimsel bir bozukluk olarak tanımlamış; ancak konuya ilişkin derinlemesine bilgiye sahip olmadıklarını belirtmiştir.	OSB'ye yönelik farkındalık bulunmakla birlikte sınırlıdır; öğretmenler özellikle eğitim süreci, BEP uygulamaları ve sınıf içi destek konusunda zorlanmaktadır.	Öğretmenlerin OSB konusunda bilgi düzeylerinin artırılması, hizmet içi eğitimlerin düzenlenmesi, sınıf mevcutlarının azaltılması ve aile-uzman iş birliğinin güçlendirilmesi önerilmiştir.
Baş (2025)[37]	Okul Öncesi ve Sınıf Öğretmeni Adayları	Türkiye'deki Üniversitelerin Eğitim Fakültesi Öğrencilerinin Otizm Farkındalığı Hakkında Anket	Öğretmen adaylarının OSB hakkında deneyim ve bilgilerinin kısıtlı olduğu, bilgilerini uygulamada yetersiz hissettikleri belirlenmiştir.	OSB farkındalık düzeylerinde cinsiyete göre anlamlı fark yoktur; bölüm ve üniversite değişkenlerine göre anlamlı farklılık vardır.	Öğretmen adaylarının aldıkları eğitimi yeterli görmedikleri ve daha fazla eğitime ihtiyaç duydukları sonucuna ulaşılmıştır. Öğretmen yetiştirme programlarına OSB'ye yönelik ders ve içeriklerin eklenmesi önerilmiştir.
Uz (2025)[38]	Okul Öncesi Öğretmenliği, Sınıf Öğretmenliği, Zihin Engelliler Öğretmenliği, Rehberlik ve Psikolojik Danışmanlık Öğretmenliği	Otizm Farkındalık Ölçeği	Öğretmen adaylarının otizm farkındalıklarının bölüm, sınıf düzeyi ve özel eğitim dersi alma durumuna göre değiştiği belirlenmiştir.	Cinsiyet, yaş, ekonomik durum, yaşanılan şehir, otizmi bilme ve otizm deneyimi değişkenlerine göre anlamlı fark yoktur; bölüm, sınıf düzeyi ve özel eğitim dersi alma değişkenlerine göre anlamlı fark vardır.	Otizm farkındalığının artırılması için özellikle sınıf öğretmenliği ve okul öncesi öğretmenliği gibi alanlarda programların güçlendirilmesi, eğitim fakültelerinde otizme yönelik içeriklerin daha kapsamlı ve uygulamalı biçimde verilmesi önerilmiştir.

Tablo 4'te, öğretmenlerin otizm spektrum bozukluğu (OSB) konusundaki bilgi ve farkındalık düzeylerinin genel olarak sınırlı olduğu görülmektedir. Çalışmaların çoğunda öğretmenlerin OSB'nin belirtileri, nedenleri, tanı süreci ve eğitim uygulamaları hakkında yeterli bilgiye sahip olmadıkları belirtilmiştir. Özellikle okul öncesi ve sınıf öğretmenlerinde bilgi eksikliği daha belirgin görünmektedir. Bununla birlikte, OSB konusunda eğitim alan, özel eğitim alanında çalışan veya deneyim sahibi olan öğretmenlerin bilgi ve farkındalık düzeylerinin daha yüksek olduğu anlaşılmaktadır.



Şekil 2. Araştırmaya dahil edilen OSB konusundaki çalışmaların örneklem grubu

Şekil 2 incelendiğinde, otizm spektrum bozukluğu konusunda öğretmenlerle yapılan çalışmaların farklı öğretmen gruplarıyla yürütüldüğü görülmektedir. En fazla araştırma okul öncesi öğretmenleri ile gerçekleştirilirken, sınıf öğretmenleri, öğretmen adayları ve farklı branşlardaki öğretmenler de örneklem grupları arasında yer almıştır.

Zihinsel Yetersizlikler (ZY) konusunda öğretmenlerle yapılan çalışmaların 2012, 2015, 2018, 2019, 2020, 2021 ve 2024 yıllarında gerçekleştirildiği belirlenmiştir. Bu çalışmaların konusu, yöntem/deseni, yayın türü ile öğretmenlerin bilgi ve farkındalıkları Tablo 5 ve Tablo 6'da; örneklem grubu Şekil 3'te sunulmuştur. İncelenen çalışmaların; çalışma sayısının en yüksek olduğu yıl 2018 olup bu yılda iki araştırma yer almaktadır. Diğer yıllarda ise birer çalışma bulunmaktadır.

Tablo 5. Araştırmaya dahil edilen ZY konusundaki çalışmaların konusu, yöntem/desen, yayın türü

Yazar(lar) ve Yılı	**Çalışma Konusu**	**Yöntem/ Desen**	**Yayın Türü**
Süngü (2012)[20]	Beden eğitimi öğretmen adaylarının zihinsel engelli çocuklara yönelik tutumları	Betimsel Yöntem/ Nicel	Yüksek Lisans Tezi
Tortop vd., (2015)[39]	Öğretmen adaylarının zihinsel engelli birey kavramına yönelik algıları	Fenomonolojik Desen/Nitel	Araştırma Makalesi
Karademir vd., (2018)[22]	Beden eğitimi öğretmen adaylarının zihinsel engelli çocuklara yönelik tutumları	Tarama Modeli/ Nicel	Araştırma Makalesi
Özcan ve Özer (2018)[21]	Beden eğitimi öğretmenlerinin zihinsel engelli çocuklara yönelik tutumlarını etkileyen faktörler	Betimsel Yöntem/ Nitel	Araştırma Makalesi

Gülünay vd., (2019)[40]	Beden eğitimi öğretmeni adaylarının zihinsel engelli çocuklara yönelik tutumlarının çeşitli değişkenlere göre incelenmesi	Betimsel Tarama Modeli/ Nicel	Araştırma Makalesi
Karatağ (2020)[41]	Zihinsel engelliler özel eğitim uygulama okullarında çalışan müzik öğretmenlerinin karşılaştıkları sorunlar ve çözüm önerileri	Görüşme Yöntemi/ Nitel	Araştırma Makalesi
Gün (2021)[42]	Beden eğitimi ve spor öğretmen adaylarının zihinsel engelli çocuklara yönelik tutumlarının incelenmesi	Betimsel Tarama Modeli/ Nicel	Yüksek Lisans Tezi
Uslu (2024)[23]	Beden eğitimi öğretmenlerinin zihinsel engelli çocuklara yönelik tutumlarda demografik değişkenler	Betimsel Yöntem/ Nicel	Yüksek Lisans Tezi

Tablo 5 incelendiğinde, zihinsel yetersizlikler konusunda öğretmenlerle yapılan çalışmaların ağırlıklı olarak öğretmen ve öğretmen adaylarının zihinsel yetersizliği olan bireylere yönelik tutumlarını incelemeye odaklandığı görülmektedir. Araştırmalarda çoğunlukla nicel yöntemler kullanılmış; yalnızca sınırlı sayıda çalışmada nitel yöntemlere yer verilmiştir. Çalışmaların önemli bir kısmı beden eğitimi öğretmenleri ve öğretmen adaylarıyla yürütülmüş olup, araştırma makalesi ve yüksek lisans tezi türündeki yayınlar öne çıkmaktadır.

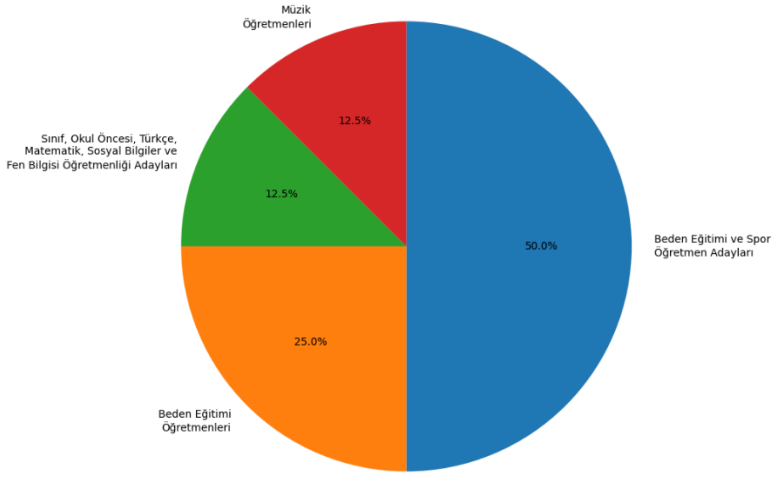
Tablo 6. Araştırmaya dahil edilen ZY konusundaki çalışmalarda öğretmenlerin ZY hakkındaki bilgi ve farkındalıkları

Yazar(lar) ve Yılı	**Katılımcı Grubu**	**Ölçüm Aracı**	**Bilgi Durumu**	**Farkındalık Seviyesi**	**Sonuç ve Öneriler**
Süngü (2012)[20]	Beden Eğitimi ve Spor Öğretmen Adayları	"Zihinsel Engelli Çocuklara Yönelik Tutum Ölçeği" (ZEÇTÖ) geliştirilmiş ve uygulanmıştır.	Öğretmen adaylarının zihinsel engelli çocuklara yönelik bilgi düzeyleri doğrudan ölçülmemiştir.	Engelli bireylerle deneyim, farkındalık düzeylerini olumlu yönde etkilemiştir.	Olumlu tutum geliştirmek için uygulamalı eğitim programları önerilmiştir. Ölçeğin olumsuz tutumları belirlemek için kullanılabileceği belirtilmiştir.
Tortop vd., (2015)[39]	Sınıf, Okul Öncesi, Türkçe, Matematik, Sosyal Bilgiler ve Fen Bilgisi Öğretmenliği Adayları	İçerik Analizi ve Betimsel Yöntem	Zihinsel engelli bireyleri sosyal yaşamda eksik gören algılar	Algılarda çeşitlilik ve kısmi farkındalık	Olumsuz algılar pozitif hale getirilmesi önerilmiştir.

Karademir vd., (2018)[22]	Beden Eğitimi ve Spor Öğretmen Adayları	Zihinsel Engelli Çocuklara Yönelik Tutum Ölçeği	Özel eğitim alanında bilgi ihtiyacı yüksek	Kadın öğretmen adaylarında farkındalık daha yüksek	Kadın öğretmen adaylarının yüksek tutumunun örnek alınması gerekliliği belirtilmiştir.
Özcan ve Özer (2018)[21]	Beden Eğitimi Öğretmenleri	Tutum Ölçeği ve Demografik Anket	Deneyim ve öz yeterlik, olumlu tutumla ilişkili	Deneyim ve öz duyarlık farkındalığı artırıyor	Tutumları artırmak için deneyim fırsatları sunulması gerekliliği belirtilmiştir.
Gülünay vd., (2019)[40]	Beden Eğitimi ve Spor Öğretmen Adayları	Kişisel Bilgi Formu ve Zihinsel Engelli Çocuklara Yönelik Tutum Ölçeği	Özel eğitim bilgisi/ders alma durumu incelenmiştir; 191 öğrenci ders almış, 91 öğrenci almamıştır	Farkındalık doğrudan ölçülmemiştir; zihinsel engelli çocuklara yönelik tutum düzeyi değerlendirilmiştir.	Cinsiyet, sınıf düzeyi, özel eğitim bilgisi, engelli yakını olma ve çalışma deneyimi değişkenlerine göre anlamlı fark bulunmamıştır. Engelliler için beden eğitimi ve spor dersinin müfredatının geliştirilmesi ve özel eğitim kurumlarıyla iş birliği yapılarak uygulama boyutunun artırılması önerilmiştir.
Karatağ (2020)[41]	Müzik Öğretmenleri	Nitel Görüşme	Müzik eğitimi ile katkı sağlanabilir ancak bilgi eksiklikleri var	Eğitim ortamında farkındalık yetersiz	Müzik eğitimi için yeterli kaynak ve desteğin sağlanması gerekliliği belirtilmiştir.
Gün (2021)[42]	Beden Eğitimi ve Spor Öğretmen Adayları	Zihinsel Engelli Çocuklara Yönelik Tutum Ölçeği (ZEÇYTÖ)	Zihinsel engelli çocuklarla ilgili ders alma durumu" incelenmiş. Ders alma durumuna göre tutum puanlarında anlamlı fark bulunmuş	Tutum/farkındalık düzeyinde yaş, ders alma ve çalışma isteği değişkenlerinde anlamlı fark bulunmuştur	Engellilerle ilgili derslerin artırılması, seminer/konferans düzenlenmesi ve öğrencilerin engelli bireylerle daha fazla uygulama/staj yapması önerilmiştir.
Uslu (2024)[23]	Beden Eğitimi Öğretmenleri	Likert Tipi Tutum Ölçeği	Özel eğitimle deneyim, olumlu tutum geliştiriyor	Farkındalık deneyim ve eğitimle artıyor	Öğretmenlerin öz yeterliklerini geliştirecek eğitimlerin düzenlenmesi önerilmiştir.

Tablo 6 incelendiğinde, öğretmenlerin ve öğretmen adaylarının zihinsel yetersizlikler konusundaki bilgi ve farkındalık düzeylerinin çoğunlukla tutum, deneyim ve özel eğitim bilgisi değişkenleri üzerinden ele

alındığı görülmektedir. Çalışmalarda bilgi düzeyinin her zaman doğrudan ölçülmediği, ancak özel eğitim dersi alma, engelli bireylerle çalışma deneyimi ve uygulamalı eğitim süreçlerinin farkındalık üzerinde etkili olduğu anlaşılmaktadır.



Şekil 3. Araştırmaya dahil edilen ZY konusundaki çalışmaların örneklem grubu

Şekil 3 incelendiğinde, zihinsel yetersizlikler konusunda öğretmenlerle yapılan çalışmaların örneklem grubunu ağırlıklı olarak beden eğitimi ve spor öğretmen adaylarının oluşturduğu görülmektedir (%50). Beden eğitimi öğretmenleri ise çalışmaların %25'ini oluşturmaktadır. Daha az sayıda araştırmada müzik öğretmenleri ile farklı branşlardaki öğretmen adaylarına yer verilmiştir.

Öğrenme Güçlükleri (ÖG) konusunda öğretmenlerle yapılan çalışmaların 2013-2025 yılları arasında gerçekleştirildiği belirlenmiştir. Bu çalışmaların konusu, yöntem/deseni, yayın türü ile öğretmenlerin bilgi ve farkındalıkları Tablo 7 ve Tablo 8'de; örneklem grubu Şekil 4'te sunulmuştur. Çalışma sayılarının özellikle son yıllarda artış gösterdiği görülmektedir. En fazla çalışma 2025 yılında gerçekleştirilmiş, bunu 2023 ve 2024 yılları izlemiştir.

Tablo 7. Araştırmaya dahil edilen ÖG konusundaki çalışmaların konusu, yöntem/desen, yayın türü ve temel sonuçları

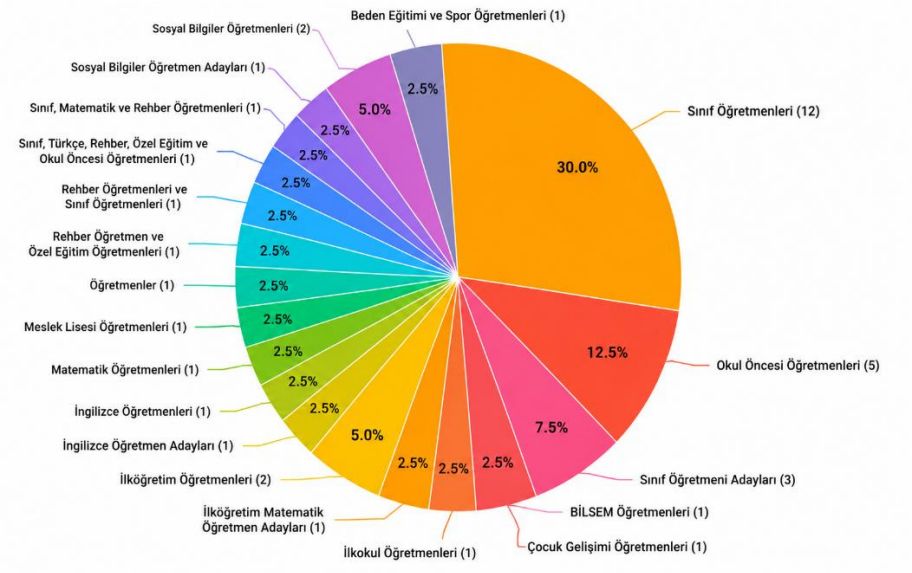
Yazar(lar) ve Yılı	**Çalışma Konusu**	**Yöntem/ Desen**	**Yayın Türü**
Karadeniz (2013)[43]	Diskalkuliye yönelik öğretmen görüşleri	Durum Çalışması/ Nitel	Araştırma Makalesi
Yangın vd., (2016)[25]	Sınıf öğretmenleri ve öğretim elemanlarında öğrenme güçlüklerine yönelik farkındalık	Karma Yöntem/ Karma	Araştırma Makalesi
Altun ve Uzuner (2016)[44]	Sınıf öğretmenlerinin Özel öğrenme güçlüğü olan öğrencilerin eğitimine yönelik görüşleri	Durum Çalışması/ Nitel	Araştırma Makalesi
Yürümez vd., (2016)[45]	Öğretmenlerin ÖÖG'ye ilişkin bilgi düzeyleri ve damgalama eğilimleri	Çok Merkezli Anket Çalışması/Nicel	Araştırma Makalesi
Kaçar (2017)[46]	Meslek lisesi öğretmenlerinin öğrenme güçlüğü bilgisi	Nedensel-Karşılaştırma Deseni/ Nicel	Yüksek Lisans Tezi

Akdemir (2018)[47]	Yeni mezun okul öncesi öğretmenlerinin öğrenme güçlüğü görüşleri	Fenomenolojik Desen/ Nitel	Yüksek Lisans Tezi
Başar ve Göncü (2018)[28]	Sınıf Öğretmenlerinin öğrenme güçlüğü kavram yanılgılarının giderilmesi	Betimsel Tarama Modeli Ve Tek Gruplu Öntest-Sontest Desen/Karma	Araştırma Makalesi
Birol ve Zor (2018)[48]	Sınıf öğretmenlerinin ÖÖG tanılı öğrencilerle yaşadıkları sorunlar	Yarı Yapılandırılmış Görüşme/Nitel	Araştırma Makalesi
Kuruyer vd., (2019)[49]	Sınıf öğretmeni adaylarının okuma ve matematik güçlüklerine yönelik farkındalıkları	Durum Çalışması/ Nitel	Araştırma Makalesi
Şahin (2019)[26]	Sınıf öğretmenlerinin disleksiye yönelik bilgi ve tutumları	Kesitsel Tarama Deseni/ Nicel	Yüksek Lisans Tezi
Balcı (2019)[50]	Disleksi hakkındaki öğretmen görüşleri ve sorunlar	İçerik Analizi/ Nitel	Araştırma Makalesi
Nurkan ve Yazıcı (2020)[51]	Matematik öğretmenlerinin Diskalkuli farkındalığı	Durum Çalışması/ Nitel	Araştırma Makalesi
Emre vd., (2020)[52]	Öğrenme güçlüğü, öz yeterlik ve pozitif öğretmenlik ilişkisi	İlişkisel Tarama Modeli/ Nicel	Araştırma Makalesi
Çoğaltay ve Çetin (2020)[53]	Sınıf öğretmenlerinin özel öğrenme güçlüğüne ilişkin yeterlilikleri	Vaka Çalışması/ Nitel	Araştırma Makalesi
Kabasakal ve Uygur (2021)[27]	Öğretmenlerin özel öğrenme güçlüğüne ilişkin bilgi düzeyleri ve kavram yanılgıları	Eş Zamanlı Üçgenleme Deseni/ Karma	Araştırma Makalesi
Susam ve Bayrakçı (2021)[54]	Özel öğrenme güçlüğü yaşayan öğrencilerin eğitimine yönelik öğretmen görüşleri	Fenomenolojik Desen/ Nitel	Araştırma Makalesi
Baldemir vd., (2022)[55]	Diskalkuliye ilişkin öğretmen adaylarının görüşleri	Nitel Araştırma Yöntemi/ Nitel	Araştırma Makalesi
Döşlü ve Bağlama (2022)[29]	Öğretmenlerin öğrenme güçlüğünün erken belirtilerine ilişkin görüşleri	Durum Çalışması/ Nitel	Araştırma Makalesi
Apak (2022)[56]	Okul öncesi öğretmenlerinin özel öğrenme güçlüğü farkındalık düzeyleri	Tarama Modeli/ Nitel	Yüksek Lisans Tezi
Reis ve Kansu (2022)[57]	Sınıf öğretmeni adaylarının özel öğrenme güçlüğü yaşayan öğrencilere yönelik yeterlikleri	Tarama Modeli/ Nitel	Araştırma Makalesi
Sivrikaya Giray (2023)[58]	Bilim ve Sanat Merkezi öğretmenlerinin özgül öğrenme güçlüğü ve disleksi hakkındaki bilgi ve öz yeterlikleri	Betimsel Tarama Modeli/ Nicel	Yüksek Lisans Tezi

Sivrikaya (2023)[59]	Okul öncesi öğretmenlerinin özgül öğrenme güçlüğü hakkındaki bilgi ve öz yeterlikleri	Sıralı Açıklayıcı Karma Yöntem/ Karma	Yüksek Lisans Tezi
Ürün vd.,(2023)[60]	Özel öğrenme güçlüğü yaşayan öğrencilerin özellikleri ve eğitimlerine yönelik görüşler	Fenomenolojik Desen/ Nitel	Araştırma Makalesi
Kuzan vd., (2023)[61]	Özel öğrenme güçlüğü konusundaki öğretmen yeterlilikleri	Fenomenolojik Desen/ Nitel	Araştırma Makalesi
Demir (2023)[62]	Sınıf öğretmenlerinin okuma güçlüklerine ilişkin farkındalık düzeylerinin incelenmesi	Durum Çalışması/ Nitel	Yüksek Lisans Tezi
Ülger (2023)[63]	Sınıf öğretmenlerinin özel öğrenme güçlüğü yeterlik düzeyleri ve diskalkuliye ilişkin görüşleri	Açıklayıcı Desen/ Karma	Yüksek Lisans Tezi
Okur vd., (2024)[30]	Özel öğrenme güçlüğüne ilişkin öğretmen ve rehber görüşleri	Durum Çalışması/ Nitel	Araştırma Makalesi
Tansel Günal (2024)[64]	Sınıf, matematik ve rehber öğretmenlerinin diskalkuliye yönelik farkındalıkları	Örnek Olay Tarama Modeli/Nicel	Yüksek Lisans Tezi
Mangır (2024)[65]	Öğrenme güçlüğü yaşayan öğrencilere ilişkin sınıf öğretmenlerinin görüş ve yeterlilikleri	Nicel Tarama Modeli Ve Nitel Fenomenoloji/ Karma	Yüksek Lisans Tezi
Akbaş (2024)[66]	Özel eğitim ve rehabilitasyon merkezinde çalışan çocuk gelişimi mezunlarının ÖÖG alanındaki yeterlik algıları	Tarama Modeli/Nicel	Yüksek Lisans Tezi
Aydoğmuş (2024)[67]	Sınıf öğretmeni adaylarının disleksi hakkındaki bilgi ve inanç düzeyleri	Tarama Modeli/Nicel	Araştırma Makalesi
Çelik (2025)[68]	Öğrenme güçlüğüne ilişkin okulöncesi öğretmenlerin yeterlilikleri	Nicel	Yüksek Lisans Tezi
Şaşmaz (2025)[69]	Sosyal bilgiler öğretmen adaylarının öğrenme güçlüğü olan öğrenciler hakkındaki farkındalıklarının incelenmesi	Tarama Modeli/Nicel	Yüksek Lisans Tezi
Turan (2025)[70]	Sosyal bilgiler öğretmenlerinin ÖÖG'ye ilişkin bilgi düzeyleri, tutumları ve görüşleri	Karma Yöntem	Doktora Tezi
Çoban (2025)[71]	Beden eğitimi ve spor öğretmenlerinin öğrenme güçlüğüne yönelik yeterlilik ve farkındalıkları	Tarama Modeli/Nicel	Araştırma Makalesi
Çelik Çoban (2025)[72]	İlköğretim öğretmenlerinin disleksi ile ilgili bilgi ve inançları	Kesitsel Çalışma/ Nicel	Tıpta Uzmanlık Tezi

Akbaba (2025)[73]	RAM personellerinin özel öğrenme güçlüğü alanındaki yeterlikleri	Tarama Modeli/Nicel	Yüksek Lisans Tezi
Turan ve Ortak (2025)[74]	Sosyal bilgiler öğretmenlerinin ÖÖG yaşayan öğrencilere yönelik tutumları	Genel Tarama Deseni/ Nicel	Araştırma Makalesi

Tablo 7 incelendiğinde, ÖG konusunda öğretmenlerle yapılan çalışmaların çoğunlukla öğretmenlerin bilgi düzeyleri, farkındalıkları, tutumları ve yeterliliklerine odaklandığı görülmektedir. Araştırmalarda nicel ve nitel yöntemlerin yanı sıra karma yöntemlere de yer verilmiştir. Çalışmaların büyük bölümü araştırma makalesi ve yüksek lisans tezi niteliğindedir.



Şekil 4. Araştırmaya dahil edilen ÖG konusundaki çalışmaların örneklem grubu

Şekil 4 incelendiğinde, ÖG konusunda yapılan çalışmaların en çok sınıf öğretmenleri ile yürütüldüğü görülmektedir. Bunun yanında okul öncesi öğretmenleri, sınıf öğretmeni adayları ve sosyal bilgiler öğretmenleri de araştırmalarda yer almaktadır. Ayrıca farklı branşlardan öğretmenler, rehber öğretmenler ve öğretmen adaylarıyla gerçekleştirilen çalışmalar da bulunmaktadır.

Tablo 2. Araştırmaya dahil edilen ÖG konusundaki çalışmalarda öğretmenlerin ÖG hakkındaki bilgi ve farkındalıkları

Yazar(lar) ve Yılı	**Katılımcı Grubu**	**Ölçüm Aracı**	**Bilgi Durumu**	**Farkındalık Seviyesi**	**Sonuç ve Öneriler**
Karadeniz (2013)[43]	Sınıf Öğretmenleri	Yarı Yapılandırılmış Görüşme	Diskalkuli hakkında sınırlı bilgiye sahipler. 'Diskalkuli' kavramı yerine yanlış terimler kullanmışlardır.	Düşük: Öğrencilerin ihtiyaçlarını anlamakta güçlük çekiyorlar.	Öğretmenlere diskalkuli hakkında özel eğitimler düzenlenmesi önerilmiştir.
Yangın vd., (2016)[25]	Sınıf Öğretmeni Adayları ve Öğretim Elemanları	Farkındalık Ölçeği ve Yarı Yapılandırılmış Görüşme	Öğrenme güçlükleriyle ilgili bilgi düzeyleri yetersiz.	Çok düşük: Eğitim ihtiyaçları yüksek seviyede.	Müfredata öğrenme güçlüklerine yönelik ders eklenmesi önerilmiştir.

Altun ve Uzuner (2016)[44]	Sınıf Öğretmenleri	Yarı Yapılandırılmış Mülakat	Özel öğrenme güçlükleriyle ilgili eksik bilgiye sahipler.	Düşük: Veli-öğretmen iş birliği zayıf.	Veli-öğretmen iş birliği artırmaya yönelik farkındalık eğitimlerinin düzenlenmesi önerilmiştir.
Yürümez vd., (2016)[45]	İlköğretim Öğretmenleri	Araştırmacılar tarafından hazırlanan anket	Öğretmenlerin ÖÖG hakkındaki bilgi düzeyleri yeterli değildir; yanlış bilgiler yaygındır.	Farkındalık sınırlıdır; bazı öğretmenlerde damgalama ve dışlama eğilimi görülmüştür.	Öğretmenlere yönelik bilgilendirme çalışmaları yapılmalı, damgalamayı azaltacak eğitim programları hazırlanmalıdır.
Kaçar (2017)[46]	Meslek Lisesi Öğretmenleri	Öğrenme Güçlüğü Bilgi Formu	Bilgi düzeyleri düşük, hizmet içi eğitime ihtiyaç duyulmaktadır.	Düşük: Kaynaştırma eğitimleri konusunda bilgi eksikliği var.	Hizmet içi eğitimler artırılarak, özel eğitim dersleri eklenmesinin gerekliliği belirtilmiştir.
Akdemir (2018)[47]	Okul Öncesi Öğretmenleri	Yarı Yapılandırılmış Görüşme	Doğru bilgiye sahipler ancak bu bilgiler yeterli seviyede değil.	Orta düzey: Öğrenme güçlüğünü tanımada yeterli değiller.	Lisans eğitiminde özel eğitim derslerinin kapsamının genişletilmesi önerilmiştir.
Başar ve Göncü (2018)[28]	Sınıf Öğretmenleri	Kelime İlişkilendirme Testi ve Öğrenme Güçlüğü Bilgi Testi	Kavram yanılgıları mevcut.	Düşük: Kavram yanılgıları giderilmiştir.	Eğitim sonrası kavram yanılgılarının giderildiği gözlemlenmiştir.
Birol ve Zor (2018)[48]	Sınıf Öğretmenleri	Yarı yapılandırılmış mülakat formu	Öğretmenlerin ÖÖG'ye ilişkin eğitim ve bilgi düzeyleri yetersizdir.	Öğretmenler sorunların farkındadır ancak uygulamada yetersizlik yaşamaktadır.	Destek sınıfları oluşturulmalı, kalıcı destek öğretmeni görevlendirilmeli, rehabilitasyon merkezleri desteklenmeli ve veliler bilgilendirilmelidir.
Kuruyer vd., (2019)[49]	Sınıf Öğretmeni Adayları	Anket ve Görüşme	Okuma ve matematik güçlükleri hakkında eksiklikler var.	Düşük: Matematik ve okuma güçlüklerinin tespitinde zorlanıyorlar.	Müfredat geliştirilerek farkındalık artırıcı içerik eklenmesi önerilmiştir.
Şahin (2019)[26]	Sınıf Öğretmenleri	Disleksi Tutum Anketi	Disleksiye dair temel bilgilere sahipler ancak bu bilgiler eksik.	Düşük: Disleksi belirtilerini tanımada güçlük yaşıyorlar.	Hizmet içi eğitimler düzenlenmesi önerilmiştir.

Balcı (2019)[50]	Sınıf, Türkçe, rehber, özel eğitim ve okul öncesi öğretmenleri	Yarı Yapılandırılmış Görüşme	Disleksi hakkında sınırlı bilgiye sahipler.	Düşük: Özel eğitim yöntemleri konusunda bilgi eksikliği var.	Disleksi eğitimi verilmesi önerilmiştir.
Nurkan ve Yazıcı (2020)[51]	Matematik öğretmenleri	Durum Çalışması	Diskalkuli konusunda kısmi bilgiye sahipler.	Kısmi bilgi: Matematik öğrenme güçlüğünü tanımakta zorlanıyorlar.	Diskalkuli farkındalığı artırılmasına yönelik hizmet içi eğitim verilmesi önerilmiştir.
Emre vd., (2020)[52]	İlkokul Öğretmenleri	Anket ve Pozitif Öğretmen Ölçeği	Orta düzey; öz-yeterlik kaynaklarında eksiklik.	Düşük-orta; olumlu tutumlar görülmüş.	Pozitif öğretim becerilerini artırmaya yönelik eğitim düzenlenmesi önerilmiştir.
Çoğaltay ve Çetin (2020)[53]	Sınıf Öğretmenleri	Yarı Yapılandırılmış Görüşme Formu	Eksik ve hatalı bilgiler mevcut.	Özel öğrenme güçlüğü farkındalığı düşük.	Öğretmen eğitimlerinin desteklenmesi önerilmiştir.
Kabasakal ve Uygur (2021)[27]	Öğretmenler	Anket ve Görüşme Formu	Eğitim almış olanlar daha bilinçli.	Orta düzeyde; mitlere dayalı kavram yanılgıları.	Mitlerin giderilmesi ve eğitim içeriklerinin geliştirilmesine yönelik eğitimler önerilmiştir.
Susam ve Bayrakçı (2021)[54]	Sınıf Öğretmenleri	Yarı Yapılandırılmış Görüşme Formu	Özel öğrenme güçlüğüne yönelik temel düzeyde bilgiye sahip.	Matematik ve Türkçe derslerinde güçlük yaşayan öğrenciler üzerine farkındalık.	Aile iş birliği ve bireyselleştirilmiş eğitim vurgusuna değinilmiştir.
Baldemir vd., (2022)[55]	İlköğretim Matematik Öğretmen Adayları	Yarı Yapılandırılmış Görüşme Formu	Diskalkuli terimlerini tanımada zayıf.	Düşük; sürece ilişkin bilgi eksikliği.	Lisansa 'öğrenme güçlükleri' dersi eklenmesi önerilmiştir.
Döşlü ve Bağlama (2022)[29]	Okul Öncesi Öğretmenleri	Yarı Yapılandırılmış Görüşme Formu	Öğretmenlerin öğrenme güçlüğü hakkında bilgi düzeylerinin sınırlı olduğu ve bu konuda daha fazla eğitime ihtiyaç duydukları görülmüştür.	Öğretmenlerin öğrenme güçlüğü belirtilerine yönelik farkındalık düzeylerinin genel olarak yeterli olduğu, ancak bu farkındalığın uygulamada tutarlı şekilde	Öğrenme güçlüğünün erken tanısının ve müdahalesinin önemini vurgulayarak öğretmenlerin bilgi ve farkındalık düzeylerini artıracak hizmet içi eğitimler ile aile iş birliğinin güçlendirilmesi

				yansıtılamadığı görülmüştür.	gerektiği önerilmektedir
Apak (2022)[56]	Okul Öncesi Öğretmenleri	Kişisel Bilgi Formu ve Özel Öğrenme Güçlüğü Soru Listesi	Öğretmenlerin genel bilgi düzeyi yüksektir ancak farklı alt boyutlarda eksiklikler bulunmaktadır.	Daha önce özel öğrenme güçlüğü olan bir öğrenciyle karşılaşan öğretmenlerin farkındalık düzeyi anlamlı derecede yüksek bulunmuştur.	Öğretmenlerin özel öğrenme güçlüğü farkındalıklarını artırmak için kapsamlı eğitim programları hazırlanması önerilmiştir.
Reis ve Kansu (2022)[57]	Sınıf Öğretmeni Adayları	Öğretmen Yeterlikleri Ölçeği	Katılımcıların özgül öğrenme güçlüğü yaşayan öğrencilerle ilgili bilgi düzeyleri yüksek bulunmuştur.	Cinsiyet ve sınıf düzeyi değişkenleri fark yaratmamış, ancak genel farkındalık seviyesi yüksek bulunmuştur.	Üniversitelerde özel eğitime yönelik ders sayısının artırılması ve ders içeriklerinin daha etkin hale getirilmesi önerilmiştir.
Sivrikaya Giray (2023)[58]	Okul Öncesi Öğretmenleri	Özel Öğrenme Güçlüğü Alanı Öğretmen Yeterlik Ölçeği, Öğrenme Güçlüğü Erken Belirtileri Tarama Ölçeği, Özgül Öğrenme Güçlüğüne Yönelik Öğretmen Görüşme Formu	Öğretmenlerin özel öğrenme güçlüğü tanılama yöntemleri ve eğitimlerine yönelik bilgilerinin yetersiz olduğu tespit edilmiştir.	Çoğu öğretmenin farkındalık düzeyleri sınırlı bulunmuş, özellikle tanılama süreçleri ve eğitim müdahaleleri hakkında bilgi eksikliği olduğu tespit edilmiştir.	Öğretmenlerin bilgi eksikliklerini gidermek için uygulamalı eğitim programları geliştirilmesi önerilmiştir.
Sivrikaya (2023)[59]	BİLSEM Öğretmenleri	Özel Öğrenme Güçlüğü Alan Öğretmen Yeterlik Ölçeği, Disleksi Bilgi Düzeyi Belirleme Anketi.	Öğretmenlerin disleksi bilgi düzeyi düşükken, özgül öğrenme güçlüğü öz yeterlikleri yüksektir.	Özgül öğrenme güçlüğü konusunda genel farkındalık ortalama düzeyde bulunmuş, ancak disleksi farkındalığı düşüktür.	Disleksi konusunda eğitim materyalleri geliştirilmesi ve farkındalık artırıcı etkinlikler düzenlenmesi önerilmektedir.
Ürün vd., (2023)[60]	Sınıf Öğretmenleri	Yarı Yapılandırılmış Görüşme Formu	Öğretmenler özel öğrenme güçlüğü yaşayan öğrencilerle ilgili bilgi sahibi olduklarını belirtse de pratikte sınıf yoğunluğundan dolayı yeterli	Katılımcılar, sınıf yoğunluğu ve sınırlı bilgi nedeniyle farkındalık düzeylerini düşük ifade etmişlerdir.	Öğretmenlerin sınıf kapasitelerinin azaltılması ve bireysel eğitime yönelik daha fazla kaynak sağlanması önerilmiştir.

			ilgiyi gösteremediklerini ifade etmişlerdir.		
Kuzan vd., (2023)[61]	Sınıf Öğretmenleri	Yarı Yapılandırılmış Görüşme Formu	Öğretmenler, özel öğrenme güçlüğü belirtilerini tanımlamakta zorlanmakta ve bu konuda yetersiz bilgiye sahip olduklarını düşünmektedir.	Öğretmenler, özel öğrenme güçlüğü tanısının belirtileri ve müdahale yöntemleri konusunda farkındalık eksikliği yaşamaktadır.	Öğretmenlerin bu alandaki bilgi ve farkındalık düzeylerini artırmak için hizmet içi eğitimler düzenlenmeli, rehberlik servisleri ve uzman desteğiyle iş birliği artırılmalıdır.
Ülger (2023)[63]	Sınıf Öğretmenleri	Özel Öğrenme Güçlüğü Alanı Öğretmen Yeterlik Ölçeği ve yarı yapılandırılmış görüşme formu	ÖÖG eğitimi alan öğretmenlerin bilgi ve öğretim bilgisi yeterlikleri daha yüksektir.	Orta; eğitim ve deneyime göre değişmektedir	ÖÖG eğitimi ve deneyimi öğretmen yeterliğini artırmaktadır; hizmet içi eğitimler önerilmiştir.
Demir (2023)[62]	Sınıf Öğretmenleri	Yarı yapılandırılmış görüşme formu	Öğretmenlerin okuma güçlüğü kavramını az düzeyde bildiği, bazı kavram yanılgılarına sahip olduğu görülmüştür.	Düşük	Lisans düzeyinde okuma güçlükleri dersi, hizmet içi eğitim ve atölye çalışmaları önerilmiştir.
Okur vd., (2024)[30]	Rehber Öğretmenleri ve Sınıf Öğretmenleri	Yarı Yapılandırılmış Görüşme Formu	Öğretmenlerin özel öğrenme güçlüğü tanı ve müdahale süreçleri hakkında bilgi eksikliği olduğu belirtilmiştir.	Çoğu öğretmenin farkındalık düzeyi yetersizdir; tanılama ve müdahale süreçlerine yönelik eksiklikler bulunmaktadır.	Öğretmenlere yönelik özel öğrenme güçlüğü eğitimlerinin artırılması, öğretimsel uyarlamaların teşvik edilmesi ve erken müdahale uygulamalarının yaygınlaştırılması önerilmiştir.
Akbaş (2024)[66]	Çocuk Gelişimi Öğretmenleri	ÖÖG Alanı Öğretmen Yeterlik Ölçeği	ÖÖG yeterlik algıları bazı değişkenlere göre farklılaşmaktadır.	Orta / geliştirilmesi gerekli	Hizmet içi eğitim, seminer ve kamu farkındalığı çalışmaları önerilmiştir.
Tansel Günal (2024)[64]	Sınıf, Matematik ve Rehber Öğretmenleri	Diskalkuli farkındalığına yönelik açık uçlu görüşme formu	Öğretmenlerin yaklaşık %54'ü diskalkulinin anlamını bilmektedir; %44'ü bilmemektedir.	Orta düzey	Diskalkuli konusunda eğitim, erken tanı ve müdahale yeterliklerinin artırılması önerilmiştir.

Mangır (2024)[65]	Sınıf Öğretmenleri	Öğrenme Güçlüğü Yaşayan Öğrencilere Yönelik Öğretmen Yeterliliği Ölçeği ve görüşme formu	Disleksi hakkında bilgi sahibi, dispraksi hakkında ise yeterli bilgiye sahip değildirler.	Nicel olarak yüksek; nitel olarak bazı alanlarda yetersizlik var	Görsel destek, destek eğitim ve sınıf yönetimi konusunda öğretmenlerin desteklenmesi önerilmiştir.
Aydoğmuş (2024)[67]	Sınıf Öğretmeni Adayı	Disleksi Bilgi ve İnanç Ölçeği	Genel bilgi düşük; tanı orta; tedavi orta düzeye yakın	Genel olarak orta düzey	Disleksiye yönelik bilgilendirici eğitimler ve kaynak kitaplar önerilmiştir.
Çelik (2025)[68]	Okul Öncesi Öğretmenleri	Okul Öncesi Öğretmenlerin Öğrenme Güçlüğü Alan Bilgisi Yeterlilik Ölçeği	Öğretmenlerin genel bilgiye sahip olduğu; ancak yeterliliklerinin istenen düzeyde olmadığı belirlenmiştir.	Düşük / sınırlı	Hizmet içi eğitimlerin artırılması, öğrenme güçlüğü olan öğrencilerle çalışma deneyiminin desteklenmesi önerilmiştir.
Şaşmaz (2025)[69]	Sosyal Bilgiler Öğretmen Adayları	Öğrenme güçlüğü farkındalık ölçeği	Öğrenme güçlüğü bilgisi olan adayların bazı alt boyutlarda daha yüksek puan aldığı görülmüştür.	Sınırlı	ÖÖG ve kapsayıcı eğitim içeriklerinin artırılması önerilmiştir.
Turan (2025)[70]	Sosyal Bilgiler Öğretmenleri	Öğretmen Bilgi Anketi, ÖÖG Soru Listesi, ÖÖG Tutum Ölçeği ve yarı yapılandırılmış görüşme soruları	ÖÖG bilgi düzeyleri orta seviyededir.	Orta düzey	Bilgi düzeyi arttıkça tutumların olumlu yönde geliştiği; ÖÖG bilgi ve tutumlarının artırılması gerektiği belirtilmiştir.
Çoban (2025)[71]	Beden Eğitimi ve Spor Öğretmenleri	Kişisel Bilgi Formu, ÖÖG Soru Listesi, Öğretmen Yeterlilik Ölçeği	Öğretmenler öğrenme güçlüğü hakkında bilgi sahibidir; ancak bu bilgiyi uygulamaya aktarmada eksiklikler vardır.	Öğrenme güçlüğünü tanıma konusunda farkındalık vardır; fakat BEP ve uyarlanmış fiziksel aktiviteler konusunda sınırlıdır.	BEP ve uyarlanmış fiziksel aktiviteler konusunda hizmet içi eğitim önerilmiştir.
Çelik Çoban (2025)[72]	İlköğretim Öğretmenleri	Disleksi Bilgi İnanç Ölçeği	Öğretmenlerin önemli bir bölümünde disleksiye ilişkin bilgi eksikliği vardır; eğitim alanların bilgi	Disleksili öğrenciyi destekleme konusunda kendini yetersiz gören öğretmen oranı yüksektir.	Hizmet öncesi ve hizmet içi disleksi eğitimleri artırılmalıdır

			puanları daha yüksektir.		
Akbaba (2025)[73]	Rehber Öğretmen ve Özel Eğitim Öğretmenleri	Demografik Bilgi Formu, ÖÖG Öğretmen Yeterlik Ölçeği	RAM personelinin ÖÖG alanındaki yeterlikleri genel olarak kabul edilebilir düzeydedir; hizmet içi eğitim ve deneyim yeterliği artırmaktadır.	ÖÖG tanılı öğrencilerle çalışma deneyimi olan personelin farkındalık ve yeterlik algısı daha yüksektir.	Hizmet içi eğitimlerin yaygınlaştırılması ve uygulama deneyimlerinin artırılması önerilmiştir.
Turan ve Ortak (2025)[74]	Sosyal Bilgiler Öğretmenleri	Özgül Öğrenme Güçlüğü Tutum Ölçeği	Çalışma doğrudan bilgi düzeyinden çok tutumları incelemiştir.	Öğretmenlerin ÖÖG'li öğrencilere yönelik tutumları orta düzeydedir.	Öğretmenlerin ÖÖG konusunda bilgi ve tutumlarını geliştirmeye yönelik eğitimler verilmelidir.

Tablo 8'de, öğretmenlerin ÖG konusunda sınırlı bilgiye sahip olduğunu ve tanılama, müdahale süreçlerinde eksiklik yaşadıklarını ortaya koymaktadır. Özellikle disleksi ve diskalkuli gibi alt alanlarda bilgi eksikliği ve kavram yanılgılarının yaygın olduğu görülmüştür. Öğretmenlerin farkındalık düzeylerinin genellikle düşük olduğu, ancak daha önce ÖG ile ilgili bir deneyime sahip olanların farkındalıklarının anlamlı şekilde daha yüksek olduğu belirtilmiştir.

TARTIŞMA

Araştırma kapsamında incelenen çalışmalar, öğretmenlerin nörogelişimsel bozukluklara ilişkin bilgi ve farkındalık düzeylerinin genel olarak yeterli olmadığını, ancak eğitim ve mesleki deneyimle geliştirilebildiğini göstermektedir. Dikkat Eksikliği ve Hiperaktivite Bozukluğu (DEHB), Otizm Spektrum Bozukluğu (OSB), zihinsel yetersizlikler (ZY) ve Öğrenme Güçlüğü (ÖG) alanlarında gerçekleştirilen çalışmaların ortak sonucu, öğretmenlerin bu bozukluklara ilişkin bilgi, tanılama ve eğitim süreçlerinde çeşitli eksiklikler yaşadıklarını ortaya koymaktadır.

DEHB alanındaki çalışmalar, öğretmenlerin bilgi ve farkındalık düzeylerinin düşük ile orta düzey arasında değiştiğini göstermektedir.[10,11,12] Bununla birlikte, eğitim ve mesleki gelişim faaliyetlerinin öğretmenlerin farkındalıklarını artırmada önemli bir rol oynadığı belirtilmektedir.[13,14] Genel olarak, bu çalışmalar, öğretmenlerin DEHB farkındalıklarının yıllar içinde sınırlı bir gelişim gösterdiğini, ancak eğitim ve mesleki gelişim programlarının farkındalık düzeylerini artırarak sınıf ortamını iyileştirme ve öğrencilerin akademik ve sosyal başarısına katkı sağlama açısından kritik bir araç olduğunu ortaya koymaktadır.[75]

OSB alanındaki araştırmalar da öğretmenlerin bilgi düzeylerinin yetersiz olduğunu, ancak eğitim programlarının bilgi, farkındalık ve tutumlar üzerinde olumlu etkiler oluşturduğunu ortaya koymaktadır.[15,16,17,18] Ayrıca öğretmenlerin bilgi düzeylerinin erken tanılama ve uygun yönlendirme süreçlerinde kritik öneme sahip olduğu vurgulanmaktadır.[19] Tüm bu bulgular, öğretmen eğitim programlarında OSB konusuna daha fazla yer verilmesi gerektiğini güçlü bir şekilde ortaya koymaktadır.

Zihinsel yetersizlikler konusunda yapılan çalışmalar, öğretmenlerin özel gereksinimli bireylere yönelik tutumlarının bilgi düzeyi, deneyim ve öz yeterlik algısından etkilendiğini göstermektedir.[20,21,22,23] Öğretmenlerin bilgi ve farkındalık düzeylerinin zihinsel engelli bireyler ve özel gereksinimli öğrencilerle etkileşimlerinde kritik bir rol oynadığını ortaya koymaktadır. Mısır'da yapılan bir müdahale çalışması,[24] yalnızca bilgiye dayalı eğitimlerin yetersiz olduğunu ve bilişsel-davranışsal müdahalelerin bir arada daha etkili sonuçlar verdiğini göstermiştir. Benzer şekilde, Güney Afrika'daki bir araştırma [76]

ise kapsayıcı eğitim politikalarının öğretmenler için bir stres kaynağı olduğunu ve bu stresin azaltılması için destekleyici eğitim ortamlarının önemini vurgulamaktadır. Sonuç olarak, öğretmenlerin bilgi ve farkındalık düzeylerinin artırılması için lisans eğitimi sırasında uygulamalı ve kapsamlı özel eğitim programlarının geliştirilmesi gerektiği, bu programların yalnızca bilgi sağlamaktan öte deneyim ve öz yeterliği güçlendiren yaklaşımlar içermesi gerektiği anlaşılmaktadır.

ÖG alanındaki araştırmalar ise öğretmenlerin disleksi ve diskalkuli gibi özel öğrenme güçlüklerine ilişkin bilgi eksiklikleri ve kavram yanılgıları yaşadıklarını ortaya koymaktadır. [25,26,27] Bu eksikliklerin erken tanılama ve müdahale süreçlerini olumsuz etkileyebildiği, hizmet içi eğitimler ve farkındalık çalışmalarının ise öğretmen yeterliklerini artırdığı belirtilmektedir.[28,29,30] Bulgular, öğretmenlerin bilgi ve farkındalık düzeylerini artırmaya yönelik hem lisans hem de hizmet içi eğitimlerde kapsamlı düzenlemelere, disiplinler arası iş birliğine ve bireyselleştirilmiş materyallerin yaygınlaştırılmasına [30,44,52] ihtiyaç duyulduğunu ortaya koymaktadır. Bu tür eğitimlerin yaygınlaşması, öğretmenlerin öz yeterlik algılarını ve çocuklarla olan etkileşimlerini olumlu yönde etkilediği ifade edilmektedir. [32,46,54]

SONUÇ VE ÖNERİLER

Sonuç olarak Türkiye'de 2025 yılına kadar yapılan çalışmalar öğretmenlerin nörogelişimsel bozukluklara ilişkin bilgi ve farkındalık düzeylerinin çoğunlukla düşük ya da orta düzeyde olduğunu göstermektedir. Öğrenim düzeyi, mesleki deneyim ve özel eğitim alanında alınan eğitimlerin öğretmenlerin bilgi, farkındalık ve öz yeterlik algıları üzerinde olumlu etkiler yarattığı görülmekle birlikte, bu gelişmelerin yaygın ve sürdürülebilir olmadığı anlaşılmaktadır. Özellikle OSB ve ÖG alanlarında formal eğitim süreçlerinin yetersizliği nedeniyle öğretmenlerin bilgiyi çoğu zaman kişisel deneyimler veya informal kaynaklardan edinmek zorunda kaldıkları görülmektedir. Bu bulgular doğrultusunda, öğretmen yetiştirme programlarında nörogelişimsel bozukluklara yönelik ders içeriklerinin güçlendirilmesi, hizmet içi eğitimlerin yaygınlaştırılması, disiplinler arası iş birliğinin desteklenmesi ve uygulamalı eğitim fırsatlarının artırılması önerilebilir. Ayrıca erken tanı ve bireyselleştirilmiş eğitim uygulamalarının güçlendirilmesi, öğretmenlere yönelik destek mekanizmalarının geliştirilmesi ve farkındalık çalışmalarının yaygınlaştırılması, özel gereksinimli öğrencilerin eğitim süreçlerine daha etkili katkı sağlanmasına yardımcı olabilir.

KAYNAKÇA

1. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders: DSM-5. Köroğlu E, trans. Ankara, Türkiye: Hekimler Yayın Birliği; 2013.
2. Merwe VM, Fourie JV, Yoro AJ. Learning support strategies for learners with neurodevelopmental disorders: Perspectives of recently qualified teachers. Afr J Disabil. 2020;9(1):1-10.
3. Honda H, Sasayama D, Niimi T, Shimizu A, Toibana Y, Kuge R, et al. Awareness of children's developmental problems and sharing of concerns with parents by preschool teachers and childcare workers: The Japanese context. Child Care Health Dev. 2024;50(1).
4. Akyıldız S. Öğretmen adaylarının engelli bireylere yönelik tutumlarının incelenmesi. Sos Polit Çalışmaları Derg. 2017;17(39):141-169.
5. Singh R, Gautam SK. Towards a more inclusive classroom: A qualitative exploration of teacher awareness of ADHD, autism, and learning disabilities. Int J Indian Psychol. 2024;12(2).
6. Mulholland S. ADHD-specific knowledge and attitudes of teachers (ASKAT): Development and validation of a new research instrument. Int J Educ Res. 2016;77:109-116.
7. Farooq Z, Imran N, Warraich S, Baloch AS, Hussain R. Awareness and knowledge about autism spectrum disorder among mainstream and special school teachers in Lahore. Pak Pediatr J. 2018;42(4):247-254.
8. Adebowale OF, Moye GP. Teachers' knowledge of and attitude towards learning disabilities. Online Educ J. 2013.
9. McKenzie K, Tanfield Y, Murray G, Sandhu R. Facilitating the identification of intellectual disability in schools: A qualitative study of stakeholder views. J Appl Res Intellect Disabil. 2024;37(1).
10. Almacıoğlu D. Yönetsel Bir Sorun Olarak Dikkat Eksikliği ve Hiperaktivite Bozukluğu Olan Öğrencilerin Sınıf ve Psikolojik Danışma ve Rehberlik Öğretmenleri Tarafından Tanınma Yeterliliklerinin İncelenmesi [yüksek lisans tezi]. Gaziantep: Gaziantep Üniversitesi Sosyal Bilimler Enstitüsü; 2007.
11. Göl İ, Bayık A. İlköğretim sınıf öğretmenlerinin çocuklarda dikkat eksikliği ve hiperaktivite bozukluğunu tanıma yeterlilikleri. DEÜ Hemşirelik Fak Elektronik Derg. 2013;6(4):207-213.
12. Beşkardeşler E. Okul Öncesi ve Sınıf Öğretmenlerinin Çocuklarda Dikkat Eksikliği ve Hiperaktivite Bozukluğunu Tanımaya Yönelik Bilgi Düzeylerinin İncelenmesi [yüksek lisans tezi]. Lefkoşa: Yakın Doğu Üniversitesi Eğitim Bilimleri Enstitüsü; 2017.
13. Küçük S, Uludaşdemir D, Aydın H, Kırçı T, Kibar E. Öğretmenlerin 6-12 yaş arası çocukların bilişsel gelişim özelliklerini bilme ve dikkat eksikliği ve hiperaktivite bozukluğu tanıma yeterlilikleri incelenmesi. J Acad Soc Sci. 2020;(107):229-241.
14. Biçer M, Çetin B. Öğretmenlerin dikkat eksikliği ve hiperaktivite bozukluğunu tanıma yeterlilikleri. Gaziantep Univ J Educ Sci. 2024;8(1):1-28.
15. Yumak E. İlköğretimde Görev Yapan Yönetici ve Öğretmenlerin Özel Eğitime Gereksinimi Olan Otistik Çocuklara Bakış Açısının İncelenmesi [yüksek lisans tezi]. İstanbul: Yeditepe Üniversitesi Sosyal Bilimler Enstitüsü; 2009.
16. Er-Sabuncuoğlu DM. Otizm bilgi düzeyi: Okul öncesi eğitimcileri. Hacettepe Univ Sağlık Bil Fak Derg. 2016;3(1):28-52.
17. Hacıibrahimoğlu YB, Ustaoğlu A. Okul öncesi öğretmen adaylarının otizm spektrum bozukluğu olan çocuklara ilişkin bilgi ve tutumlarının incelenmesi. İnönü Univ Educ Fac J. 2019;20(2):491-506.
18. Aral N, Deleş B, Aydoğdu F. Öğretmenlerin otizm spektrum bozukluğuna yönelik tutumlarının incelenmesi. In: 2nd International Contemporary Scientific Research Congress Proceedings; 2022:429-435.
19. Asma A. Öğretmenlerin Otizm Spektrum Bozukluğu Hakkındaki Bilgi ve Tutumlarının İncelenmesi [tıpta uzmanlık tezi]. İzmir: Sağlık Bilimleri Üniversitesi; 2023.
20. Süngü B. Beden Eğitimi ve Spor Öğretmen Adaylarının Zihinsel Engelli Çocuklara Yönelik Tutumlarıyla İlgili Bir Ölçek Geliştirme Çalışması [yüksek lisans tezi]. Çanakkale: Çanakkale Onsekiz Mart Üniversitesi Sağlık Bilimleri Enstitüsü; 2012.
21. Özcan HG, Özer D. Beden eğitimi ve spor öğretmenlerinin zihinsel engelli çocuklara yönelik tutumlarını etkileyen faktörlerin incelenmesi. Sağlık Spor Bil Derg. 2018;1(1):39-51.

22. Karademir T, Açak M, Türkçapar Ü, Eroğlu H. Beden eğitimi öğretmen adaylarının zihinsel engellilere yönelik tutumlarının belirlenmesi. Beden Eğitimi Spor Bil Derg. 2018;20(3):103-112.
23. Uslu Y. Beden Eğitimi Öğretmenlerinin Zihinsel Engelli Çocuklara Yönelik Tutumlarının Demografik Değişkenler Üzerinden İncelenmesi [yüksek lisans tezi]. Edirne: Trakya Üniversitesi Sağlık Bilimleri Enstitüsü; 2024.
24. Hassanein EEA. Changing teachers' negative attitudes toward persons with intellectual disabilities. Behav Modif. 2015;39(3):367-389.
25. Yangın S, Yangın N, Önder V, Şavlığ A. Sınıf öğretmeni adaylarının ve öğretim elemanlarının çeşitli öğrenme güçlüklerine yönelik farkındalıkları. NWSA Educ Sci. 2016;11(4):243-266.
26. Şahin R. Sınıf Öğretmenlerinin Disleksiye Yönelik Bilgi ve Tutumlarının İncelenmesi [yüksek lisans tezi]. Tokat: Tokat Gaziosmanpaşa Üniversitesi Eğitim Bilimleri Enstitüsü; 2019.
27. Kabasakal HZ, Uygur SS. Öğretmenlerin özel öğrenme güçlüğüne ilişkin bilgi düzeyleri, görüş ve kavram yanılgılarının incelenmesi. Int Soc Ment Health Res Thinkers J. 2021;7(51):2736-2754.
28. Başar M, Göncü A. Sınıf öğretmenlerinin öğrenme güçlüğüyle ilgili kavram yanılgılarının giderilmesi ve öğretmen görüşlerinin değerlendirilmesi. Hacettepe Univ J Educ. 2018;33(1):185-206.
29. Döşlü KP, Bağlama B. Okul öncesi öğretmenlerinin öğrenme güçlüğünün erken belirtilerine ilişkin görüşlerinin incelenmesi. Ulusal Eğitim Derg. 2022;2(2):361-388.
30. Okur M, Topuz A, Aksoy G. İlkokulda çalışan rehber öğretmenlerin ve sınıf öğretmenlerinin özel öğrenme güçlüğüne ilişkin görüşleri. Trakya Educ J. 2024;14(3):1813-1830.
31. Şimşek Ş, Yıldırım V, Bostan R. Psikolojik danışmanlık ve rehberlik öğretmenlerinin dikkat eksikliği ve hiperaktivite bozukluğu hakkındaki bilgi ve inançları. Van Med J. 2015;22(1):34-40.
32. Kıranşal N. İlköğretim Öğretmenlerinin Dikkat Eksikliği ve Hiperaktivite Bozukluğu Hakkındaki Damgalama Algıları ve İlişkili Faktörler [yüksek lisans tezi]. Kars: Kafkas Üniversitesi Sağlık Bilimleri Enstitüsü; 2019.
33. Batum S. Otizm Spektrum Bozukluğuna Yönelik Toplumsal Tutumlar Ölçeği'nin Türkçe Uyarlaması ve Öğretmenlerin OSB'ye Yönelik Tutumlarının Değerlendirilmesi [yüksek lisans tezi]. İstanbul: Marmara Üniversitesi Eğitim Bilimleri Enstitüsü; 2019.
34. Akgül EM, Mertoğlu H. Öğretmen yetiştirme programlarında otizm farkındalığı: Fen bilgisi eğitimi örneği. J Individ Differ Educ. 2020;2(1):31-41.
35. Burak Y, Özden E, Sardroud EM. Okul öncesi öğretmenlerin otizm spektrum bozukluğu bilgileriyle problem davranışlardan rahatsız olma düzeyleri arasındaki ilişkinin incelenmesi. Trakya Educ J. 2022;12(1):366-380.
36. Efe E. Sınıf Öğretmenlerinin Otizm Spektrum Bozukluğu Konusundaki Bilgi Düzeylerinin Belirlenmesi [yüksek lisans tezi]. Bolu: Bolu Abant İzzet Baysal Üniversitesi Lisansüstü Eğitim Enstitüsü; 2024.
37. Baş M. Okul Öncesi ve Sınıf Öğretmeni Adaylarının Otizm Spektrum Bozukluğu Farkındalık Düzeylerinin Belirlenmesi [yüksek lisans tezi]. Trabzon: Trabzon Üniversitesi Lisansüstü Eğitim Enstitüsü; 2025.
38. Uz Z. Farklı Branşlardaki Öğretmen Adaylarının Otizm Farkındalık Düzeylerinin Karşılaştırılması [yüksek lisans tezi]. Burdur: Burdur Mehmet Akif Ersoy Üniversitesi Eğitim Bilimleri Enstitüsü; 2025.
39. Tortop HS, Kandemir B, Kaya ÖE, Demir F. Öğretmen adaylarının zihinsel engelli birey kavramına ilişkin algıları. Abant İzzet Baysal Univ Educ Fac J. 2015;15:307-322.
40. Gülünay Yİ, Kayışoğlu N, İlhan L. Beden eğitimi öğretmeni adaylarının zihinsel engelli çocuklara yönelik tutumlarının çeşitli değişkenlere göre incelenmesi. Karabük Univ J Soc Sci Inst. 2019;9(2):626-639.
41. Karatağ M. Zihinsel engelliler özel eğitim uygulama okullarında çalışan müzik öğretmenlerinin karşılaştıkları sorunlar ve çözüm önerileri. J Art Human. 2020;4(1).
42. Gün E. Beden Eğitimi ve Spor Öğretmen Adaylarının Zihinsel Engelli Çocuklara Yönelik Tutumlarının İncelenmesi: Malatya İli Örneği [yüksek lisans tezi]. Malatya: İnönü Üniversitesi Sağlık Bilimleri Enstitüsü; 2021.
43. Karadeniz HM. Diskalkuli yaşayan öğrencilere ilişkin öğretmen görüşlerinin değerlendirilmesi. Educ Sci. 2013;8(2):193-208.

44. Altun T, Uzuner FG. Sınıf öğretmenlerinin özel öğrenme güçlüğü olan öğrencilerin eğitimine yönelik görüşleri. J Acad Soc Sci Stud. 2016;44:33-49.
45. Gül H, Yürümez E, Gül A, Kılıç HT, Ay MG. Öğretmenlerin özgül öğrenme güçlüğü ile ilgili bilgi düzeyleri ve damgalama: Çok merkezli bir çalışma. Ortadogu Med J. 2016;8(2).
46. Kaçar E. Meslek Lisesi Öğretmenlerinin Öğrenme Güçlüğü Hakkındaki Bilgi Düzeylerinin Çeşitli Değişkenler Açısından İncelenmesi [yüksek lisans tezi]. Eskişehir: Anadolu Üniversitesi Eğitim Bilimleri Enstitüsü; 2017.
47. Akdemir Y. Öğrenme Güçlüğü: Yeni Mezun Okul Öncesi Öğretmenlerinin Görüşlerinin İncelenmesi [yüksek lisans tezi]. Eskişehir: Anadolu Üniversitesi Eğitim Bilimleri Enstitüsü; 2018.
48. Birol ZN, Aksoy Zor E. Sınıf öğretmenlerinin özel öğrenme güçlüğü tanılı öğrencileriyle yaşadıkları sorunlara ilişkin görüşleri. Gazi Univ Educ Fac J. 2018;38(3):887-918.
49. Kuruyer HG, Çakıroğlu A, Özsoy G. Sınıf öğretmeni adaylarının okuma ve matematik güçlüklerine ilişkin pedagojik farkındalıklarının ve öğretimsel bakış açılarının belirlenmesi. Kastamonu Educ J. 2019;27(4):1659-1678.
50. Balcı E. Disleksi hakkında öğretmen görüşleri ve karşılaştıkları sorunlar. Ege Educ J. 2019;20(1):162-179.
51. Nurkan MA, Yazıcı E. Matematik öğretmenlerinin matematik öğrenme güçlüğü (diskalkuli) farkındalıklarının belirlenmesine ilişkin bir durum çalışması. Çağdaş Yönetim Bil Derg. 2020;7(1):95-109.
52. Emre O, Ulutaş A, İnci R, Coşanay B, Ayanoğlu M, Kaçmaz C, et al. Öğretmenlerin öğrenme güçlüğü yaşayan öğrencilere yönelik yeterlikleri, öz yeterlik kaynakları ve pozitif öğretmenlik becerileri arasındaki ilişki. Celal Bayar Univ Sos Bil Derg. 2020;18(1):205-218.
53. Çoğaltay N, Çetin İ. Sınıf öğretmenlerinin özel öğrenme güçlüğüne ilişkin yeterlilikleri: Nitel bir araştırma. Academia Eğit Araş Derg. 2020;5(1):126-140.
54. Bayrakçı M, Susam B. Sınıf öğretmenlerinin özel öğrenme güçlüğü yaşayan öğrencilerin özelliklerine ve eğitimlerine yönelik görüşleri. Akdeniz Univ Educ Fac Derg. 2021;4(2):45-56.
55. Baldemir B, İç Ü, Tutak T. İlköğretim matematik öğretmen adaylarının diskalkuliye ilişkin görüşleri. Abant İzzet Baysal Univ Educ Fac J. 2022;22(1):485-505.
56. Apak Ö. Okul Öncesi Öğretmenlerinin Özel Öğrenme Güçlüğü Hakkında Farkındalıkları [yüksek lisans tezi]. İstanbul: Maltepe Üniversitesi Lisansüstü Eğitim Enstitüsü; 2022.
57. Reis ÇT, Kansu ÇC. Sınıf öğretmeni adaylarının özel öğrenme güçlüğü yaşayan öğrencilere yönelik yeterliklerinin incelenmesi. Eurasian J Teach Educ. 2022;3(3):172-186.
58. Sivrikaya AG. Bilim ve Sanat Merkezinde Görev Yapan Öğretmenlerin Özgül Öğrenme Güçlüğü ve Disleksi Hakkındaki Bilgi ve Öz Yeterliklerinin İncelenmesi [yüksek lisans tezi]. Edirne: Trakya Üniversitesi Sosyal Bilimler Enstitüsü; 2023.
59. Sivrikaya O. Okul Öncesi Öğretmenlerinin Özgül Öğrenme Güçlüğü Hakkındaki Bilgi ve Öz Yeterliklerinin İncelenmesi [yüksek lisans tezi]. Edirne: Trakya Üniversitesi Sosyal Bilimler Enstitüsü; 2023.
60. Ürün YM, Ürün GG, Doğan U. Sınıf öğretmenlerinin özel öğrenme güçlüğü yaşayan öğrencilerin özelliklerine ve eğitimlerine yönelik görüşleri. Ulusal Eğitim Derg. 2023;3(2):520-521.
61. Kuzan İ, Özer M, Dada Ü, Dada B. Sınıf öğretmenlerinin özel öğrenme güçlüğüne ilişkin yeterlilikleri hakkında görüşleri. Ulusal Eğitim Derg. 2023;3(8):1187-1209.
62. Demir E. Sınıf Öğretmenlerinin Okuma Güçlüklerine İlişkin Farkındalık Düzeylerinin İncelenmesi [yüksek lisans tezi]. Ordu: Ordu Üniversitesi Sosyal Bilimler Enstitüsü; 2023.
63. Ülger M. Sınıf Öğretmenlerinin Özel Öğrenme Güçlüğü Alanına İlişkin Yeterlik Düzeylerinin Belirlenmesi ve Diskalkuliye İlişkin Görüşlerinin İncelenmesi [yüksek lisans tezi]. Malatya: İnönü Üniversitesi Eğitim Bilimleri Enstitüsü; 2023.
64. Günal TP. Sınıf, Matematik ve Rehber Öğretmenlerinin Diskalkuliye Yönelik Farkındalıklarının Belirlenmesi [yüksek lisans tezi]. Ankara: Başkent Üniversitesi Eğitim Bilimleri Enstitüsü; 2024.
65. Mangır M. Öğrenme Güçlüğü Yaşayan Öğrencilere İlişkin Sınıf Öğretmenlerinin Görüş ve Yeterlilikleri [yüksek lisans tezi]. Alanya: Alanya Alaaddin Keykubat Üniversitesi Lisansüstü Eğitim Enstitüsü; 2024.

66. Akbaş TS. Özel Eğitim ve Rehabilitasyon Merkezinde Çalışan Çocuk Gelişimi Mezunlarının Özel Öğrenme Güçlüğü Alanındaki Yeterlik Algılarının İncelenmesi [yüksek lisans tezi]. İstanbul: İstanbul Gelişim Üniversitesi Lisansüstü Eğitim Enstitüsü; 2024.
67. Aydoğmuş M. Sınıf öğretmeni adaylarının disleksi hakkındaki bilgi ve inanç düzeylerinin incelenmesi. Mehmet Akif Ersoy Univ Educ Bil Enst Derg. 2024;12(15):23-40.
68. Çelik İT. Eğitimde Öğrenme Güçlüğüne İlişkin Okul Öncesi Öğretmenlerin Yeterliliklerine Yönelik Çalışma: Kırşehir İli Okul Öncesi Öğretmenleri Örneği [yüksek lisans tezi]. Kırşehir: Kırşehir Ahi Evran Üniversitesi Sosyal Bilimler Enstitüsü; 2024.
69. Şaşmaz S. Sosyal Bilgiler Öğretmen Adaylarının Öğrenme Güçlüğü Olan Öğrenciler Hakkındaki Farkındalıklarının İncelenmesi [yüksek lisans tezi]. Ankara: Gazi Üniversitesi Eğitim Bilimleri Enstitüsü; 2025.
70. Turan M. Sosyal Bilgiler Öğretmenlerinin Özgül Öğrenme Güçlüğüne İlişkin Bilgi Düzeyleri ile Tutumları Arasındaki İlişki ve Özgül Öğrenme Güçlüğüne Yönelik Görüşleri [doktora tezi]. Afyonkarahisar: Afyon Kocatepe Üniversitesi Sosyal Bilimler Enstitüsü; 2025.
71. Çoban Ü. Beden eğitimi ve spor öğretmenlerinin öğrenme güçlüğüne yönelik yeterlilik ve farkındalıklarının incelenmesi. Spor Performans Araş Derg. 2025;16(1):71-87.
72. Çoban ÇA. İlköğretim Öğretmenlerinin Disleksi ile İlgili Bilgi ve İnançlarının Araştırılması [tıpta uzmanlık tezi]. Gaziantep: Gaziantep Üniversitesi; 2025.
73. Akbaba U. Rehberlik ve Araştırma Merkezleri Personellerinin Özel Öğrenme Güçlüğü Alanındaki Yeterliklerinin İncelenmesi [yüksek lisans tezi]. İstanbul: Biruni Üniversitesi Lisansüstü Eğitim Enstitüsü; 2025.
74. Turan M, Ortak Ş. Sosyal bilgiler öğretmenlerinin özgül öğrenme güçlüğü yaşayan öğrencilere yönelik tutumlarının incelenmesi. Uluslararası Sosyal ve Eğitim Bilimleri Derg. 2025;23:159-181.
75. Matthew MA, Nasri NM. Teachers' readiness and knowledge about ADHD students among mainstream school teachers: A systematic literature review. Int J Acad Res Prog Educ Dev. 2022;11(3):1584-1598.
76. Engelbrecht P, Oswald M, Swart E, Eloff I. Including learners with intellectual disabilities: Stressful for teachers? Int J Disabil Dev Educ. 2003;50(3):293-308.

COMPREHENSIVE SCIENTIFIC EVALUATION OF THE PRINCIPAL CLINICAL, DIAGNOSTIC, AND THERAPEUTIC DIMENSIONS OF ENDOVASCULAR INTERVENTIONAL MANAGEMENT IN GASTROINTESTINAL AND DUODENAL ULCER HEMORRHAGE: A CONCISE CASE-BASED ANALYTICAL REPORT

Nodar Sulashvili

MD, PhD, Doctor of Pharmaceutical and Pharmacological Sciences in Medicine, Professor of Medical and Clinical Pharmacology of International School of Medicine at Alte University, https://orcid.org/0000-0002-9005-8577

Gocha Chankseliani

MD, PhD, Doctor of Medical Sciences, Tbilisi State University, Faculty of Medicine, Tbilisi, Georgia https://orcid.org/0000-0001-8731-9206

Lali Patsia

MD, PhD, Doctor of Medical Sciences, Doctor Cardiologist at Republican Hospital, Invited Professor of Tbilisi State Medical University, https://orcid.org/0009-0007-7125-6862

Abstract

Gastrointestinal bleeding secondary to peptic and duodenal ulcer disease remains one of the most significant medical and surgical emergencies worldwide, contributing substantially to morbidity, mortality, prolonged hospitalization, recurrent hemorrhage, and healthcare expenditure. Despite considerable progress in pharmacotherapy, endoscopic hemostatic techniques, intensive care management, and minimally invasive therapeutic modalities, ulcer-related hemorrhage continues to represent a major challenge in modern gastroenterology and interventional medicine. In recent decades, endovascular surgical approaches, particularly transcatheter arterial embolization, have emerged as highly effective alternatives to conventional surgical intervention in patients with refractory, recurrent, or life-threatening gastrointestinal and duodenal ulcer bleeding. The increasing integration of advanced angiographic technologies, selective catheterization techniques, embolic biomaterials, and multidisciplinary treatment algorithms has significantly enhanced therapeutic outcomes while reducing perioperative complications and procedure-associated mortality. The present scientific discourse provides a comprehensive analytical overview of the essential clinical, pathophysiological, diagnostic, and therapeutic aspects of endovascular surgery in the management of gastrointestinal and duodenal ulcer hemorrhage, accompanied by a concise case-based evaluation illustrating practical interventional application. Special emphasis is placed on contemporary endovascular therapeutic techniques and their growing role in minimally invasive hemorrhage control. The scientific discussion evaluates selective arterial embolization, superselective catheterization, coil embolization, gelatin sponge application, polyvinyl alcohol particle utilization, liquid embolic agents, and combined embolization methods targeting branches of the gastroduodenal, left gastric, and pancreaticoduodenal arteries. The article further examines indications, contraindications, technical considerations, procedural planning, perioperative optimization, and post-procedural monitoring strategies associated with endovascular interventions. Comparative perspectives between endovascular treatment and traditional open surgical management are also analyzed, highlighting the reduced invasiveness, shorter recovery time, lower complication rates, preservation of gastrointestinal anatomy, and improved tolerability in elderly and critically ill patients undergoing transcatheter interventions. The presented brief case report describes a patient with severe recurrent duodenal ulcer bleeding resistant to pharmacological stabilization and repeated endoscopic hemostatic attempts. Ongoing hematemesis, progressive anemia, hypotension, and hemodynamic deterioration necessitated urgent angiographic assessment and selective embolization of the bleeding arterial branch. Successful endovascular intervention achieved complete hemostasis, stabilization of vital parameters, and prevention of emergency laparotomy. The clinical outcome demonstrated the effectiveness of multidisciplinary collaboration among gastroenterologists, interventional radiologists, vascular specialists, anesthesiologists, and critical care physicians in optimizing patient-centered therapeutic management. The article explores current innovations and future

perspectives in endovascular surgery, including artificial intelligence-assisted angiographic navigation, robotic catheter systems, bioresorbable embolic materials, image-guided precision embolization, and personalized vascular intervention strategies. The significance of evidence-based protocols, early diagnosis, individualized risk assessment, and integrated multimodal treatment pathways is emphasized as essential for improving survival rates and minimizing recurrent bleeding episodes. The scientific analysis also addresses potential complications such as ischemia, rebleeding, contrast-induced nephropathy, embolization failure, and vascular injury, together with preventive measures and long-term follow-up recommendations. The endovascular surgical management has become an indispensable component of contemporary treatment algorithms for gastrointestinal and duodenal ulcer hemorrhage, particularly in patients with high surgical risk or failed endoscopic therapy. Advances in interventional radiology, vascular imaging, and embolization technology continue to expand the therapeutic capabilities of minimally invasive procedures in acute gastrointestinal bleeding control. Comprehensive multidisciplinary coordination, technological innovation, and individualized therapeutic planning remain fundamental determinants of successful clinical outcomes and future progress in the field of endovascular gastrointestinal hemorrhage management.

Key Words: Endovascular surgery, gastrointestinal duodenal, ulcer bleeding, treatment.

Introduction

Acute gastrointestinal (GI) bleeding represents a frequent medical emergency that may range from mild self-limited hemorrhage to severe, life-threatening conditions requiring urgent intervention. Endoscopy remains the first-line diagnostic and therapeutic modality for both upper and lower gastrointestinal bleeding. Conventional treatment strategies include conservative medical management, therapeutic endoscopy, transcatheter embolization, and surgical intervention. In cases where endoscopic therapy fails or recurrent bleeding occurs, transcatheter embolization and surgical procedures are considered alternative therapeutic approaches. However, both methods may be associated with significant complications and varying degrees of procedural risk [1-3].

The selection of an appropriate management strategy largely depends on the patient's clinical status, hemodynamic stability, and underlying comorbidities. Emergency surgical intervention has traditionally been associated with relatively high morbidity and mortality rates. In recent decades, advances in interventional radiology and catheter-based techniques have significantly improved the safety and effectiveness of superselective transcatheter embolization, making it an increasingly preferred treatment modality for the management of acute gastrointestinal bleeding. This review highlights the expanding role of interventional radiology in the diagnosis and treatment of GI hemorrhage [4-6].

Technological developments in catheter systems, embolization materials, and imaging guidance have enhanced the feasibility and precision of angiographic embolization for both upper and lower gastrointestinal bleeding. Transcatheter embolization has demonstrated high technical success and favorable clinical outcomes, particularly in patients who do not respond to endoscopic or pharmacological therapy. Multidetector computed tomography (MDCT) has also emerged as a valuable diagnostic tool for identifying bleeding sources and evaluating the anatomical characteristics of the gastrointestinal tract in hemodynamically stable patients [7-8].

Effective management of gastrointestinal bleeding requires close multidisciplinary collaboration among interventional radiologists, gastroenterologists, and diagnostic radiologists. Endovascular embolization has been shown to significantly reduce mortality in high-risk patients who would otherwise require open surgical procedures following unsuccessful endoscopic treatment. Nevertheless, further clinical investigations are necessary to optimize treatment protocols and to better define the long-term outcomes of these minimally invasive therapeutic approaches [9-10].

The article discusses the epidemiological burden and pathogenesis of peptic ulcer bleeding, emphasizing the role of Helicobacter pylori infection, chronic nonsteroidal anti-inflammatory drug exposure, anticoagulant therapy, physiological stress, vascular abnormalities, and systemic comorbidities in ulcerogenesis and hemorrhagic progression. Particular attention is directed toward the hemodynamic instability and microvascular disruption associated with acute upper gastrointestinal bleeding, as well

as the mechanisms underlying recurrent hemorrhage and failed endoscopic hemostasis. Modern diagnostic strategies are reviewed in detail, including upper gastrointestinal endoscopy, contrast-enhanced computed tomography angiography, digital subtraction angiography, laboratory monitoring, and risk stratification systems utilized for evaluating bleeding severity, transfusion requirements, and prognostic outcomes [11-12].

Gastrointestinal (GI) bleeding represents one of the most frequent and potentially life-threatening emergencies encountered in clinical gastroenterology and surgical practice. It is defined as hemorrhage occurring within the gastrointestinal tract, extending from the esophagus to the rectum, and may manifest clinically as hematemesis, melena, hematochezia, or occult blood loss detected through laboratory investigations. The severity of gastrointestinal bleeding varies widely, ranging from mild and self-limiting bleeding episodes to massive hemorrhage associated with hemodynamic instability, shock, and significant mortality risk. Despite remarkable progress in diagnostic and therapeutic modalities, gastrointestinal bleeding continues to pose major challenges to clinicians due to its complex etiology, unpredictable clinical course, and high recurrence rate.Upper gastrointestinal bleeding is generally defined as bleeding originating proximal to the ligament of Treitz, including hemorrhage from the esophagus, stomach, and duodenum. The most common causes of upper GI bleeding include peptic ulcer disease, erosive gastritis, esophageal varices, Mallory–Weiss tears, and malignancies of the upper digestive tract. Among these etiologies, peptic ulcer disease remains one of the leading causes of acute upper gastrointestinal hemorrhage worldwide. In contrast, lower gastrointestinal bleeding arises distal to the ligament of Treitz and may result from conditions such as diverticulosis, angiodysplasia, colorectal cancer, inflammatory bowel disease, and ischemic colitis. Regardless of its anatomical origin, gastrointestinal bleeding requires prompt evaluation, accurate localization of the bleeding source, and rapid implementation of appropriate therapeutic interventions [13-15].

The clinical significance of gastrointestinal bleeding is reflected in its substantial morbidity, mortality, and healthcare burden. Acute GI hemorrhage often necessitates urgent hospitalization, intensive monitoring, blood transfusion, and multidisciplinary management involving gastroenterologists, surgeons, interventional radiologists, and critical care specialists. In severe cases, uncontrolled hemorrhage may lead to hypovolemic shock, organ dysfunction, and death if not treated promptly. Moreover, recurrent bleeding episodes significantly increase the risk of complications and prolong hospital stays, thereby contributing to increased healthcare costs and resource utilization. Consequently, continuous advancements in diagnostic technologies and therapeutic strategies are essential to improve patient outcomes and optimize the management of gastrointestinal bleeding [16-17].

Historically, the management of gastrointestinal hemorrhage relied heavily on conservative medical therapy and surgical intervention. Pharmacological treatment aimed at stabilizing the patient and reducing gastric acid secretion has long played a central role in the initial management of peptic ulcer bleeding. Proton pump inhibitors, vasoactive agents, and hemostatic drugs are frequently administered to stabilize the bleeding source and reduce the risk of recurrent hemorrhage. However, while medical therapy may be effective in certain cases, it is often insufficient for controlling active bleeding or preventing recurrence in patients with severe or persistent hemorrhage [18-20].

The introduction and rapid development of endoscopic techniques revolutionized the management of gastrointestinal bleeding. Endoscopy currently serves as both a diagnostic and therapeutic modality, allowing direct visualization of the gastrointestinal mucosa and enabling various hemostatic interventions. Endoscopic therapies such as injection therapy, thermal coagulation, mechanical clipping, and combination approaches have significantly improved the success rate of bleeding control. Endoscopic hemostasis is considered the first-line treatment for most cases of upper gastrointestinal bleeding, particularly those caused by peptic ulcers. Nevertheless, despite its high efficacy, endoscopic therapy may fail in a subset of patients, particularly when bleeding is massive, recurrent, or associated with complex vascular lesions [21-22].

When endoscopic management fails to achieve adequate hemostasis, alternative therapeutic approaches must be considered. Traditionally, emergency surgical intervention was the primary option in such situations. Surgical procedures such as oversewing of bleeding ulcers, gastrectomy, or vascular ligation were performed to control hemorrhage and prevent further blood loss. Although surgical treatment can

be life-saving, it is associated with significant morbidity and mortality, especially in elderly patients or individuals with severe comorbid conditions. Postoperative complications, prolonged recovery periods, and increased risk of infection further limit the widespread use of surgery as a primary treatment option for gastrointestinal bleeding [23-24].

Over the past several decades, significant technological advances in diagnostic imaging and interventional radiology have transformed the therapeutic landscape of gastrointestinal bleeding management. Among these innovations, endovascular techniques have emerged as highly effective and minimally invasive alternatives to conventional surgical treatment. Endovascular surgery refers to a group of catheter-based procedures performed within the vascular system using image-guided techniques. These procedures allow clinicians to access the bleeding vessel through percutaneous vascular entry and deliver targeted therapeutic interventions directly at the site of hemorrhage [25-27].

One of the most important endovascular procedures used in the treatment of gastrointestinal bleeding is transcatheter arterial embolization (TAE). This technique involves selective catheterization of the arterial supply to the bleeding region followed by the administration of embolic agents that occlude the affected vessel and stop the hemorrhage. Advances in catheter technology, microcatheter systems, guidewires, and embolization materials have significantly enhanced the precision and safety of this approach. Superselective catheterization enables interventional radiologists to target small branches of the mesenteric or gastric arteries while preserving blood flow to surrounding tissues, thereby minimizing the risk of ischemic complications [28-30].

Transcatheter embolization has demonstrated high technical and clinical success rates in the treatment of both upper and lower gastrointestinal bleeding. The procedure is particularly valuable in patients who are poor surgical candidates due to advanced age, comorbid diseases, or hemodynamic instability. Furthermore, embolization can be repeated if necessary and is often associated with shorter recovery times compared with open surgical procedures. The growing adoption of this technique reflects the broader trend toward minimally invasive therapeutic strategies in modern medicine [31-33].

Another key advancement in the diagnostic evaluation of gastrointestinal bleeding is the use of multidetector computed tomography (MDCT). MDCT angiography has become an essential imaging modality for detecting and localizing active bleeding sites within the gastrointestinal tract. This noninvasive technique provides high-resolution visualization of vascular structures and allows rapid identification of contrast extravasation, vascular malformations, or other pathological changes responsible for hemorrhage. In hemodynamically stable patients, MDCT plays a crucial role in guiding subsequent therapeutic interventions, including endovascular embolization or targeted endoscopic treatment [34-36].

The integration of advanced imaging technologies with interventional radiology techniques has significantly improved the overall management of gastrointestinal bleeding. Modern diagnostic algorithms often incorporate MDCT angiography as an early diagnostic step, particularly when endoscopy fails to identify the bleeding source. The combination of imaging-guided diagnosis and catheter-based therapy enables rapid localization and treatment of hemorrhage, thereby reducing the need for invasive surgical procedures [37-39].

Despite these significant advancements, several challenges remain in the management of gastrointestinal bleeding. Accurate identification of the bleeding source may be difficult in cases of intermittent or low-volume hemorrhage. Additionally, patients with complex vascular anatomy or multiple bleeding sites may require repeated diagnostic and therapeutic procedures. The risk of complications, including bowel ischemia, rebleeding, and contrast-related adverse reactions, must also be carefully considered when selecting the appropriate treatment strategy [40-42]

The successful management of gastrointestinal bleeding therefore requires a multidisciplinary approach involving close collaboration among gastroenterologists, surgeons, radiologists, and critical care specialists. Each discipline contributes unique expertise to the diagnostic and therapeutic process. Gastroenterologists play a central role in endoscopic diagnosis and treatment, while interventional radiologists provide minimally invasive vascular interventions when endoscopic therapy fails. Surgeons remain essential for managing cases in which both endoscopic and endovascular treatments are unsuccessful or contraindicated [43-45].

Recent research has focused on improving the safety and effectiveness of endovascular procedures through the development of novel embolic materials, enhanced imaging technologies, and refined catheterization techniques. New embolization agents, including microcoils, polyvinyl alcohol particles, liquid embolic materials, and absorbable gelatin sponges, have expanded the range of therapeutic options available to interventional radiologists. These materials allow precise control of vascular occlusion and enable tailored treatment strategies based on the specific characteristics of the bleeding lesion [46-48].

Furthermore, the increasing use of hybrid operating rooms and advanced imaging platforms has facilitated real-time integration of diagnostic and therapeutic procedures. These technological developments support more efficient patient management and allow rapid transition from diagnostic imaging to endovascular intervention when active bleeding is detected. As a result, patients with severe gastrointestinal hemorrhage can receive timely and targeted treatment, significantly improving clinical outcomes [49-51].

In addition to technological progress, growing emphasis has been placed on the development of evidence-based clinical guidelines for the management of gastrointestinal bleeding. International gastroenterology and radiology societies have published recommendations outlining optimal diagnostic pathways, treatment algorithms, and post-treatment monitoring strategies. These guidelines aim to standardize clinical practice, reduce variability in patient care, and ensure that patients receive the most effective and appropriate treatment based on current scientific evidence [52-53].

The present study focuses on the key clinical and technical aspects of endovascular surgery and interventional treatment in patients with gastrointestinal and duodenal ulcer bleeding. Particular attention is given to the diagnostic role of imaging techniques, the therapeutic effectiveness of transcatheter embolization, and the clinical outcomes associated with minimally invasive vascular interventions. By analyzing contemporary approaches to endovascular management, this work seeks to highlight the growing importance of interventional radiology in the treatment of gastrointestinal hemorrhage [54-56].

Understanding the advantages, limitations, and clinical indications of endovascular therapy is essential for optimizing patient management and improving survival outcomes in individuals with severe gastrointestinal bleeding. As medical technology continues to evolve, endovascular procedures are expected to play an increasingly prominent role in the multidisciplinary treatment of this challenging and potentially life-threatening condition [57-59].

Acute gastrointestinal bleeding is a common medical emergency that ranges from minor, uncontrollable bleeding to potentially life-threatening bleeding. The site of bleeding can be located anywhere in the gastrointestinal tract, which makes it difficult to determine its exact location. Patients with upper gastrointestinal bleeding usually have hematemesis or melena with the bleeding point proximal to the ligament of Treitz, while patients with lower gastrointestinal bleeding usually have melena or hematochezia with the bleeding point distal to the ligament of Treitz. Endoscopy is a first-line diagnostic procedure with 100% sensitivity to detect upper gastrointestinal bleeding. However, it has only 60% sensitivity for diagnosing lower gastrointestinal bleeding. Therapeutic options for treating acute GI bleeding include conservative treatment, therapeutic endoscopy, transcatheter embolization, and surgery. Transcatheter embolization and surgery are both options for recurrent GI bleeding [60-61]. When therapeutic endoscopy fails. The both options were associated with several complications and risk of bleeding. The choice of management depends on the patient's status (for example, the degree of hemodynamic instability or hypotension, or whether resuscitation is required). Emergency surgery is usually associated with high rates of morbidity and mortality. However, recent technical improvements in superselective transcatheter embolization have increased the safety of the procedure, and it is widely used in the treatment of acute gastrointestinal bleeding. This review article describes the role of interventional radiology in the emergency management of acute GI bleeding [62-63].

Upper gastrointestinal bleeding is defined as bleeding originating from the distal esophagus, stomach, or duodenum (ie, proximal to the ligament of Treitz). The most common cause of upper GI bleeding is peptic ulcer disease, but the differential diagnosis is varied and includes benign and malignant tumors,

ischemia, gastritis, arteriovenous malformations, Mallory-Weiss tears, trauma such as a Dieulafoy injury, and iatrogenic causes [64-66].

Upper gastrointestinal bleeding is a potentially fatal condition, so immediate management and accurate diagnosis of the location and etiology of bleeding is essential. The primary diagnostic procedure for upper gastrointestinal bleeding is endoscopy, which has high sensitivity and specificity for locating bleeding lesions in the upper gastrointestinal tract. Once a bleeding lesion is identified, therapeutic endoscopic techniques such as thermal coagulation or hemoclip placement can be used to achieve acute hemostasis. Endoscopic management achieves hemostasis in most patients, but 10% to 30% of patients experience recurrent bleeding for various reasons [67-69].

When hemostasis is not achieved with endoscopic management, other options are surgery and transarterial embolization. Surgery has long been the standard of care, but with the development of interventional radiology, more and more patients are now being referred for embolotherapy. Transarterial embolization can prevent unnecessary resection of the upper gastrointestinal tract and should be considered as an alternative to surgery [70-71].

The evolution of minimally invasive therapeutic strategies has significantly reshaped the clinical management paradigm of gastrointestinal hemorrhage during the past two decades. Among these innovations, endovascular surgery and catheter-based interventional radiology procedures have gained substantial recognition as effective alternatives to traditional surgical treatment. The rapid development of high-resolution imaging modalities, microcatheter technology, and advanced embolic materials has enabled clinicians to achieve accurate localization and precise occlusion of bleeding vessels with minimal trauma to surrounding tissues. These advancements have contributed to improved clinical outcomes, reduced procedural complications, and shorter hospital stays for patients suffering from severe gastrointestinal bleeding [72-73].

Endovascular interventions are particularly valuable in situations where conventional therapeutic approaches prove ineffective or contraindicated. In patients with persistent bleeding after endoscopic therapy, transcatheter arterial embolization provides an important second-line treatment option. The procedure is typically performed under fluoroscopic guidance, during which a catheter is introduced through a percutaneous arterial access point, most commonly the femoral or radial artery. The catheter is then navigated through the arterial system toward the vascular territory supplying the bleeding site. Once the responsible vessel has been identified through angiographic visualization, embolic materials are delivered through a microcatheter to achieve targeted vascular occlusion and cessation of hemorrhage [74-75].

One of the major advantages of endovascular treatment lies in its ability to selectively control bleeding without requiring extensive surgical exposure or tissue resection. Superselective catheterization techniques allow the interventional radiologist to isolate the precise arterial branch responsible for the hemorrhage, thereby minimizing the risk of ischemic injury to surrounding gastrointestinal tissues. This targeted approach is particularly beneficial in elderly patients or those with multiple comorbidities who may not tolerate major surgical procedures. Furthermore, because the intervention is performed through a small percutaneous puncture, recovery times are generally shorter, and postoperative complications are less frequent compared with traditional surgery [76-78].

In addition to its therapeutic applications, angiography plays an important diagnostic role in the evaluation of gastrointestinal bleeding. Conventional catheter-based angiography allows real-time visualization of arterial blood flow and can detect active bleeding through the appearance of contrast extravasation within the gastrointestinal lumen. This imaging modality is particularly useful when the bleeding source cannot be identified through endoscopic examination. In cases of intermittent bleeding, angiography may also reveal indirect signs of vascular pathology, such as pseudoaneurysms, arteriovenous malformations, or abnormal vascular networks associated with inflammatory or neoplastic processes [79-81].

The integration of angiographic diagnosis with immediate therapeutic intervention represents one of the key strengths of endovascular management. Once the bleeding vessel is identified during angiographic evaluation, embolization can be performed in the same procedural session, thereby eliminating the need for additional surgical exploration. This rapid transition from diagnosis to treatment is especially

important in patients experiencing massive hemorrhage, where prompt hemostasis is critical for preventing hemodynamic collapse and reducing mortality risk [82-83].

Another important factor contributing to the success of endovascular treatment is the wide range of embolic materials currently available to interventional radiologists. These materials are specifically designed to occlude blood vessels of varying sizes and can be selected according to the anatomical characteristics of the bleeding source. Mechanical embolic agents, such as metallic coils, function by inducing thrombosis within the targeted vessel. Particulate embolic agents, including polyvinyl alcohol particles and calibrated microspheres, provide distal vessel occlusion and are often used when diffuse bleeding occurs within small vascular branches. Temporary embolic agents, such as gelatin sponge particles, can also be used in certain clinical situations where reversible vascular occlusion is desirable [84-86].

Liquid embolic materials, including cyanoacrylate-based adhesives and ethylene vinyl alcohol copolymers, represent another important category of embolization agents. These substances rapidly solidify upon contact with blood, forming a durable intravascular cast that effectively blocks blood flow through the affected vessel. The use of liquid embolic agents has expanded the therapeutic capabilities of interventional radiology, particularly in complex cases involving high-flow vascular lesions or pseudoaneurysms. However, their application requires considerable technical expertise due to the risk of unintended embolization of adjacent vessels [87-89].

Despite the numerous advantages associated with endovascular therapy, the procedure is not entirely free from complications. One of the most significant risks is the development of intestinal ischemia resulting from excessive or nonselective vascular occlusion. Although superselective catheterization techniques significantly reduce this risk, careful evaluation of collateral blood supply is essential before embolization is performed. Other potential complications include access-site hematoma, contrast-induced nephropathy, allergic reactions to contrast agents, and rebleeding following incomplete embolization [90-92].

Rebleeding remains an important clinical concern in the management of gastrointestinal hemorrhage. While transcatheter embolization demonstrates high initial technical success rates, recurrent bleeding may occur in a subset of patients due to collateral vessel formation, incomplete occlusion of the bleeding artery, or progression of the underlying pathological condition. In such cases, repeat angiographic evaluation and secondary embolization procedures may be required. Nevertheless, even when repeat interventions are necessary, endovascular treatment generally remains less invasive and safer than emergency surgical alternatives [93-95].

Another critical component of modern gastrointestinal bleeding management is the use of multidetector computed tomography angiography (MDCTA). This imaging technique provides rapid and noninvasive evaluation of the abdominal vasculature and has become an essential diagnostic tool in many clinical settings. MDCTA can detect active bleeding at rates as low as 0.3–0.5 mL per minute and offers excellent spatial resolution for identifying vascular abnormalities. In addition, the three-dimensional reconstruction capabilities of MDCTA allow detailed visualization of mesenteric vascular anatomy, which is invaluable for planning subsequent endovascular interventions [96-97].

The growing use of MDCTA has led to significant improvements in the diagnostic workflow for patients with suspected gastrointestinal bleeding. In hemodynamically stable patients, CT angiography is often performed prior to endoscopic or angiographic evaluation to localize the bleeding source and determine the most appropriate therapeutic approach. This strategy not only improves diagnostic accuracy but also reduces unnecessary invasive procedures. Furthermore, CT findings can help predict the likelihood of successful embolization by identifying the specific arterial territory involved in the hemorrhage [98-99].

The importance of multidisciplinary collaboration cannot be overstated in the effective management of gastrointestinal bleeding. Optimal patient outcomes are achieved when gastroenterologists, surgeons, interventional radiologists, and intensive care specialists work together to develop individualized treatment strategies. Such collaboration allows for rapid decision-making and ensures that each patient receives the most appropriate combination of diagnostic and therapeutic interventions [100-101].

For example, in cases of upper gastrointestinal bleeding caused by peptic ulcer disease, initial management typically involves endoscopic hemostasis combined with pharmacological therapy using proton pump inhibitors. If endoscopic treatment fails or if the bleeding recurs despite repeated attempts at hemostasis, the patient may be referred for angiographic embolization. Surgical intervention is generally reserved for cases in which both endoscopic and endovascular treatments are unsuccessful or when complications such as perforation or uncontrolled hemorrhage occur [102-103].

Similarly, in lower gastrointestinal bleeding, the diagnostic approach often involves colonoscopy as the first-line investigation. However, in situations where colonoscopy is inconclusive or technically difficult due to active bleeding or inadequate bowel preparation, CT angiography and catheter-based angiography may provide valuable diagnostic information. Endovascular embolization can then be performed to control bleeding originating from branches of the superior or inferior mesenteric arteries [104-106].

The ongoing development of novel imaging technologies and embolization techniques continues to expand the therapeutic potential of endovascular interventions. Emerging innovations such as cone-beam CT integrated within angiographic suites allow real-time three-dimensional imaging during catheter-based procedures, improving the accuracy of vessel targeting and embolic material delivery. In addition, robotic-assisted catheter navigation systems are being explored as a means of enhancing procedural precision and reducing radiation exposure for both patients and medical personnel [107-108].

Future research in the field of interventional radiology is also focusing on the development of bioresorbable embolic materials and drug-eluting embolization agents. These advanced materials may offer improved therapeutic control while minimizing long-term vascular complications. Furthermore, the integration of artificial intelligence and advanced image-processing algorithms into diagnostic imaging platforms has the potential to enhance the detection and characterization of gastrointestinal bleeding sources, thereby facilitating earlier and more effective intervention [109-110].

The rapid advancement of endovascular surgery and interventional radiology techniques has fundamentally transformed the clinical management of gastrointestinal bleeding. These minimally invasive procedures provide highly effective alternatives to conventional surgical treatment and have significantly improved patient outcomes in cases of severe or refractory hemorrhage. The continued refinement of diagnostic imaging modalities, catheterization technologies, and embolization materials is expected to further enhance the safety, precision, and clinical effectiveness of endovascular therapy [111-113].

As healthcare systems increasingly emphasize minimally invasive treatment strategies, the role of endovascular interventions in the management of gastrointestinal bleeding will continue to expand. Ongoing research, technological innovation, and interdisciplinary collaboration will be essential for optimizing treatment protocols and ensuring that patients benefit from the full potential of these advanced therapeutic approaches [114-115].

Aim of the research was to study the key issue aspects of features of endovascular surgery and treatment for gastrointestinal and duodenal ulcer bleeding and brief case report.

Materials and Methods

The material of the article was the data from scientific publications, which were processed, analyzed, overviewed and reviewed by generalization and systematization. Research studies are based on a review/overview assessment of the development of critical visibility and overlook of the modern scientific literature. Use the following databases: (for extensive literature searches to identify key issue aspects of features of endovascular surgery and treatment for gastrointestinal and duodenal ulcer bleeding and brief case report). PubMed, Web of Science, Clinical Key, Tomson Reuters, Google Scholar, Cochrane library, and Elsevier foundations. National and international policies and guidelines were also reviewed and as well as grey literature.

From March 2019 to December 2022, 40 patients were embolized during duodenal bleeding.

These patients were divided into the following groups:

➢ Massive, active bleeding.

➢ Recurrence of bleeding in clinic and endoscopy was unsuccessful.

➢ Unstable hemodynamics and solid hemostasis could not be achieved during endoscopy.

➢ Failed to evacuate stomach contents and failed to see a bleeding ulcer.

➢ High risk of bleeding recurrence (Forest classification).

➢ Elderly and patients burdened with co-morbidities, with whom operative.

Result and Discussion

The present study examined the clinical features, diagnostic pathways, and therapeutic outcomes associated with the use of endovascular techniques in the management of gastrointestinal bleeding, particularly hemorrhage related to duodenal ulcer disease. Gastrointestinal bleeding remains a major clinical challenge due to its sudden onset, variable severity, and potentially life-threatening consequences. The findings of the present analysis highlight the growing role of endovascular interventions, especially transcatheter arterial embolization, as an effective therapeutic strategy for controlling bleeding when conventional methods such as pharmacological therapy and endoscopic intervention prove insufficient.

The clinical evaluation of patients included in this investigation demonstrated that the majority of cases presented with typical symptoms of acute upper gastrointestinal bleeding, including hematemesis, melena, and signs of acute blood loss such as hypotension, tachycardia, and decreased hemoglobin concentration. In many patients, the bleeding was associated with duodenal ulceration, which is widely recognized as one of the most common causes of upper gastrointestinal hemorrhage. Duodenal ulcers are often linked to Helicobacter pylori infection, chronic use of nonsteroidal anti-inflammatory drugs, stress-related mucosal injury, and various systemic conditions that compromise mucosal integrity. The results observed in this study support existing evidence indicating that ulcerative lesions in the gastroduodenal region frequently involve erosion of arterial branches, particularly those arising from the gastroduodenal artery, thereby creating a high risk of severe bleeding.

Initial management of the patients involved standard resuscitative measures aimed at stabilizing hemodynamic parameters and correcting acute blood loss. Intravenous fluid replacement, transfusion of packed red blood cells when necessary, and pharmacological therapy with proton pump inhibitors were administered in accordance with established clinical guidelines. These interventions are essential components of the early treatment algorithm for gastrointestinal bleeding because they help maintain circulatory stability while diagnostic investigations are performed. In the majority of patients, upper gastrointestinal endoscopy served as the primary diagnostic modality, allowing direct visualization of the bleeding site and facilitating immediate endoscopic hemostasis.

Endoscopic treatment methods included injection therapy, thermal coagulation, and mechanical clipping of bleeding vessels. In many cases, these procedures successfully achieved primary hemostasis. However, a subset of patients experienced persistent or recurrent bleeding despite endoscopic intervention. This observation is consistent with previous clinical reports demonstrating that although endoscopic therapy is highly effective, it may fail in approximately 10–20% of severe bleeding cases. Factors contributing to endoscopic treatment failure include large ulcer size, arterial spurting, coagulopathy, hemodynamic instability, and difficult anatomical localization of the bleeding source.

In patients where endoscopic hemostasis proved unsuccessful, endovascular intervention was considered the next therapeutic step. Angiographic evaluation was performed using digital subtraction angiography to identify the vascular origin of the hemorrhage. The angiographic findings frequently demonstrated active contrast extravasation within the duodenal region or abnormal vascular patterns corresponding to the arterial supply of the gastroduodenal artery and its branches. In several cases, the bleeding source originated from branches of the pancreaticoduodenal arteries, which form a complex vascular network supplying the duodenum and adjacent pancreatic structures.

The technical success of angiographic localization was high, allowing interventional radiologists to precisely identify the responsible vessel and perform selective catheterization. Superselective catheterization was achieved through the use of microcatheter systems that enabled access to small arterial branches with minimal disruption of surrounding vascular structures. Once the bleeding vessel had been successfully catheterized, embolization was performed using appropriate embolic materials. These materials included metallic coils, gelatin sponge particles, and other embolization agents designed to induce thrombosis and achieve permanent or temporary vascular occlusion.

The results of the embolization procedures demonstrated a high rate of immediate hemostasis. In most patients, bleeding ceased promptly following the delivery of embolic materials into the targeted vessel. The rapid effectiveness of this intervention underscores the clinical value of transcatheter embolization as a minimally invasive alternative to emergency surgical procedures. Furthermore, the procedure was generally well tolerated by patients, and the majority of individuals experienced stabilization of their clinical condition shortly after the intervention.

One of the most important findings of this investigation relates to the safety profile of endovascular treatment. Complications associated with embolization were relatively rare and generally manageable. The most significant potential complication is intestinal ischemia, which may occur if embolization inadvertently compromises the blood supply to extensive segments of the gastrointestinal tract. However, the use of superselective catheterization techniques significantly reduces this risk by limiting embolization to the specific arterial branch responsible for the bleeding. In the present study, careful angiographic assessment of collateral circulation was performed prior to embolization in order to preserve adequate perfusion to adjacent tissues.

Another important consideration in the interpretation of the results is the possibility of recurrent bleeding following embolization. Although the majority of patients achieved durable hemostasis, a small number of cases experienced rebleeding during the follow-up period. Recurrent hemorrhage may occur due to incomplete occlusion of the bleeding vessel, development of collateral circulation, or progression of the underlying ulcerative disease. In such situations, repeat angiographic evaluation and secondary embolization may be required. Despite this possibility, the rate of rebleeding observed in the present analysis remained within the range reported in previous clinical studies.

The diagnostic contribution of multidetector computed tomography angiography also deserves special attention in the discussion of the results. In several cases, CT angiography was used prior to catheter angiography to identify the approximate location of the bleeding source. This imaging modality provided valuable information regarding the anatomical relationships between the gastrointestinal tract and surrounding vascular structures. The ability of CT angiography to detect active bleeding through visualization of contrast extravasation significantly facilitated the planning of subsequent endovascular intervention. Furthermore, the noninvasive nature of CT imaging makes it particularly suitable for use in hemodynamically stable patients during the initial stages of diagnostic evaluation.

The integration of CT imaging with angiographic intervention represents a major advancement in the modern management of gastrointestinal bleeding. By combining rapid diagnostic visualization with targeted therapeutic intervention, clinicians are able to control hemorrhage more efficiently and reduce the need for invasive surgical procedures. The findings of this study reinforce the concept that multidisciplinary collaboration between gastroenterologists, radiologists, and surgeons is essential for achieving optimal patient outcomes.

From a broader clinical perspective, the results of the present investigation contribute to the growing body of evidence supporting the use of endovascular techniques in the treatment of gastrointestinal hemorrhage. Over the past two decades, numerous studies have reported high technical success rates for transcatheter arterial embolization, often exceeding 85–90%. These findings demonstrate that embolization is not only effective in achieving immediate hemostasis but also capable of significantly reducing the need for emergency surgical intervention. Considering the substantial risks associated with surgery in critically ill patients, the availability of a minimally invasive alternative represents a major advancement in therapeutic practice.

Another important aspect of the discussion concerns the economic and organizational implications of endovascular treatment. Although angiographic procedures require specialized equipment and trained

personnel, they often result in shorter hospital stays and reduced postoperative complications compared with traditional surgery. Consequently, the overall cost of patient care may be lower when endovascular therapy is used as part of a comprehensive treatment strategy for gastrointestinal bleeding. Additionally, the minimally invasive nature of the procedure contributes to faster patient recovery and earlier return to normal physiological function.

Technological innovations continue to expand the therapeutic capabilities of interventional radiology in this field. Modern microcatheter systems provide improved flexibility and navigational control, allowing clinicians to access increasingly small and complex vascular territories. Similarly, the development of advanced embolic materials with enhanced biocompatibility and controlled occlusion properties has improved the safety and effectiveness of embolization procedures. These advancements suggest that endovascular treatment will play an even greater role in the management of gastrointestinal bleeding in the future.

Despite the promising results observed in the present study, certain limitations must also be acknowledged. The success of endovascular treatment depends heavily on the availability of specialized radiological infrastructure and the expertise of experienced interventional radiologists. In healthcare settings where such resources are limited, access to angiographic intervention may be restricted. Furthermore, although embolization is highly effective in controlling acute bleeding, it does not directly address the underlying pathological process responsible for ulcer formation. Therefore, long-term management strategies, including eradication of Helicobacter pylori infection and modification of ulcerogenic medication use, remain essential for preventing recurrence.

Overall, the results of this investigation highlight the significant therapeutic potential of endovascular techniques in the management of gastrointestinal bleeding associated with duodenal ulcer disease. The ability to achieve rapid hemostasis through minimally invasive vascular intervention represents a major advancement in modern clinical practice. When integrated into a multidisciplinary treatment framework that includes endoscopic evaluation, pharmacological therapy, and appropriate surgical backup, endovascular embolization offers a highly effective and safe method for controlling severe gastrointestinal hemorrhage.

The continuing development of imaging technologies, embolization materials, and catheter-based techniques is expected to further enhance the precision and clinical success of endovascular procedures. Future research should focus on refining patient selection criteria, optimizing embolization strategies, and evaluating long-term outcomes in larger patient populations. Such investigations will contribute to the development of evidence-based clinical guidelines and will help ensure that patients with gastrointestinal bleeding receive the most effective and appropriate treatment available.

Acute gastrointestinal bleeding is a common medical emergency that ranges from minor to potentially life-threatening bleeding. Endoscopy is the first-line diagnostic procedure for upper and lower gastrointestinal bleeding. Treatment options for acute GI bleeding include conservative management, therapeutic endoscopy, transcatheter embolization, and surgery. Transcatheter embolization and surgery are both options for recurrent GI bleeding when therapeutic endoscopy fails. However, both options are associated with several complications and risk of bleeding. The choice of management depends on the patient's status. Emergency surgery is usually associated with high rates of morbidity and mortality. Recently, superelective transcatheter embolization has become a safer procedure and is now widely used to treat acute gastrointestinal bleeding. This review article describes the role of interventional radiology in the management of acute GI bleeding. Improvements in catheter technology, development of more compatible embolization devices, and expansion of embolization techniques have led to angiography and embolization for the treatment of upper and lower gastrointestinal bleeding. Transcatheter embolization therapy for the treatment of acute GI bleeding is a safe procedure with high technical performance and clinical success, but it should be reserved as a treatment option for patients who have failed endoscopic and medical management. MDCT imaging is a useful tool for identifying the site of bleeding and evaluating the anatomical structure of the gastrointestinal tract in stable patients. Close working relationships between interventional radiologists, gastroenterologists, and diagnostic radiologists are essential for the optimal management of patients with GI bleeding. Endovascular

embolization dramatically reduces the mortality rate in high-risk patients who require open surgery after failed endoscopy, further studies are needed to fully address these objectives.

Lower gastrointestinal bleeding is defined as bleeding originating from a source distal to the ligaments of Treitz. About 80% of all lower GI bleeding comes from a colorectal source and 5% to 10% from a small intestinal source; 10% to 15% are classified as blood of upper gastrointestinal tract origin. A small bowel bleeding source is more likely than a colorectal bleeding source to be obscure or occult.

A common cause of lower GI bleeding is a colonic diverticulum. Differential diagnoses include colitis or enteritis, anorectal abnormalities (hemorrhoids, proctitis), tumors, arteriovenous malformations or angiodysplasia, and postpolyectomy bleeding.

Therapeutic colonoscopy is currently the first-line intervention for colonic bleeding. Colonoscopy is the diagnostic method of choice in patients with lower gastrointestinal bleeding, but therapeutic endoscopy can also be successful in a limited number of patients. Therapeutic colonoscopy fails in approximately 32% of cases due to the presence of stool or blood clots, or technical difficulties such as time required to prepare patients. Further disadvantages include the fact that small bowel bleeding cannot be accessed through colonoscopy and that colonoscopy is relatively ineffective when performed in patients with significant bleeding without bowel preparation. If bleeding cannot be stopped by therapeutic colonoscopy, transarterial embolization is the next line of therapy to control hemostasis. As with upper gastrointestinal bleeding, transarterial embolization is the first-line therapy for patients with lower gastrointestinal bleeding. The efficacy of transarterial embolization in the treatment of acute gastrointestinal bleeding when medical or endoscopic techniques are inadequate has been demonstrated in several large studies. For both upper and lower gastrointestinal bleeding, surgery is usually reserved as a last-line treatment for patients whose bleeding has failed to respond to previous treatments.

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In angiography, vascular access is usually obtained by transfemoral catheterization with a 4- or 5-Fr catheter and sheath. Diagnostic visceral arteriography, which includes angiography of the celiac trunk, superior mesenteric artery, and inferior mesenteric artery, is performed to examine the suspected vascular region, and then a microcatheter is inserted coaxially for superselective cannulation of the bleeding artery. In upper gastrointestinal bleeding, the source of the bleeding is usually identified by endoscopy. Therefore, angiography is most often performed only as a precursor to transcatheter embolotherapy. Angiograms are considered positive when they show direct angiographic evidence of active GI bleeding (eg, contrast medium extravasation) or indirect angiographic evidence of bleeding (eg, pseudoaneurysm). For embolization, the appropriate position of the catheter is selected, and transcatheter vessel occlusion is performed with embolized material. Embolization is carried out as

selectively as possible, the catheter is technically possible near the site of bleeding. The goal is to achieve proximal and distal control of the bleeding lesion (embolization of both inflow and outflow vessels) to reduce the risk of recurrent bleeding via collateral circulation. Embolization will continue to the occlusive angiographic endpoint without antegrade arterial blood flow in the embolized artery. Post-embolization arteriography is performed to confirm completion of the procedure. The most common embolic material used to treat upper gastrointestinal bleeding is a fibrous platinum microcoil, which is usually placed in the bleeding artery distally proximal to the angiographic position.

Extravasation of the contrast medium is stopped and complete occlusion of the bleeding vessel occurs. Coiling of the gastroduodenal artery from the celiac axis may be inadequate because the gastroduodenal artery may be fed by collateral branches of the superior mesenteric artery. A "sandwich" technique has been proposed, in which the gastroduodenal artery is looped distally proximally. Sandwich occlusion can be used at the level of the gastroduodenal artery with the catheter directed toward the origin of the right gastroepiploic artery, and when the catheter is removed the coils are inserted into the proximal gastroduodenal artery. Complete embolization of the gastroduodenal artery, including proximal and distal embolization and exclusion of its two side branches, is the technical end point.

Selective superior mesenteric arteriography is performed after embolization to ensure that the bleeding site is not secured. If extravasation is detected, superselective catheterization of the lower pancreatic duodenal artery and side branch is performed with a microcatheter. Over the past 10 years, significant improvements in this technique have made superelective embolization a safer procedure by minimizing the risk of intestinal ischemia.

The development of sophisticated rotating wires and coaxial microcatheters, along with advances in digital fluoroscopic imaging, now allow for more precise vascular interventions. In a recent report, transarterial embolization for upper gastrointestinal bleeding was associated with a high technical success rate (93%) and a minimal complication rate (9%). In addition, a recently published international consensus recommendation considers transarterial embolization as an alternative therapy for the treatment of upper gastrointestinal bleeding in patients who have failed an endoscopic hemostatic procedure or who have recurrent bleeding.

Transarterial embolization for the treatment of lower GI bleeding was first introduced in 1974 and involved the non-elective injection of an autologous clot. In 1977, Gelfoam and Oxycel injection were described for embolization of diverticular bleeding. Although injection of autogal clot or gelatin sponge has been shown to achieve hemostasis, these early embolization techniques were characterized by high rates of intestinal infarction. The development of coaxial microcatheters has increased interest in the use of embolization to control lower GI bleeding. The use of a microcatheter, delivered via a 4- or 5-wire guide catheter, to a specific margin near the bleeding site in the arteries or vas rectus can be obtained to remove embolic material. Because this technique is superselective, the risk of intestinal infarction is significantly lower than nonselective embolic techniques or vasopressin infusion, and there are no vasopressin-related systemic side effects. In addition, the risk of bleeding from collateral vessels is reduced as embolic material is delivered to the site of bleeding.

The most common embolic materials for lower GI bleeding, used alone or in combination, are microcoil, polyvinyl alcohol (PVA) particles, and gelatin sponge. Microcoils are persistent embolic agents that can be superselectively placed near the bleeding site and are easily identified under fluoroscopy. However, due to the small caliber of the target vessels, positioning these coils correctly can be difficult. Coils can back out of small vessels and provoke ischemia if they enter a large feeding vessel. PVA is a permanent embolic agent that is less selective than microcol. The basis for PVA embolization with respect to flow is that PVA particles preferentially flow to the area of least resistance (ie, the bleeding site). Defrin et al demonstrated in 10 patients that lesions inaccessible by superelective catheterization could be safely embolized by flow-directed PVA embolization. However, a consensus on the optimal PVA particle size for embolization in lower GI bleeding has not yet been reached. Previous reports have recommended a PVA particle size of 300 to 500 μm, as early animal studies have shown that smaller particles may be associated with a higher risk of intestinal ischemia. The choice of embolic agent in relation to the characteristics of the bleeding vessel is important, but which embolic agent is best among coils, cyanoacrylate glue, gelatin sponge, and calibrated particles remains a matter of debate. In our

department, microcoil, 1000 μm gelatin sponge particles, and cyanoacrylate glue are used to treat acute GI bleeding. Unlike PVA, the gelatin sponge is a temporary embolic agent that allows recanalization of the vessel from a few days to a few weeks. If the angiogram is negative for active bleeding, empiric embolization is performed based on discussion with the gastroenterologist or surgeon. For empiric embolization, if endoscopy showed that the bleeding source was located in the proximal stomach, the left gastric artery was selectively embolized. If endoscopy shows that the source of bleeding is in the distal stomach or duodenum, the gastroduodenal artery, the right gastroepiploic artery, the pancreaticoduodenum, or all three are selectively embolized. If endoscopic intervention fails to control bleeding, radioplaque clips are positioned as guides to the bleeding site via colonoscopy and transarterial embolization is performed.

Bleeding, deposition of coils is guided by endoscopy with pre-placed hemoclips. As a result, angiography and embolization of vessels causing GI bleeding have been gradually adopted and have revolutionized the management of lower GI bleeding.

Complications associated with embolization include angiography itself (eg, hematoma, arterial thrombosis, dissection, embolism, and pseudoaneurysm) as well as intestinal infarction. Early transcatheter intervention involved vasopressin infusion, but the high rate of rebleeding and high complication rates led to its reduced use. Higher rates of complications and bleeding have been described in patients treated with vasopressin. Although the first embolic techniques improved hemostasis, their use was limited by the high incidence of intestinal infarction. Until the advent and development of microcatheter technology, transarterial embolization became a safer, more effective method for managing gastrointestinal bleeding. Improvements in microcatheter systems have enabled more selective delivery of embolic material near bleeding sites. This overcame the systemic side effects of vasopressin and resulted in a reduced risk of intestinal infarction and vascular bleeding. Recently, many reports have suggested that superelective embolization for the management of gastrointestinal bleeding rapidly stops bleeding with minimal risk of ischemia. However, the risk of ischemia after embolization is increased in patients with a history of surgical intervention in the same area or when the therapeutic intervention involves embolic agents that may advance into the vascular bed. Such agents include liquids (for example, fabric adhesives such as cyanoacrylate) or very small particles.

In stable patients, multidetector computed tomography (MDCT) imaging is a useful tool to identify bleeding sites and assess the anatomical structure of the gastrointestinal tract, thereby allowing for more targeted intervention. Scintigraphy of red blood cells has a sensitivity and specificity of more than 90%. However, its simulated resolution does not provide an accurate diagnosis. Computed tomography angiography (CTA) is also used (sensitivity up to 86%) in the diagnosis of acute GI bleeding and can be used to pinpoint the location and etiology of bleeding and thus direct further management. A positive MDCT angiogram may be useful in selecting patients suitable for rapid targeted embolization. Visualization of active extravasation of contrast medium in the gastrointestinal tract requires careful attention to technique, including the use of fine collimation, rapid administration of contrast medium, and appropriate scan times. Additionally, multimodal reconstruction and three-dimensional imaging are useful in determining the exact source of bleeding. Although further studies are needed to determine which course of action is best when bowel preparation is not possible, CTA may be useful in this situation to identify the site of bleeding [18,34, 45,74].

The idea of embolization of duodenal bleeding as an alternative use of surgery belongs to Roche (1972). Since then, arterial embolization has been considered as an effective diagnostic and surgical method

- ❖ Common causes of duodenal bleeding:
- ➢ Arteriovenous malformation
- ➢ Visceral aneurysms/pseudoaneurysm
- ➢ Angiodysplasia
- ➢ Aortoenteric fistula
- ➢ Hemophilia
- ➢ Intestinal diverticula
- ➢ Inflammatory bowel disease (ulcer disease)
- ➢ Benign anorectal lesions

The main causes of duodenal bleeding. (See Illustration-1).

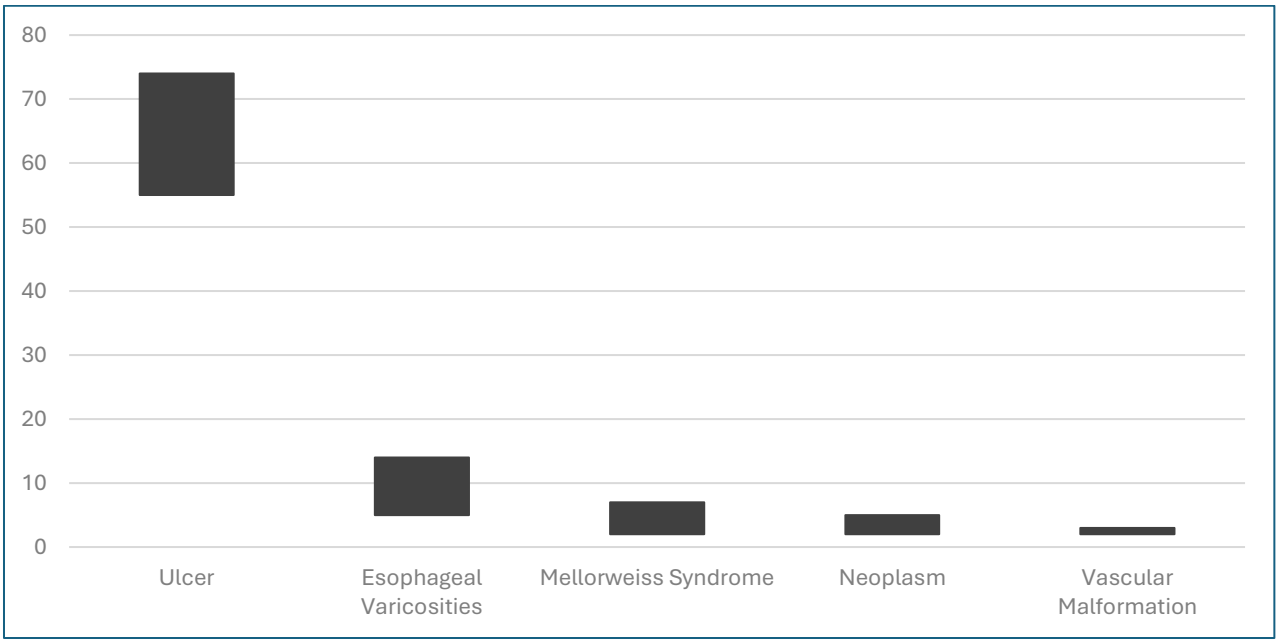


Illustration-1. Transcatheter arterial embolization for acute nonvariceal upper gastrointestinal bleeding: Indications, techniques and outcomes.

❖ Frequency of duodenal bleeding:

- 375 cases per 100,000 population
- Acute case of bleeding-75%
- 70% of patients are >65 years old
- Recurrent bleeding-25%
- Mortality is 19-40%
- Ratio male 2:1 female

❖ Clinical manifestations of duodenal bleeding

- Hematemesis
- Color brownish vomit
- Melena
- Anemia
- Tachycardia (if blood loss > 500 ml)
- Hypotension (if blood loss > 500 ml)
- Systemic shock (if blood loss is more than 15% of circulating blood volume).

Case Report

A middle-aged patient was admitted to the emergency department with clinical manifestations suggestive of acute upper gastrointestinal bleeding. The patient presented with symptoms including hematemesis, melena, generalized weakness, dizziness, and signs of progressive hemodynamic instability. Initial physical examination revealed pallor, tachycardia, and a moderate decrease in arterial blood pressure, indicating significant blood loss. Laboratory investigations demonstrated reduced hemoglobin levels and hematocrit values consistent with acute hemorrhage. Immediate resuscitative measures were initiated, including intravenous fluid therapy, blood transfusion when required, and pharmacological treatment with proton pump inhibitors in order to stabilize the patient's clinical condition.

Following initial stabilization, urgent upper gastrointestinal endoscopy was performed to determine the source of bleeding. Endoscopic examination revealed the presence of a duodenal ulcer with active bleeding. The ulcerative lesion was located in the duodenal bulb and showed signs of arterial erosion, which is a well-recognized cause of severe gastrointestinal hemorrhage. Endoscopic hemostatic techniques were attempted, including injection therapy and mechanical clipping. Although temporary bleeding control was achieved during the procedure, recurrent hemorrhage occurred within a short period of time, indicating failure of endoscopic therapy.

Given the persistence of bleeding and the risk of further hemodynamic deterioration, the patient was referred for angiographic evaluation and possible endovascular intervention. Digital subtraction angiography of the celiac trunk and superior mesenteric artery was performed to identify the vascular source of the hemorrhage. Angiographic imaging revealed contrast extravasation from a branch of the gastroduodenal artery, confirming the presence of active arterial bleeding in the duodenal region.

A microcatheter was advanced selectively into the affected arterial branch under fluoroscopic guidance. Superselective catheterization allowed precise localization of the bleeding vessel while preserving blood flow to adjacent vascular territories. Once the catheter position was confirmed, embolization was performed using metallic coils and additional embolic materials to occlude the bleeding artery. The embolic agents induced rapid thrombosis within the targeted vessel, effectively stopping the hemorrhage.

Control angiography performed immediately after embolization demonstrated complete cessation of contrast extravasation and successful occlusion of the bleeding vessel. The patient's hemodynamic status improved significantly following the procedure, and no further episodes of bleeding were observed during the subsequent monitoring period. Post-procedural management included continued proton pump inhibitor therapy, monitoring of hemoglobin levels, and evaluation for underlying etiological factors contributing to ulcer formation.

The patient recovered without major complications and was discharged in stable condition after appropriate observation and follow-up assessment. This case illustrates the clinical effectiveness of transcatheter arterial embolization as a minimally invasive therapeutic approach for the management of severe gastrointestinal bleeding when endoscopic treatment fails.

Diagnosis by fibrogastroscopy. See Photo-1-2.

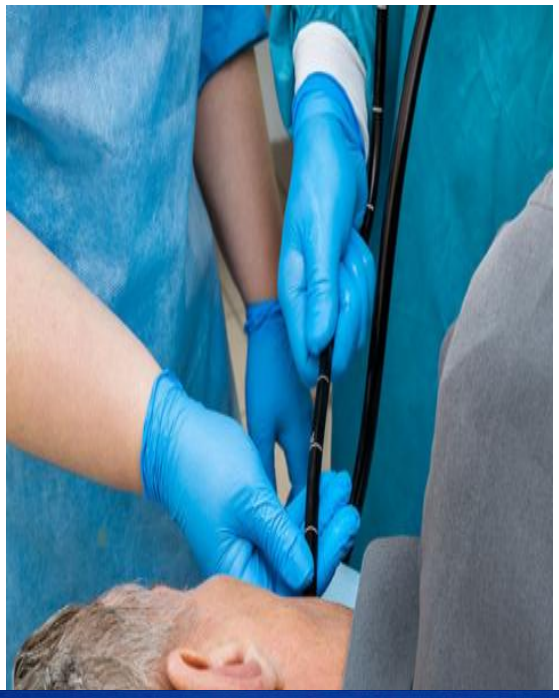




Photo-1-2. Fibrogastroscopy technics.

Angiography as a method of determining bleeding and result. (See Photo-3).

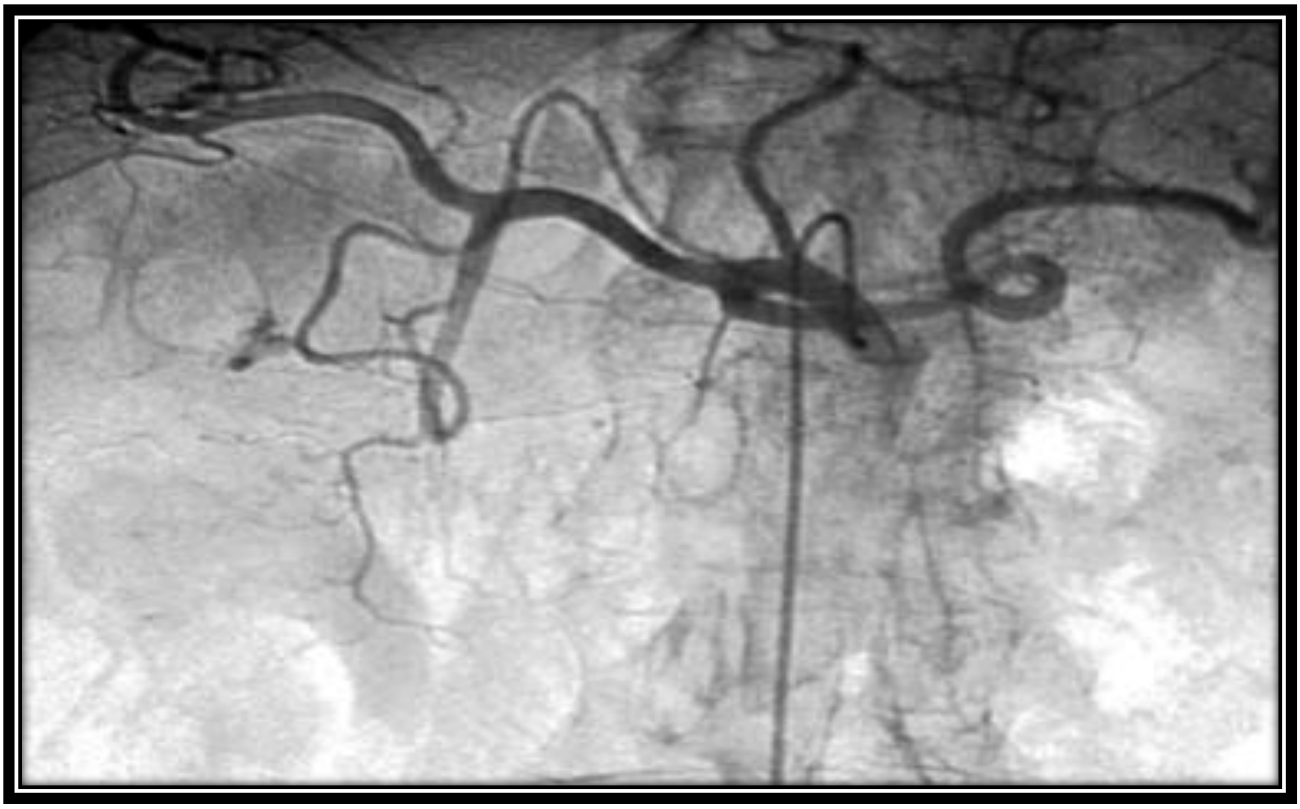


Photo-3. Angiography as a method of determining bleeding and result.

Angiographic signs of acute duodenal bleeding

- ❖ Direct:
- ➢ Contrast extravasation into the intestinal lumen

- ❖ Indirect:
- ➢ "Aneurysms/pseudoaneurysms
- ➢ Asymmetry of the blood vessel
- ➢ Arteriovenous/arterioportal shunting
- ➢ Neovascular

Our Purpose was to improvement of the results of surgical treatment of duodenal ulcer bleeding based on the use of endovascular embolization:

The task

- ➢ To determine indications for endovascular occlusion in ulcer patients complicated by gastroduodenal bleeding.
- ➢ The technique of endovascular interventions should be perfected.
- ➢ To evaluate the effectiveness of the endovascular occlusion method compared to the surgical method of treatment in high-risk patients.
- ➢ The tactics of surgical treatment of the mentioned patients should be developed based on the use of the endovascular occlusion method.

- ❖ Forrest's classification during endoscopy
- ➢ Forrest IA
- ➢ Forrest IB

- Forrest IIA
- Forrest IIB
- Forrest IIC
- Forrest III

Risk of rebleeding according to the Forrest classification. (See Illustration-2).

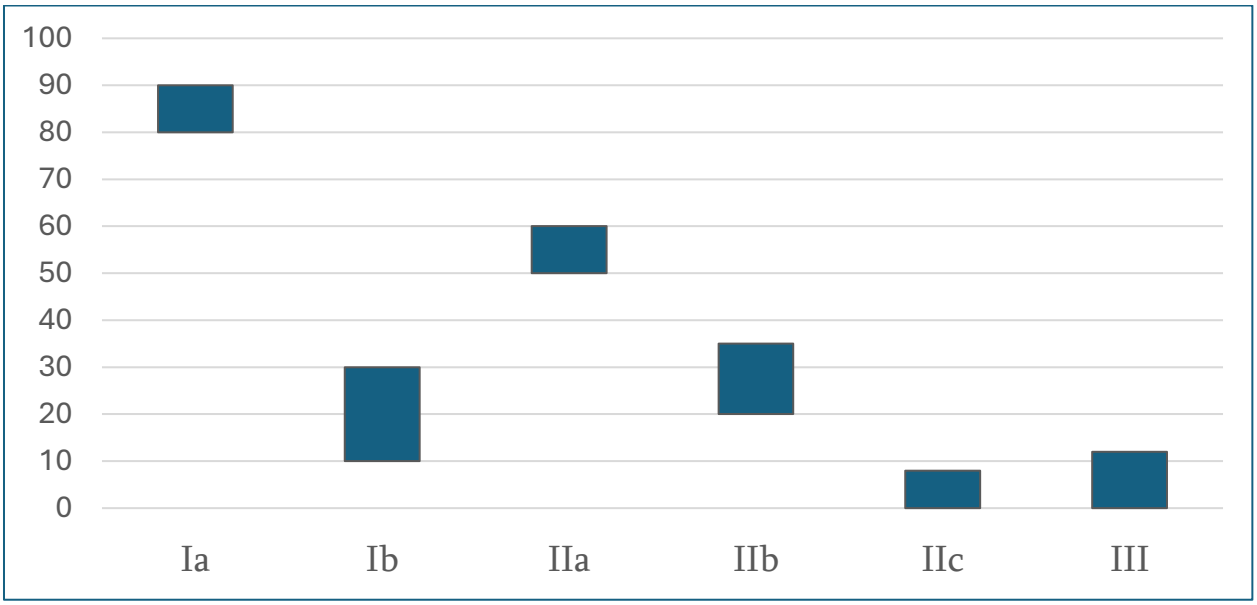


Illustration-2. Risk of rebleeding according to the Forrest classification.

❖ **Testimonials**

- Low-risk patients - surgical treatment
- And high-risk patients - endovascular surgery
- Recurrent bleeding after surgery - endovascular surgery

The diagnosis and management of gastrointestinal (GI) bleeding are complicated and requires a multidisciplinary approach involving gastroenterologists, interventional radiologists, and surgeons.

❖ **Testimonials**

- With active bleeding (requiring 4 units of blood transfusion in 24 hours).
- With hemodynamic instability (low systolic pressure, pulse 100 or more, hypovolemic shock) - who did not have satisfactory results during endoscopic hemostasis, in this case it will be important to calculate the Rokall score.
- A high risk of rebleeding should be used in the Forrest classification. Forrest 1A, Forrest 1B Forrest 2A and Forrest 2B
- Co-morbidities that aggravate the patient's medical history.

Graphical comparison of mean age of TAE and surgical groups in included studies. See Illustartion-3

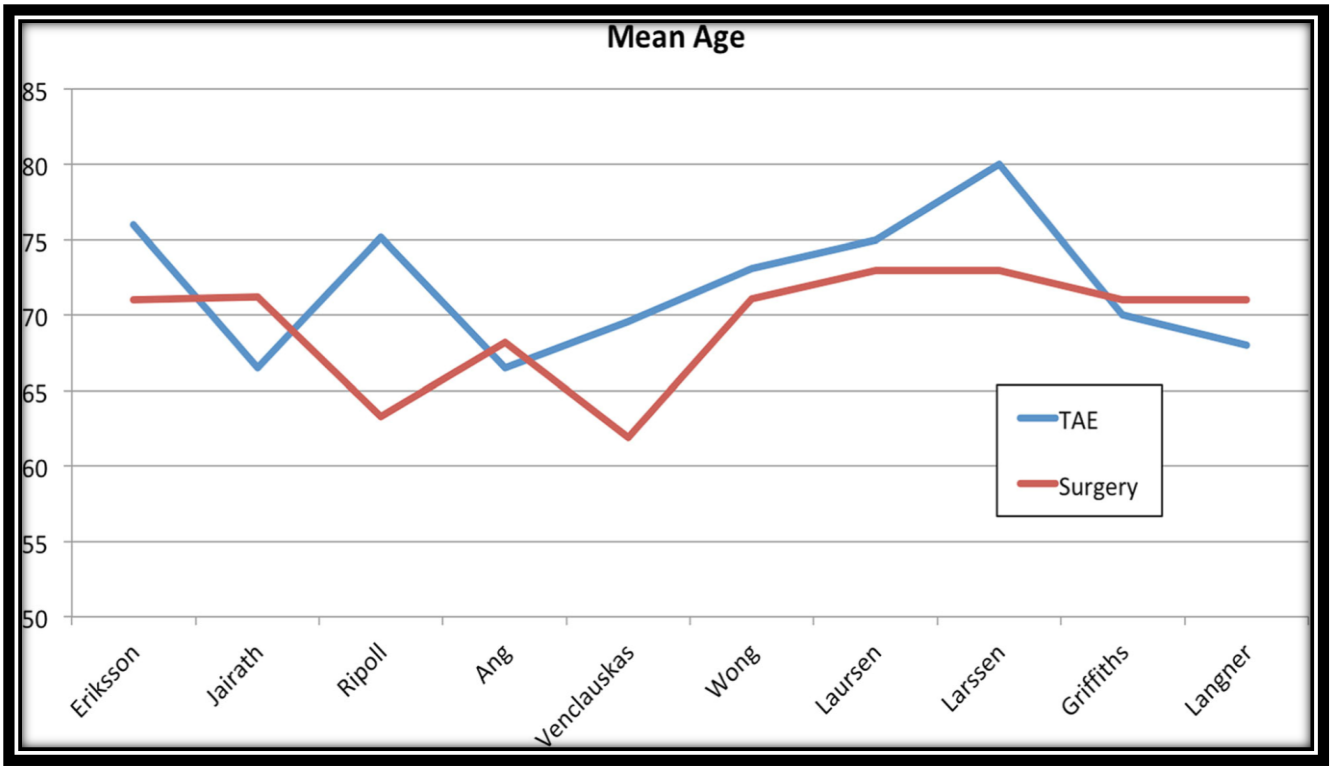


Illustration-3. Graphical comparison of mean age of TAE and surgical groups.

Material and methods**:** From March 2019 to December 2024, 40 patients were embolized during duodenal bleeding.

- These patients were divided into the following groups:
- Massive, active bleeding;
- Recurrence of bleeding in clinic and endoscopy was unsuccessful;
- Unstable hemodynamics and solid hemostasis could not be achieved during endoscopy;
- Failed to evacuate stomach contents and failed to see a bleeding ulcer;
- High risk of bleeding recurrence (Forest classification);
- Elderly and patients burdened with co-morbidities, with whom operative intervention represents a high risk of lethality.

Embolization performed according to Forrest's classification in 40 patients. See Illustration-4.

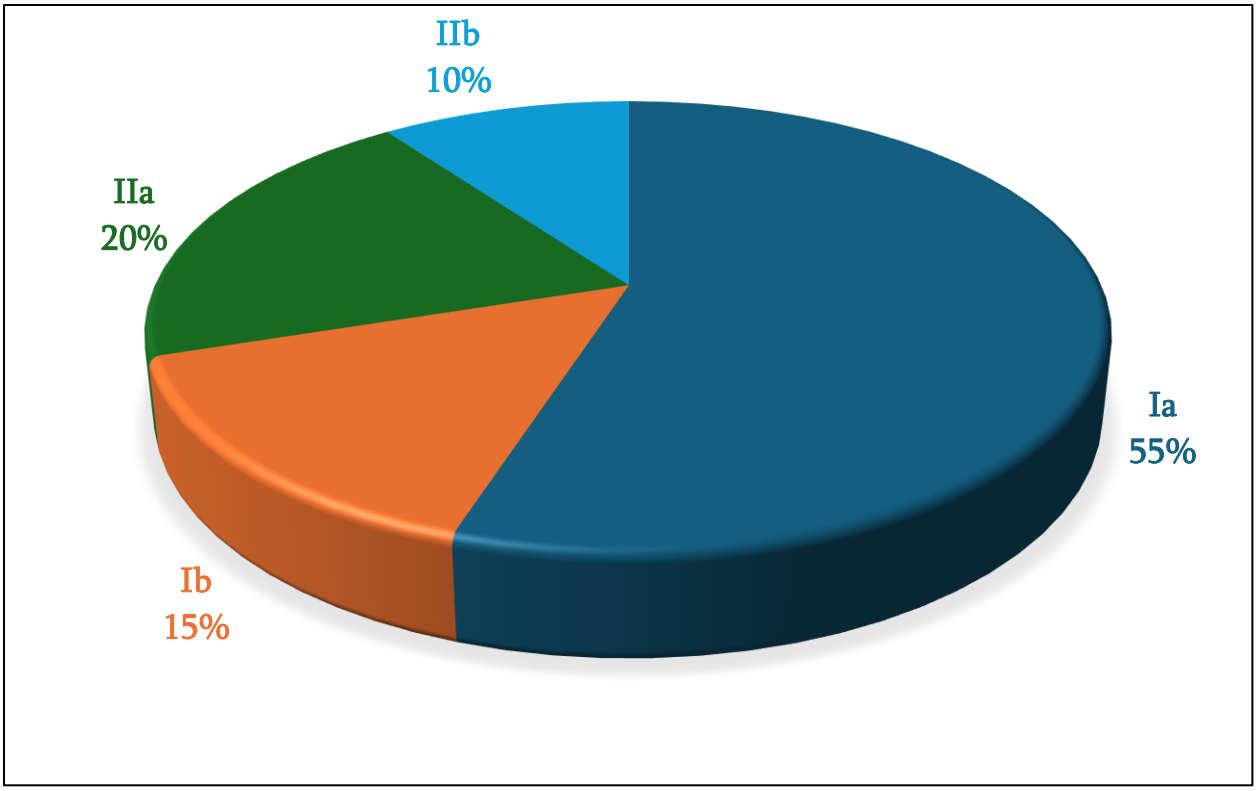


Illustration-4. Embolization performed according to Forrest's classification

- ❖ Embolization methods
  - ➢ Blind- embolization
  - ➢ Empirical embolization

- ❖ Technical aspects of embolization
  - ➢ Radial approach
  - ➢ Femoral artery approach

- ❖ Factors influencing the choice of embolic agent
  - ➢ Angiographic conclusion
  - ➢ Vascular anatomy
  - ➢ Vascular size
  - ➢ Desired level of vascular occlusion
  - ➢ Temporary or permanent occlusion is preferred
  - ➢ Catheter position
  - ➢ Operator experience

Embolization techniques. (See Illustration-5).

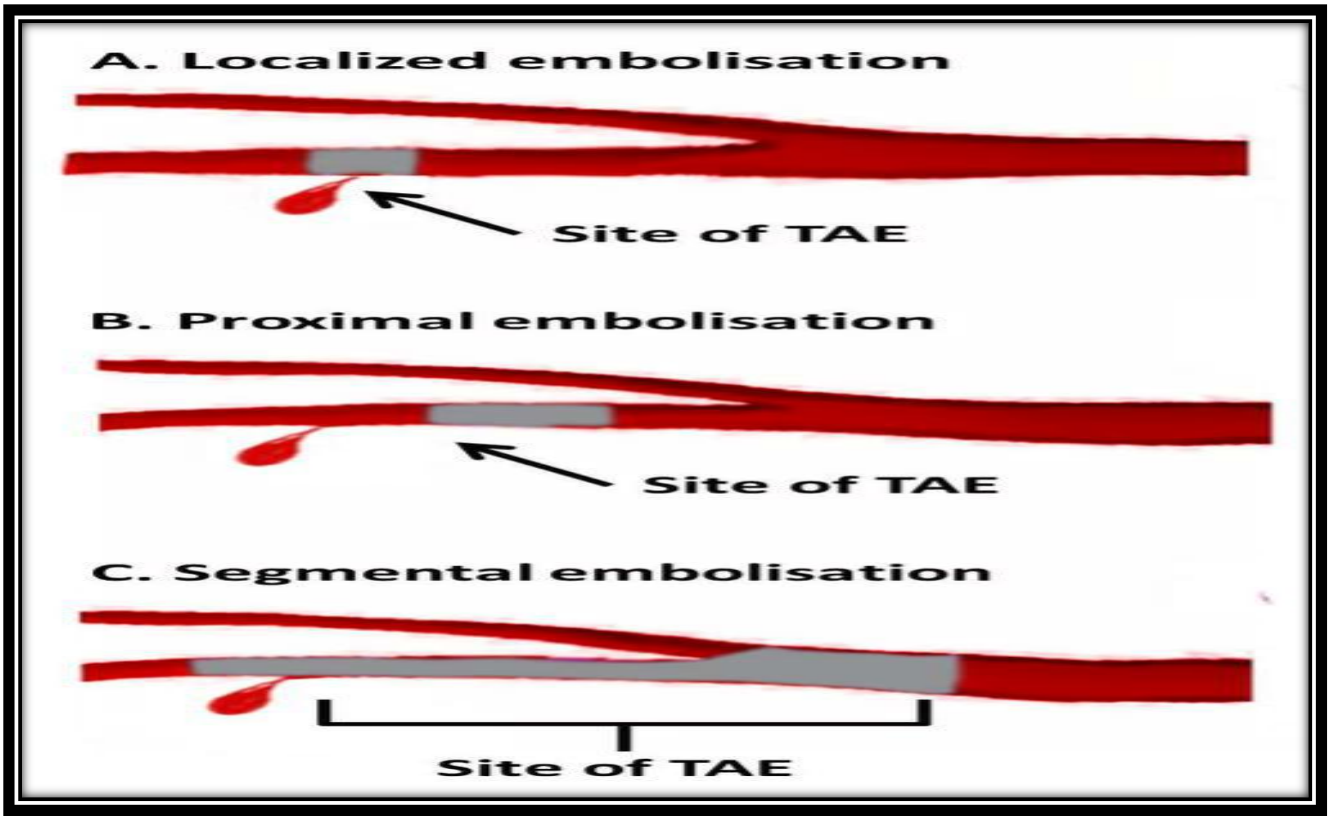


Illustration-5. Embolization techniques.

Embolization Sendvich technique. See Illustration-6.

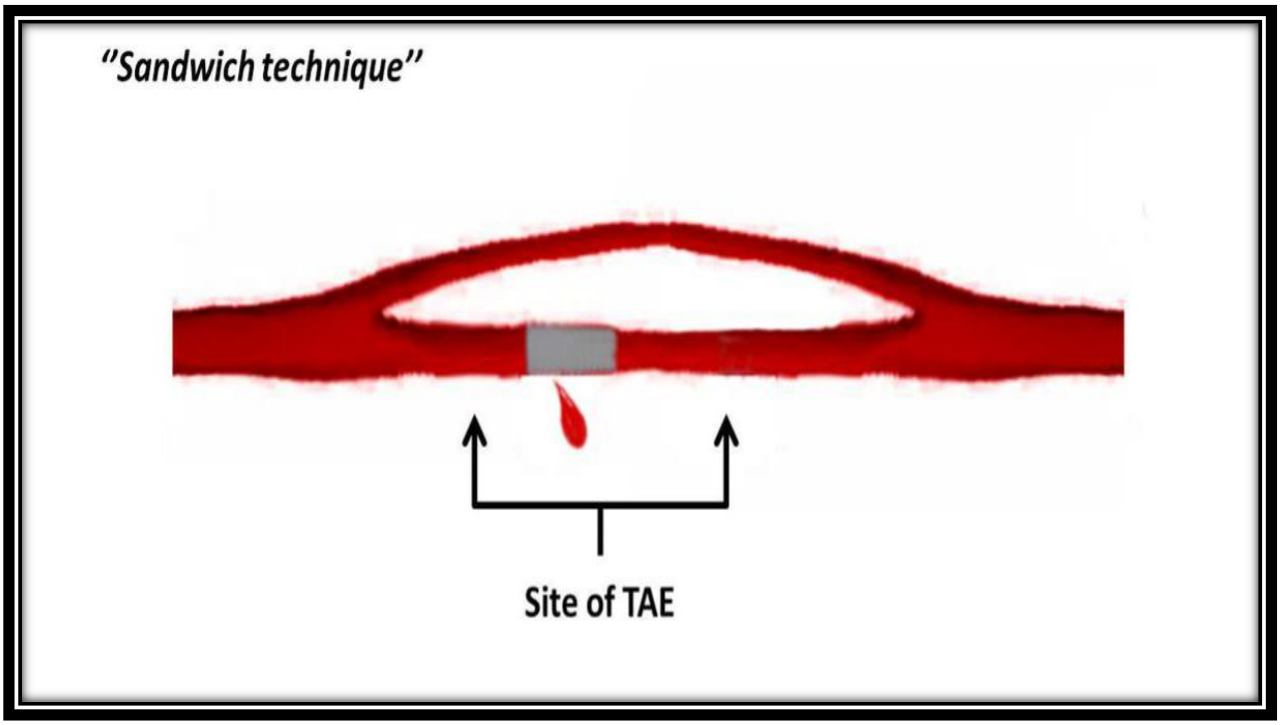


Illustration-6. Embolization Sendvich technique.

- Study Results:

- Technical success in 39 patients (97.5%).
- Technical failure in 1 patient (2.5%).

Embolization results obtained on 40 patients. (See Illustration-7).

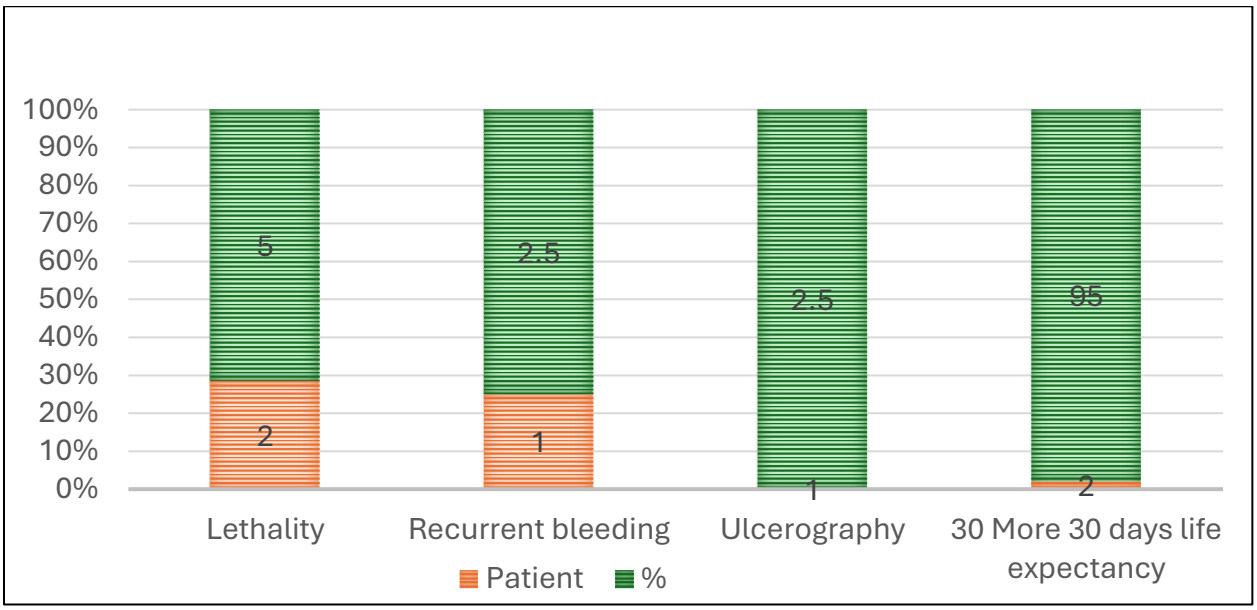


Illustration-7. Embolization results.

❖ **Case description**

- The patient is 78 years old
- Pain in the chest
- Marked respiratory failure
- Troponin 2.6 ug/L
- ST-elevation on the cardiogram

Angiography results. See Photo-4.



Photo -4. Angiography results.

- ❖ The following criteria are used to evaluate the effectiveness of endovascular hemostasis:
- ➢ Technical success - interruption of blood flow in the embolization zone.
- ➢ Clinical success - correction of bleeding recurrence and stabilization of hemodynamics
- ➢ Unsuccessful embolization.
- ➢ Studies show that coagulopathy is significantly associated with mortality after failed embolization.

The risk of rebleeding after successful embolization is three times greater in patients with coagulation problems, and for the same reason there is a 10-fold greater risk of death compared to patients with normal coagulation.

Improvements in catheter technology, development of more compatible embolization devices, and expansion of embolization techniques have led to angiography and embolization for the treatment of upper and lower gastrointestinal bleeding. Transcatheter embolization therapy for the treatment of acute GI bleeding is a safe procedure with high technical performance and clinical success, but it should be reserved as a treatment option for patients who have failed endoscopic and medical management. MDCT imaging is a useful tool for identifying the site of bleeding and evaluating the anatomical structure of the gastrointestinal tract in stable patients. Close working relationships between interventional radiologists, gastroenterologists, and diagnostic radiologists are essential for the optimal management of patients with GI bleeding. Endovascular embolization dramatically reduces the mortality rate in high-risk patients who require open surgery after failed endoscopy, further studies are needed to fully address these objectives.

Conclusion

- Gastrointestinal bleeding remains a serious and potentially life-threatening clinical condition requiring rapid diagnosis and effective therapeutic intervention. Advances in diagnostic imaging and interventional radiology have significantly improved the management of this complex medical emergency. The results of the present analysis emphasize the growing importance of endovascular techniques, particularly transcatheter arterial embolization, in the treatment of gastrointestinal hemorrhage associated with duodenal ulcer disease.
- Endoscopic therapy continues to represent the first-line treatment for most cases of upper gastrointestinal bleeding. However, when endoscopic interventions fail to achieve durable hemostasis or when bleeding recurs, alternative treatment strategies must be considered. In such circumstances, endovascular embolization provides a highly effective and minimally invasive therapeutic option that can achieve rapid control of hemorrhage while avoiding the risks associated with emergency surgical procedures.
- The clinical findings presented in this work demonstrate that angiographic embolization can successfully identify and treat bleeding vessels with a high rate of technical and clinical success. Superselective catheterization techniques allow precise occlusion of the responsible artery while preserving collateral blood supply to surrounding tissues. As a result, the risk of ischemic complications is minimized, and patient recovery is generally faster compared with traditional surgical interventions.
- Furthermore, the integration of modern imaging techniques, such as multidetector computed tomography angiography, has significantly enhanced the ability of clinicians to localize bleeding sources and plan targeted therapeutic interventions. These imaging modalities provide valuable anatomical and functional information that supports accurate diagnosis and facilitates efficient endovascular treatment.
- Overall, endovascular surgery has emerged as an essential component of the multidisciplinary approach to gastrointestinal bleeding management. The combination of advanced diagnostic imaging, endoscopic therapy, and interventional radiology techniques offers a comprehensive framework for controlling hemorrhage and improving patient outcomes. Continued technological innovation and clinical research are expected to further refine these methods and expand their applications in the treatment of gastrointestinal bleeding.

Recommendations

- The management of gastrointestinal bleeding should be based on a multidisciplinary approach involving gastroenterologists, surgeons, and interventional radiologists. Early identification of the bleeding source and prompt initiation of appropriate therapeutic measures are essential for preventing complications and reducing mortality.
- Endoscopic evaluation should remain the primary diagnostic and therapeutic modality for patients presenting with upper gastrointestinal bleeding. However, clinicians must be prepared to consider alternative treatment strategies in cases where endoscopic hemostasis is unsuccessful or when recurrent bleeding occurs.
- Endovascular embolization should be regarded as a highly effective second-line treatment for patients with persistent or recurrent gastrointestinal hemorrhage. The procedure offers several advantages, including minimal invasiveness, rapid hemostasis, and reduced postoperative morbidity compared with surgical intervention.
- Healthcare institutions should ensure the availability of modern angiographic equipment and trained interventional radiology specialists in order to provide timely and effective treatment for patients with severe gastrointestinal bleeding. The establishment of standardized clinical protocols for the management of gastrointestinal hemorrhage may also improve treatment outcomes and reduce variability in clinical practice.
- Future research should focus on evaluating long-term outcomes following endovascular treatment, optimizing embolization techniques, and developing novel embolic materials with improved safety and efficacy profiles. Such investigations will contribute to the continued advancement of minimally invasive therapies in the field of gastrointestinal bleeding management.

Acknowledgments

Declaration of Interest Statement. We confirm that the manuscript has been read and approved by all named authors and that there are no other persons who satisfied the criteria for authorship but are not listed. We further confirm that the order of authors listed in the manuscript has been approved by all of us. Conflict of interest-None.

References

1. Cherian MP, Mehta P, Kalyanpur TM, Hedgire SS, Narsinghpura KS: Arterial interventions in gastrointestinal bleeding. Semin Intervent Radiol, 2009; 26: 184-195.
2. Sheth R, Someshwar V, Warawdekar G: Treatment of acute lower gastrointestinal hemorrhage by superselective transcatheter embolization. Indian J Gastroenterol, 2006; 25: 290-294.
3. Rozycki GS, Tremblay L, Feliciano DV, etal: Three hundred consecutive emergent celiotomies in general surgery patients. Ann Surg, 2002; 235: 681-689.
4. Pennoyer WP, Vignati PV and Cohen JL: Management of angiogram positive lower gastrointestinal hemorrhage: long term follow-up of non-operative treatments. Int J Colorectal Dis, 1996; 11: 279-282.
   Schuetz A, Jauch KW: Lower gastrointestinal bleeding: therapeutic strategies, surgical techniques and results. Langenbecks Arch Surg, 2001; 386: 17-25.
5. Mirsadraee S, Tirukonda P, Nicholson A, Everett SM, McPherson SJ: Embolization for non-variceal upper gastrointestinal tract haemorrhage: a systematic review. Clin Radiol, 2011; 66: 500-509.
6. Bjorkman DJ, Zaman A, Fennerty MB, Lieberman D, Disario JA, Guest-Warnick G: Urgent vs. electiveendoscopy for acute non-variceal upper GI-bleeding: an effectiveness study. Gastrointest Endosc, 2004; 60: 1-8.
7. Church NI, Palmer KR: Diagnostic and therapeutic endoscopy. Curr Opin Gastroenterol, 1999; 15: 504.
8. Yap FY, Omene BO, Patel MN, etal: Transcatheter embolotherapy for gastrointestinal bleeding: a single center review of safety, efficacy, and clinical outcomes. Dig Dis Sci, 2013; 58: 1976-1984.
9. DeBarros J, Rosas L, Cohen J, Vignati P, Sardella W, Hallisey M: The changing paradigm for the treatment of colonic hemorrhage: superselective angiographic embo- lization. Dis Colon Rectum, 2002; 45: 802-808.
10. Lewis BS: Small intestinal bleeding. Gastroenterol Clin North Am, 1994; 23: 67-91.
11. Jenson DM, Machicado GA, Jutabha R, Kovacs TO: Urgentcolonoscopy for the diagnosis and treatment of severe diverticular hemorrhage. N Engl J Med, 2000; 342: 78-82.
12. Zuccaro G: Management of the adult patient with acute lower gastrointestinal bleeding. Am J Gastroenterol, 1998; 93: 1202-1208.
13. Angtuaco TL, Reddy SK, Drapkin S, Harrell LE, Howden CW: The utility of urgent colonoscopy in the evaluation of acute lower gastrointestinal tract bleeding: a 2-year experience from a single center. Am J Gastroenterol, 2001; 96: 1782-1785.
14. Bloomfield RD, Rockey DC, Shetzline MA: Endoscopic therapy of acute diverticular hemorrhage. Am J Gastroenterol, 2001; 96: 2367-2372.
15. Eisen GM, Dominitz JA, Faigel D, etal; American Society for Gastrointestinal Endoscopy. Standards of Practice Committee: an annotated algorithmic approach to acute lower gastrointestinal bleeding. Gastrointest Endosc, 2001; 53: 859-863.
16. Zuckerman GR, Prakash C: Acute lower intestinal bleeding. Part I: clinical presentation and diagnosis. Gastrointest Endosc, 1998; 48: 606-617.
17. Fisher L, Krinsky ML, Anderson MA, etal: The role of endoscopy in the management of obscure GI bleeding. Gastrointestinal Endoscopy, 2010; 72: 471-479.
18. Funaki B, Kostelic JK, Lorenz J, etal: Superselective microcoil embolization of colonic hemorrhage. Am J Roentgenol, 2001; 177: 829-836.
19. Funaki B: Superselective embolization of lower gastrointestinal hemorrhage: a new paradigm. Abdom Imaging, 2004; 29: 434-438.

20. Barkun AN, Bardou M, Kuipers EJ, etal: International consensus recommendations on the management of patients with nonvariceal upper gastrointestinal bleeding. Ann Intern Med, 2010; 152: 101-113.
21. Weldon DT, Burke SJ, Sun S, Mimura H, Golzarian J: Interventional management of lower gastrointestinal bleeding. Eur Radiol, 2008; 18: 857-867.
22. Mirsadraee S, Tirukonda P, Nicholson A, Everett SM, McPherson SJ: Embolization for non-variceal upper
23. Charbonnet P, Toman J, Buhler L, etal: Treatment of gastrointestinal hemorrhage. Abdom Imaging, 2005; 30: 719-726.
24. Gocha Chankseliani, Avtandil Girdaladze, Omar Gibradze, Paata Meshveliani, Kakha Chelidze, Mirian Cheishvili, Ana Kvernadze, Nodar Sulashvili. THE FEATURES OF ENDOVASCULAR SURGERY FOR DUODENAL ULCER BLEEDING. RS Global - World Science [Internet]. 2023Dec.11 [cited 2024Feb.13];(4(82). Available from: https://rsglobal.pl/index.php/ws/article/view/2690
25. Gocha Chankseliani, Avtandil Girdaladze, Omar Gibradze, Paata Meshveliani, Kakha Chelidze, Mirian Cheishvili, Ana Kvernadze, Nodar Sulashvili; THE MANIFESTATION OF SOME KEY ISSUE ASPECTS OF PECULIARITIES OF ENDOVASCULAR SURGERY BASED ON ENDOVASCULAR EMBOLIZATION FOR BLEEDING FROM GASTRO-DUODENAL ULCER AND FEATURES OF SOME ESSENTIAL PHARMACOTHERAPY; ISBN: 978-9941-9711-7-4; DOI suffix: 10.36962/IMPAS01-2023; CONFERENCE PROCEEDINGS; THE FIRST INTERNATIONAL SCIENTIFIC-PRACTICAL CONFERENCE IN HEALTH INNOVATIONS & RESEARCH: PROGNOSIS, ACHIEVEMENT AND CHALLENGES; DECEMBER 15-16, 2023. TALLINN, ESTONIA-2023. Pp:14-15.
26. G. Chankseliani, A. Girdaladze, O. Gibradze, P. Meshveliani, K. Chelidze, M. Cheishvili, A. Kvernadze, N. Sulashvili; THE MANIFESTATION OF SOME KEY ISSUE ASPECTS OF PECULIARITIES OF ENDOVASCULAR SURGERY BASED ON ENDOVASCULAR EMBOLIZATION FOR BLEEDING FROM GASTRO-DUODENAL ULCER AND FEATURES OF SOME ESSENTIAL PHARMACOTHERAPY; ISSN: 2346-8068, E-ISSN: 2346-8181; DOI: 10.36962/ALISJMSC; http://scsj.fisdd.org/index.php/ail/home/Archive_of_Issues; DOI PREFIX: 10.36962/ALISJMSC; SOUTHERN CAUCASUS SCIENTIFIC JOURNALS; AMBIANCE IN LIFE; INTERNATIONAL SCIENTIFIC JOURNAL IN MEDICINE; JOURNAL OF BEHAVIORAL MEDICINE, REFEREED AND REVIEWED JOURNAL; VOLUME 15, ISSUE -01, 2023; 15.01.2023. TBILISI-GEORGIA-2023. Pp: 20-38.
27. Gocha Chankseliani, Avtandil Girdaladze, Omar Gibradze, Paata Meshveliani, Kakha Chelidze, Nodar Sulashvili; THE SCIENTIFIC DISCUSSION SINGULARITIES OF ENDOVASCULAR SURGERY AND ENDOVASCULAR EMBOLIZATION FOR BLEEDING FROM GASTRO-DUODENAL ULCER AND TREATMENT OF COMPLICATIONS; ISBN - 978-1-955094-84-9; By Liberty Academic Publishers 2023; New York, USA; PROCEEDINGS BOOK; PROCEEDINGS BOOK OF 5 BASKENT INTERNATIONAL CONFERENCE ON MULTIDISCIPLINARY STUDIES; December 21-22, 2023, Ankara, Turkey-2023. Pp:1041-1059.
28. [Guideline] Talley NJ, Vakil N, for the Practice Parameters Committee of the American College of Gastroenterology. Guidelines for the management of dyspepsia. Am J Gastroenterol. 2005 Oct. 100(10):2324-37. [QxMD MEDLINE Link].
29. Tajima A, Koizumi K, Suzuki K, et al. Proton pump inhibitors and recurrent bleeding in peptic ulcer disease. J Gastroenterol Hepatol. 2008 Dec. 23 suppl 2: S237-41. [QxMD MEDLINE Link].
30. McConnell DB, Baba GC, Deveney CW. Changes in surgical treatment of peptic ulcer disease within a veteran's hospital in the 1970s and the 1980s. Arch Surg. 1989 Oct. 124(10):1164-7. [QxMD MEDLINE Link].
31. Gisbert JP, Calvet X, Cosme A, et al, for the H. pylori Study Group of the Asociacion Espanola de Gastroenterologia (Spanish Gastroenterology Association). Long-term follow-up of 1,000 patients cured of Helicobacter pylori infection following an episode of peptic ulcer bleeding. Am J Gastroenterol. 2012 Aug. 107(8):1197-204. [QxMD MEDLINE Link].

32. [Guideline] Tarasconi A, Coccolini F, Biffl WL, et al. Perforated and bleeding peptic ulcer: WSES guidelines. World J Emerg Surg. 2020. 15:3. [QxMD MEDLINE Link]. [Full Text].
33. Berne TV, Donovan AJ. Nonoperative treatment of perforated duodenal ulcer. Arch Surg. 1989 Jul. 124(7):830-2. [QxMD MEDLINE Link].
34. Donovan AJ, Berne TV, Donovan JA. Perforated duodenal ulcer: an alternative therapeutic plan. Arch Surg. 1998 Nov. 133(11):1166-71.[QxMD MEDLINE Link].
35. Wangensteen OH. Non-operative treatment of localized perforations of the duodenum. Proc Minn Acad Med. 1935. 18:477-80.
36. Strand DS, Kim D, Peura DA. 25 years of proton pump inhibitors: a comprehensive review. Gut Liver. 2017 Jan 15. 11(1):27-37. [QxMD MEDLINE Link]. Kajihara Y, Shimoyama T, Mizuki I. Analysis of the cost effectiveness of using vonoprazan-amoxicillin-clarithromycin triple therapy
37. For first-line Helicobacter pylori eradication. Scand J Gastroenterol. 2017 Feb. 52(2):238-41. [QxMD MEDLINE Link].
38. Ng JC, Yeomans ND. Helicobacter pylori infection and the risk of upper gastrointestinal bleeding in low dose aspirin users: systematic review and meta-analysis. Med J Aust. 2018 Sep 1. 209(7):306-11. [QxMD MEDLINE Link].
39. Mirabella A, Fiorentini T, Tutino R, et al. Laparoscopy is an available alternative to open surgery in the treatment of perforated peptic ulcers: a retrospective multicenter study. BMC Surg. 2018 Sep 25. 18(1):78. [QxMD MEDLINE Link].
40. Havens JM, Castillo-Angeles M, Nitzschke SL, Salim A. Disparities in peptic ulcer disease: A nationwide study. Am J Surg. 2018 Dec. 216(6):1127-8. [QxMD MEDLINE Link].
41. [Guideline] Satoh K, Yoshino J, Akamatsu T, et al. Evidence-based clinical practice guidelines for peptic ulcer disease 2015. J Gastroenterol. 2016 Mar. 51(3):177-94. [QxMD MEDLINE Link].
42. Lau JY, Sung J, Hill C, Henderson C, Howden CW, Metz DC. Systematic review of the epidemiology of complicated peptic ulcer disease: incidence, recurrence, risk factors and mortality. Digestion. 2011. 84(2):102-13. [QxMD MEDLINE Link].
43. Sonnenberg A. Temporal trends and geographical variations of peptic ulcer disease. Aliment Pharmacol Ther. 2005. 9 suppl 2:3-12. [QxMD MEDLINE Link].
44. Mohamed WA, Schaalan MF, Ramadan B. The expression profiling of circulating miR-204, miR-182, and lncRNA H19 as novel potential biomarkers for the progression of peptic ulcer to gastric cancer. J Cell Biochem. 2019 Aug. 120(8):13464-77. [QxMD MEDLINE Link].
45. Sanaii A, Shirzad H, Haghighian M, et al. Role of Th22 cells in Helicobacter pylori-related gastritis and peptic ulcer diseases. Mol Biol Rep. 2019 Dec. 46(6):5703-12. [QxMD MEDLINE Link].
46. Eriksson LG, Ljungdahl M, Sundbom M et al. Transcatheter arterial embolization versus surgery in the
47. treatment of upper gastrointestinal bleeding after therapeutic endoscopy failure. J Vasc Interv Radiol
48. 2008; 19: 1413–1418.
49. Wong TC, Wong KT, Chiu PW et al. A comparison of angiographic embolization with surgery after failed endoscopic hemostasis to bleeding peptic ulcers. Gastrointest Endosc 2011; 73: 900–908.
50. Stampfl U, Hackert T, Sommer CM et al. Superselective embolization for the management of
51. postpancreatectomy hemorrhage: a single-center experience in 25 patients. J Vasc Interv Radiol 2012;
52. 23: 504–510.
53. Hassold N, Wolfschmidt F et al. Effectiveness and outcome of endovascular therapy for late-onset
54. postpancreatectomy hemorrhage using covered stents and embolization. J Vasc Surg 016; 64:1373–83.
55. Kickuth R, Hoppe H, et al. Superselective transcatheter arterial embolization in patients with acute peripancreatic bleeding complications: review of 44 cases. Abdom Radiol (NY) 2016; 41:1782–92.

56. Nicholson AA, Patel J, McPherson S et al. Endovascular treatment of visceral aneurysms associated
57. with pancreatitis and a suggested classification with therapeutic implications. J Vasc Interv Radiol
58. 2006; 17: 1279–1285.
59. Lang EV, Picus D, Marx MV et al. Massive arterial hemorrhage from the stomach and lower esophagus:
60. impact of embolotherapy on survival. Radiology 1990; 177: 249–252.
61. d'Othee BJ, Surapaneni P, Rabkin D et al. Microcoil embolization for acute lower gastrointestinal
62. bleeding. Cardiovasc Intervent Radiol 2006; 29: 49–58.
63. Weldon DT, Burke SJ, Sun S et al. Interventional management of lower gastrointestinal bleeding.
64. European radiology 2008; 18: 857–867.
65. Encarnacion CE, Kadir S, Beam CA et al. Gastrointestinal bleeding: treatment with gastrointestinal
66. arterial embolization. Radiology 1992; 183: 505–508.
67. Loffroy R, Favelier S, et al. Transcatheter arterial embolization for acute nonvariceal upper gastrointestinal bleeding: Indications, techniques and outcomes. Diagn Interv Imaging 2015; 96: 731–744.
68. Augustin AM et al. Endovascular Therapy of Gastrointestinal Bleeding. Fortschr Röntgenstr 2019; 191:
69. 1073–1082.
70. 58. Loffroy R, Guiu B, Cercueil JP et al. Endovascular therapeutic embolisation: an overview of occluding
71. agents and their effects on embolised tissues. Curr Vasc Pharmacol 2009; 7: 250–263.
72. Lipof T, Sardella WV, Bartus CM et al. The efficacy and durability of super-selective embolization in the treatment of lower gastrointestinal bleeding. Dis Colon Rectum 2008; 51: 301–305.
73. Ikoma A, Kawai N, Sato M et al. Ischemic effects of transcatheter arterial embolization with N-butyl cyanoacrylate-lipiodol on the colon in a Swine model. Cardiovasc Intervent Radiol 2010; 33:1009-1015.
74. Bandi R, Shetty PC, Sharma RP et al. Superselective arterial embolization for the treatment of lower gastrointestinal hemorrhage. J Vasc Interv Radiol 2001; 12: 1399–1405.
75. Barkun AN, Almadi M, Kuipers EJ, et al. Management of nonvariceal upper gastrointestinal bleeding. Ann Intern Med. 2019;171(11):805-822.
76. Laine L, Jensen DM. Management of patients with ulcer bleeding. Am J Gastroenterol. 2012;107(3):345-360.
77. Loffroy R, Rao P, Ota S, et al. Embolization for gastrointestinal bleeding: review of current techniques and outcomes. Radiographics. 2015;35(3):701-722.
78. Defreyne L, Vanlangenhove P, De Vos M, et al. Transcatheter embolization as treatment of gastrointestinal bleeding. Acta Radiol. 2001;42(3):281-287.
79. Ripoll C, Banares R, Beceiro I, et al. Comparison of transcatheter arterial embolization and surgery for uncontrolled gastrointestinal bleeding. Am J Gastroenterol. 2004;99(10):2040-2045.
80. Schenker MP, Duszak R, Soulen MC, et al. Upper gastrointestinal hemorrhage and transcatheter embolization. J Vasc Interv Radiol. 2001;12(11):1263-1271.
81. Beggs AD, Dilworth MP, Powell SL, Atherton H. A systematic review of transcatheter arterial embolization versus emergency surgery. World J Surg. 2014;38(9):2267-2274.
82. Kim JH, Shin JH, Yoon HK, et al. Angiographic management of gastrointestinal bleeding. Radiology. 2009;251(3):739-748.
83. Loffroy R, Guiu B. Role of interventional radiology in gastrointestinal bleeding. World J Gastroenterol. 2011;17(30):3643-3651.
84. Green BT, Rockey DC, Portwood G, et al. Urgent colonoscopy for evaluation and management of acute lower gastrointestinal bleeding. Am J Gastroenterol. 2005;100(11):2395-2402.

85. Barkun AN, Almadi M, Kuipers EJ, et al. Management of nonvariceal upper gastrointestinal bleeding: guideline recommendations. Ann Intern Med. 2019;171(11):805–822.
86. Loffroy R, Rao P, Ota S, De Lin M, Kwak BK, Geschwind JF. Embolization for gastrointestinal bleeding: review of current techniques and therapeutic outcomes. Radiographics. 2015;35(3):701–722.
87. Laine L, Jensen DM. Management of patients with ulcer bleeding. Am J Gastroenterol. 2012;107(3):345–360.
88. Schenker MP, Duszak R Jr, Soulen MC, et al. Upper gastrointestinal hemorrhage and transcatheter embolization: clinical and technical factors influencing success. J Vasc Interv Radiol. 2001;12(11):1263–1271.
89. Gastroenterology Barkun AN, Almadi M, Kuipers EJ, et al. Management of nonvariceal upper gastrointestinal bleeding: guideline recommendations from the international consensus group. *Ann Intern Med.* 2019;171(11):805–822.
90. Laine L, Jensen DM. Management of patients with ulcer bleeding. *Am J Gastroenterol.* 2012;107(3):345–360.
91. Gralnek IM, Dumonceau JM, Kuipers EJ, et al. Diagnosis and management of nonvariceal upper gastrointestinal hemorrhage: European Society of Gastrointestinal Endoscopy guideline. *Endoscopy.* 2015;47(10):a1–a46.
92. Loffroy R, Guiu B, D'Athis P, et al. Arterial embolotherapy for endoscopically unmanageable acute gastroduodenal hemorrhage: predictors of early rebleeding. *Clin Gastroenterol Hepatol.* 2009;7(5):515–523.
93. Schenker MP, Duszak R Jr, Soulen MC, et al. Upper gastrointestinal hemorrhage and transcatheter embolotherapy: clinical and technical factors impacting success and survival. *J Vasc Interv Radiol.* 2001;12(11):1263–1271.
94. Defreyne L, Vanlangenhove P, Decruyenaere J, et al. Therapeutic embolization for acute upper gastrointestinal hemorrhage: results in 52 patients. *Acta Gastroenterol Belg.* 2001;64(1):6–12.
95. Ripoll C, Bañares R, Beceiro I, et al. Comparison of transcatheter arterial embolization and surgery for treatment of bleeding peptic ulcer after endoscopic treatment failure. *J Vasc Interv Radiol.* 2004;15(5):447–450.
96. Loffroy R, Rao P, Ota S, et al. Embolization in the management of gastrointestinal hemorrhage. *World J Gastroenterol.* 2012;18(11):1152–1163.
97. Beggs AD, Dilworth MP, Powell SL, Atherton H, Griffiths EA. A systematic review of transarterial embolization versus emergency surgery in treatment of major nonvariceal upper gastrointestinal bleeding. *Clin Exp Gastroenterol.* 2014;7:93–104.
98. Wong TC, Wong KT, Chiu PW, et al. A comparison of angiographic embolization with surgery after failed endoscopic hemostasis in bleeding peptic ulcers. *Gastrointest Endosc.* 2011;73(5):900–908.
99. Holster IL, Kuipers EJ. Management of acute nonvariceal upper gastrointestinal bleeding: current policies and future perspectives. *World J Gastroenterol.* 2012;18(11):1202–1207.
100. Sung JJY, Kuipers EJ, El-Serag HB. Systematic review: the global incidence and prevalence of peptic ulcer disease. *Aliment Pharmacol Ther.* 2009;29(9):938–946.
101. Lau JYW, Barkun A, Fan DMY, Kuipers EJ, Yang YS, Chan FKL. Challenges in the management of acute peptic ulcer bleeding. *Lancet.* 2013;381(9882):2033–2043.
102. Hearnshaw SA, Logan RFA, Lowe D, Travis SPL, Murphy MF, Palmer KR. Acute upper gastrointestinal bleeding in the United Kingdom: patient characteristics, diagnoses and outcomes. *Gut.* 2011;60(10):1327–1335.
103. Stanley AJ, Laine L. Management of acute upper gastrointestinal bleeding. *BMJ.* 2019;364:l536.
104. Vergara M, Catalán M, Gisbert JP, Calvet X. Meta-analysis: role of Helicobacter pylori eradication in prevention of peptic ulcer rebleeding. *Aliment Pharmacol Ther.* 2005;21(7):791–799.
105. Green BT, Rockey DC, Portwood G, et al. Urgent colonoscopy for evaluation and management of acute lower gastrointestinal hemorrhage. *Am J Gastroenterol.* 2005;100(11):2395–2402.

106. Kim JH, Shin JH, Yoon HK, et al. Angiographically negative acute arterial upper and lower gastrointestinal bleeding: incidence, predictive factors, and clinical outcomes. *Korean J Radiol.* 2009;10(4):384–390.
107. Encarnacion CE, Kadir S, Beam CA, Payne CS. Gastrointestinal bleeding: treatment with gastrointestinal arterial embolization. *Radiology.* 1992;183(2):505–508.
108. Lang EV. Angiographic interventions in gastrointestinal bleeding. *Gastroenterol Clin North Am.* 2000;29(2):429–458.
109. Funaki B. Superselective embolization of upper gastrointestinal hemorrhage. *Semin Intervent Radiol.* 2004;21(3):173–180.
110. Maleux G, Roeflaer F, Heye S, et al. Long-term outcome of transcatheter embolotherapy for acute lower gastrointestinal hemorrhage. *Am J Gastroenterol.* 2009;104(8):2042–2046.
111. Loffroy R, Estivalet L, Cherblanc V, et al. Transcatheter arterial embolization for acute nonvariceal upper gastrointestinal bleeding: indications, techniques and outcomes. *Diagn Interv Imaging.* 2015;96(7–8):731–744.
112. Jairath V, Kahan BC, Logan RFA, et al. Red blood cell transfusion practice in patients presenting with acute upper gastrointestinal bleeding. *Transfusion.* 2011;51(9):1949–1956.
113. Barkun A, Leontiadis GI, Kuipers EJ, et al. Acute upper gastrointestinal bleeding consensus recommendations. *Ann Intern Med.* 2010;152(2):101–113.
114. Sung JJY, Chiu PWY, Chan FKL, Lau JYW, Goh KL, Ho LH. Asia-Pacific working group consensus on non-variceal upper gastrointestinal bleeding: an update on management and endoscopic treatment strategies. *Gut.* 2018;67(10):1757–1768.
115. Camus M, Jensen DM, Kovacs TOG, Jensen ME, Ohning GV, Jutabha R. Independent risk factors of 30-day outcomes in patients with peptic ulcer bleeding receiving transcatheter arterial embolization after failed endoscopic hemostasis. *Gastrointest Endosc.* 2014;79(6):882–888.

Türk sivilizasiyasının formalaşmasında İpək Yolunun əhəmiyyəti

Səriyyə Abidova Elşən qızı

Elmi Araşdırmalar, Ekspozisiya fond şöbəsinin əməkdaşı, Quba şəhəri "Soyqırımı Memorial Kompleksi"

ORCID ID: 0009-0001-4236-3518

Xülasə

Bu məqalədə Böyük İpək Yolunun Türk sivilizasiyasının formalaşması və inkişafına göstərdiyi siyasi, iqtisadi və mədəni təsirlər təhlil edilir. Tədqiqat çərçivəsində İpək Yolunun yalnız beynəlxalq ticarət marşrutu deyil, eyni zamanda dövlətçilik institutlarının möhkəmlənməsi, şəhər mədəniyyətinin inkişafı və sivilizasion identikliyin təşəkkülündə mühüm amil olduğu əsaslandırılır. Türk dövlətlərinin Orta Asiya və Xəzər hövzəsi kimi strateji bölgələrdə yerləşməsi onların tranzit nəzarət imkanlarını genişləndirmiş, bu isə iqtisadi resursların siyasi gücə transformasiyasına şərait yaratmışdır. Nəticə olaraq göstərilir ki, İpək Yolu Türk sivilizasiyasının struktur və məzmun baxımından formalaşmasında sistemli və həlledici rol oynamışdır.

Açar sözlər: İpək Yolu, Türk dövlətləri, dövlətçilik, tranzit nəzarət, mədəni inteqrasiya

Summary

This article analyzes the political, economic, and cultural impact of the Great Silk Road on the formation and development of Turkic civilization. The study argues that the Silk Road functioned not only as an international trade route, but also as a significant factor in strengthening state institutions, fostering urban development, and shaping civilizational identity. The strategic location of Turkic states in Central Asia and the Caspian Basin expanded their transit control capacity, enabling the transformation of economic resources into political power. The research concludes that the Silk Road played a systematic and decisive role in the structural formation of Turkic civilization.

Key words: Silk Road, Turkic states, statehood, transit control, cultural integration

Резюме

В статье анализируется политическое, экономическое и культурное влияние Великого Шёлкового пути на процессы формирования и развития тюркской цивилизации. Обосновывается, что Шёлковый путь функционировал не только как международный торговый маршрут, но и как важный фактор укрепления государственных институтов, развития городской культуры и формирования цивилизационной идентичности. Стратегическое расположение тюркских государств в Центральная Азия и Каспийский регион способствовало расширению их транзитного контроля и превращению экономических ресурсов в политическую силу. Делается вывод о том, что Шёлковый путь сыграл системную и решающую роль в структурном формировании тюркской цивилизации.

Ключевые слова: Шёлковый путь, тюркские государства, государственность, транзитный контроль, культурная интеграция

Giriş

Dünya tarixində beynəlxalq əlaqələrin formalaşmasına və sivilizasiyalararası qarşılıqlı təsir proseslərinə mühüm təsir göstərmiş amillərdən biri Böyük İpək Yolu olmuşdur. Eramızdan əvvəl II əsrdən etibarən sistemli xarakter alan bu geniş kommunikasiya şəbəkəsi Şərqi Asiyadan Aralıq dənizi hövzəsinə qədər uzanaraq Avrasiya məkanında iqtisadi, siyasi və mədəni inteqrasiyanın əsas platformasına çevrilmişdir. İpək Yolu yalnız ticarət marşrutu deyil, eyni zamanda dövlətlərarası münasibətlərin, diplomatik əlaqələrin və ideoloji mübadilənin formalaşdığı çoxşaxəli tarixi mühit kimi çıxış etmişdir.

Türk tayfaları və dövlətləri tarixən bu yolun keçdiyi əsas coğrafi ərazilərdə — xüsusilə Orta Asiya və Cənubi Qafqaz məkanında yerləşmişdir. Bu strateji mövqe türk siyasi qurumlarına tranzit nəzarət imkanı yaratmış, nəticə etibarilə onların hərbi-siyasi gücünün artmasına, iqtisadi potensialının genişlənməsinə

və dövlətçilik ənənələrinin möhkəmlənməsinə şərait yaratmışdır. İpək Yoluna nəzarət təkcə iqtisadi gəlir mənbəyi deyil, həm də geosiyasi üstünlük göstəricisi olmuşdur.

Müasir dövrdə Türk dünyasının tarixi irsinin yenidən qiymətləndirilməsi və Avrasiya məkanında inteqrasiya proseslərinin güclənməsi fonunda İpək Yolunun rolu daha da aktuallaşır. Tarixi İpək Yolunun müasir geosiyasi layihələr kontekstində yenidən gündəmə gəlməsi bu mövzunun yalnız tarixi deyil, həm də aktual elmi əhəmiyyətini artırır. Bu baxımdan, Türk sivilizasiyasının formalaşmasında İpək Yolunun rolunun sistemli şəkildə araşdırılması zəruri elmi və nəzəri problem kimi çıxış edir.

Bu məqalədə İpək Yolunun Türk sivilizasiyasının siyasi, iqtisadi və mədəni komponentlərinin təşəkkülünə təsiri kompleks yanaşma əsasında təhlil edilir və onun dövlətçilik modelinin formalaşmasında oynadığı sistemli rol əsaslandırılır.

İpək Yolunun tarixi-coğrafi mahiyyəti onun Avrasiya məkanında yalnız ticarət marşrutu kimi deyil, həm də sivilizasiyalararası əlaqələri təmin edən genişmiqyaslı kommunikasiya sistemi kimi çıxış etməsində özünü göstərir. Qədim dövrlərdən başlayaraq, eramızdan əvvəl II əsrdən etibarən daha sistemli xarakter alan İpək Yolu Şərqi Asiyadan Aralıq dənizi hövzəsinə qədər uzanan quru və dəniz yollarını əhatə etmişdir. Bu marşrut Çin, Mərkəzi Asiya, Ön Asiya və Avropa arasında iqtisadi, siyasi və mədəni inteqrasiyanın əsas coğrafi platformasına çevrilmişdir. [4.s.5]

Coğrafi baxımdan İpək Yolu vahid xətt olmayıb, bir-biri ilə əlaqəli alternativ yollar şəbəkəsi kimi fəaliyyət göstərmişdir. Şimal marşrutu Altay və Qazaxıstan çöllərindən keçərək Qara dəniz istiqamətinə yönəlmiş, orta marşrut Mərkəzi Asiya vasitəsilə Xəzər hövzəsinə çıxmış, cənub marşrutu isə İran və Mesopotamiya üzərindən Aralıq dənizi limanlarına çıxış təmin etmişdir. Bu çoxşaxəli quruluş ticarətin fasiləsizliyini və siyasi dəyişikliklərə uyğun elastik hərəkət imkanını təmin etmişdir. [7.s.74]

Tarixi baxımdan İpək Yolunun əhəmiyyəti onun müxtəlif imperiyaların və dövlətlərin formalaşma prosesində oynadığı rolda özünü göstərir. Yolun keçdiyi ərazilər geosiyasi baxımdan strateji məkan kimi qiymətləndirilmiş, bu ərazilərə nəzarət siyasi və iqtisadi üstünlük demək olmuşdur. Xüsusilə türk tayfalarının və dövlətlərinin yerləşdiyi Orta Asiya və Xəzər ətrafı bölgələr İpək Yolunun əsas qovşaq nöqtələrindən biri kimi çıxış etmişdir. [6.s.62]

Beləliklə, İpək Yolunun tarixi-coğrafi mahiyyəti onun təkcə maddi mübadilə xətti deyil, eyni zamanda geosiyasi dinamikanı formalaşdıran, dövlətlərarası münasibətləri istiqamətləndirən və sivilizasiya mərkəzlərini birləşdirən strateji məkan olması ilə müəyyən olunur. Bu xüsusiyyət İpək Yolunu dünya tarixində uzunmüddətli və sistemli təsirə malik nadir tarixi fenomenlərdən biri kimi səciyyələndirir.

İpək Yolu üzərində nəzarət orta əsrlər Avrasiya məkanında yalnız iqtisadi üstünlük deyil, eyni zamanda siyasi hakimiyyət göstəricisi hesab olunurdu. Türk dövlətlərinin yerləşdiyi coğrafi mövqe bu strateji kommunikasiya xəttinin əsas hissələrini əhatə etdiyindən, onlar təbii şəkildə tranzit nəzarət imkanına malik olmuşlar. Bu nəzarət mexanizmi hərbi, diplomatik və iqtisadi vasitələrin vəhdəti əsasında formalaşmışdır.

VI əsrdə yaranmış Göytürk Xaqanlığı Orta Asiyada əsas ticarət arteriyalarını nəzarət altına alaraq Çin ilə Bizans arasında vasitəçi mövqeyə yüksəlmişdir. Göytürk hakimləri karvan yollarının təhlükəsizliyini təmin etməklə ticarət sabitliyini qoruyur, eyni zamanda bu nəzarəti siyasi təsir alətinə çevirirdilər. Çin imperiyası ilə bağlanan müqavilələr və Bizansla qurulan diplomatik münasibətlər İpək Yolunun strateji əhəmiyyətindən qaynaqlanırdı. Bu siyasət nəticəsində türk xaqanları beynəlxalq münasibətlər sistemində balans yarada bilən güc mərkəzinə çevrilmişdir. [5. s.53]

Sonrakı mərhələdə Xəzər Xaqanlığı Qafqaz və Xəzər hövzəsində şimal marşrutuna nəzarət etməklə regionda geosiyasi sabitliyin əsas iştirakçılarından biri olmuşdur. Xəzərlər İslam xilafəti ilə Bizans arasında vasitəçi mövqe tutaraq ticarət axınlarını tənzimləmiş və tranzit rüsumları hesabına iqtisadi dayaqlarını möhkəmləndirmişlər.

İpək Yolundan əldə olunan vergi və tranzit gəlirləri türk dövlətlərinin hərbi-siyasi strukturlarının güclənməsinə, şəhər mərkəzlərinin inkişafına və idarəetmə institutlarının formalaşmasına şərait yaratmışdır. Beləliklə, İpək Yoluna nəzarət iqtisadi resursların siyasi gücə çevrilməsi mexanizmi kimi çıxış etmişdir. Bu amil Türk sivilizasiyasının yalnız köçəri hərbi model əsasında deyil, eyni zamanda

ticarətə və diplomatik münasibətlərə əsaslanan kompleks dövlətçilik sistemi kimi formalaşmasına mühüm təsir göstərmişdir. [1]

İpək Yolunun fəaliyyət göstərdiyi dövrdə iqtisadi amil türk dövlətlərinin siyasi və sosial strukturunun formalaşmasında mühüm rol oynamışdır. İpək Yolu vasitəsilə həyata keçirilən beynəlxalq ticarət yalnız malların mübadiləsi ilə məhdudlaşmamış, eyni zamanda iqtisadi institutların inkişafına təkan vermişdir. Türk dövlətlərinin nəzarət etdiyi tranzit ərazilərdən keçən karvanlar ipək, ədviyyat, metal məmulatları, atlar və digər strateji məhsulların daşınmasını təmin edir, bu isə rüsum və vergi sistemi vasitəsilə dövlət büdcəsinin formalaşmasına imkan yaradırdı. [7.s.15]

Tranzit ticarətindən əldə edilən gəlirlər hərbi qüvvələrin saxlanılmasına, diplomatik fəaliyyətin maliyyələşdirilməsinə və şəhər mərkəzlərinin inkişafına yönəldilirdi. Xüsusilə Orta Asiya və Qafqaz bölgəsində yerləşən şəhərlər ticarət qovşaqları kimi formalaşaraq iqtisadi canlanmanın mərkəzinə çevrilmişdir. Bu proses şəhərləşmənin sürətlənməsinə, sənətkarlığın inkişafına və bazar münasibətlərinin dərinləşməsinə səbəb olmuşdur. [3]

İpək Yolu həmçinin pul dövriyyəsinin genişlənməsinə və iqtisadi inteqrasiyanın artmasına şərait yaratmışdır. Müxtəlif sivilizasiyalar arasında aparılan ticarət mübadiləsi nəticəsində iqtisadi əlaqələr sabit xarakter almış, bazar münasibətləri daha sistemli formaya düşmüşdür. Türk dövlətləri bu iqtisadi dinamikanı siyasi gücə çevirməklə regional və beynəlxalq miqyasda mövqelərini möhkəmləndirmişlər. [3]

Beləliklə, İpək Yolunun iqtisadi təsiri Türk sivilizasiyasının maddi əsaslarının formalaşmasına, dövlət institutlarının möhkəmlənməsinə və şəhər mədəniyyətinin inkişafına birbaşa təsir göstərmişdir. Bu baxımdan, İpək Yolu Türk dövlətlərinin yalnız xarici ticarət platforması deyil, həm də iqtisadi dayanıqlılıq və siyasi sabitlik mənbəyi olmuşdur.

İpək Yolu yalnız ticarət və siyasi münasibətlər sistemi deyil, eyni zamanda geniş mədəni və sivilizasion qarşılıqlı təsir məkanı olmuşdur. İpək Yolu boyunca müxtəlif xalqlar, dillər, dini inanclar və mədəni ənənələr qarşılıqlı əlaqəyə girərək çoxşaxəli sivilizasion mühit formalaşdırmışdır. Türk tayfaları və dövlətləri bu prosesin passiv iştirakçısı deyil, aktiv vasitəçisi olmuşlar.

Ticarət karvanları ilə birlikdə yalnız mallar deyil, ideyalar, dini görüşlər və mədəni dəyərlər də yayılırdı. Buddizm, Manixeylik və daha sonrakı mərhələdə İslam dini türk coğrafiyasında məhz bu kommunikasiya şəbəkəsi vasitəsilə yayılmışdır. Bu proses Türk sivilizasiyasının dünyagörüşünün transformasiyasına, hüquqi və sosial institutların dəyişməsinə təsir göstərmişdir. Xüsusilə İslamın qəbulundan sonra Türk dövlətçilik modeli yeni dini-siyasi legitimlik çərçivəsində inkişaf etmişdir. [7.s.41]

İpək Yolu eyni zamanda yazı sistemlərinin, elmi biliklərin və sənət üslublarının yayılmasına şərait yaratmışdır. Müxtəlif mədəniyyətlərlə təmas nəticəsində türk xalqları həm öz mədəni irsini qorumuş, həm də digər sivilizasiya elementlərini adaptasiya etmişdir. Bu adaptasiya prosesi Türk sivilizasiyasını qapalı deyil, açıq və inteqrativ model kimi formalaşdırmışdır.

Mədəni qarşılıqlı təsir şəhər mədəniyyətinin inkişafında da özünü göstərmişdir. Ticarət mərkəzləri yalnız iqtisadi fəaliyyət zonası deyil, həm də elmi, dini və sənət mübadiləsinin baş verdiyi məkanlara çevrilmişdir. Beləliklə, İpək Yolunun təsiri nəticəsində Türk sivilizasiyası çoxmədəniyyətli və çevik struktur qazanmış, Avrasiya məkanında mədəni körpü rolunu oynayan tarixi model formalaşdırmışdır. [5.s.108]

İpək Yolu Türk sivilizasiyasının formalaşmasında yalnız maddi baza deyil, həm də ideoloji və mədəni transformasiya mexanizmi kimi çıxış etmişdir. Bu təsir Türk dövlətlərinin identiklik modelinin və sivilizasion xarakterinin təşəkküründə həlledici amillərdən biri olmuşdur.

Nəticə

Beləliklə, aparılan təhlil göstərir ki, İpək Yolu Türk sivilizasiyasının formalaşmasında çoxşaxəli və sistemli rol oynamışdır. Bu yol yalnız beynəlxalq ticarət marşrutu kimi deyil, eyni zamanda siyasi

hakimiyyətin möhkəmlənməsi, iqtisadi dayanıqlılığın təmin olunması və mədəni inteqrasiyanın genişlənməsi üçün fundamental platforma olmuşdur.

Türk dövlətlərinin Avrasiya məkanında yerləşdiyi strateji coğrafi mövqe İpək Yoluna nəzarət imkanını təmin etmiş, bu isə hərbi-siyasi gücün artmasına və beynəlxalq münasibətlər sistemində aktiv iştirakına şərait yaratmışdır. Tranzit ticarətindən əldə olunan iqtisadi resurslar dövlət institutlarının formalaşmasına, şəhər mədəniyyətinin inkişafına və sosial strukturun sabitləşməsinə təsir göstərmişdir. Eyni zamanda, yol boyunca baş verən mədəni və dini mübadilə prosesi Türk sivilizasiyasının identiklik modelini zənginləşdirərək onu açıq və inteqrativ xarakterli sivilizasiya kimi formalaşdırmışdır.

Nəticə etibarilə, İpək Yoluna nəzarət və onun yaratdığı siyasi-iqtisadi mühit Türk dövlətçiliyinin möhkəmlənməsində və sivilizasional inkişafında həlledici amillərdən biri olmuşdur. Bu baxımdan, İpək Yolunun Türk sivilizasiyasının təşəkkülündə rolu təsadüfi tarixi faktor deyil, sistemli və tarixi qanunauyğunluq kimi qiymətləndirilməlidir.

Ədəbiyyat

1. Azərbaycan Milli Elmlər Akademiyası. Böyük İpək Yolunda Azərbaycan – tarix və perspektivlər. https://science.gov.az/az/news/open/26629
2. Əfəndiyeva, G. (2021). Azərbaycan Böyük İpək Yolu üzərində. Beynəlxalq Türk Mədəniyyəti və İrsi Fondu.
3. Əzizov, Ş. (2022). Böyük İpək yolunun İnkişaf mərhələləri və Azərbaycana təsirləri
4. Feyziyev, C. (2018). İpək yolu mədəniyyəti və türklər. Tarix, İnsan və Cəmiyyət.
5. İsayev, E. (2012). Böyük İpək yolu və Naxçıvan. Elm və Təhsil.
6. Qocatürk, N. (2008). İlham Əliyev: İpək yolu sivilizasiyası və Azərbaycan diplomatiyası. Nurlan.
7. Mustafayev R. XXI. Yüzyıl İlüzyonlar Politikası. İstanbul, 2004

FUNGAL MEKANİZMALAR İLE FARMASÖTİK KALINTI GİDERİMİ

Melise İPHAR

Bilecik Şeyh Edebali Üniversitesi, Lisansüstü Eğitim Enstitüsü, Biyomühendislik Anabilim Dalı, Merkez Kampüs, Bilecik, Türkiye ORCID ID: 0009-0006-2190-5601

Ülküye Dudu GÜL

Bilecik Şeyh Edebali Üniversitesi, Mühendislik Fakültesi, Biyomühendislik Bölümü, Merkez Kampüs Bilecik, Türkiye ORCID ID: 0000-0001-6443-1633

Abstract

Pharmaceutical compounds have gained increasing importance as persistent micropollutants in environmental matrices due to their widespread use and their incomplete removal by conventional wastewater treatment systems. The accumulation of these compounds in aquatic ecosystems not only exerts toxic effects on organisms but also adversely affects ecological balance. This situation highlights the limitations of existing treatment technologies and necessitates the development of alternative, more effective, and sustainable treatment approaches. In this study, the role of fungal systems in the removal of pharmaceutical residues, their mechanisms of action, advantages, and application potential are comprehensively examined based on current knowledge.

The ability of fungi, particularly through ligninolytic enzyme systems, to degrade complex and recalcitrant organic compounds makes these organisms promising candidates for the biological treatment of pharmaceutical pollutants. Within this context, the removal performances of different fungal species toward various pharmaceutical compounds are comparatively evaluated through both enzymatic and non-enzymatic processes, and the fundamental mechanisms involved are examined in detail. In addition to enzymatic biodegradation processes, the contribution of the biosorption mechanism to pollutant removal is emphasized, highlighting the combined action of these two processes. Furthermore, the observed differences in performance among fungal species are reported to be associated with enzyme production capacity, metabolic characteristics, and environmental adaptation abilities.

In addition, this study addresses the effects of environmental and operational parameters, including pH, temperature, and contact time, on removal efficiency and demonstrates that these factors are critical determinants of process performance. However, limitations such as the incomplete mineralization of certain pharmaceutical compounds, the formation of transformation products, and variability in process efficiency are also evaluated. Overall, fungal-based treatment approaches are considered an effective alternative for the removal of pharmaceutical pollutants; nevertheless, it is concluded that treatment processes should be optimized for practical applications, the potential use of multiple fungal species in combination should be further investigated, and additional comprehensive studies are required to support their implementation.

Key Words: Biodegradation, Pharmaceutical contaminant, Fungal treatment, Water treatment.

Özet

Farmasötik bileşikler, yaygın kullanımları ve konvansiyonel atık su arıtma sistemleri tarafından tam olarak giderilememeleri nedeniyle çevresel ortamlarda kalıcı mikro kirleticiler olarak giderek artan bir önem kazanmaktadır. Bu bileşiklerin sucul ekosistemlerde birikimi, hem organizmalar üzerinde toksik etkiler oluşturmakta hem de ekosistem dengesini olumsuz yönde etkilemektedir. Bu durum mevcut arıtma teknolojilerinin yetersizliklerini ortaya koymakta ve alternatif olarak daha etkili ve sürdürülebilir arıtma yöntemlerinin geliştirilmesini gerekli kılmaktadır. Bu çalışmada, fungal sistemlerin farmasötik kalıntıların giderimindeki rolü, etki mekanizmaları, avantajları ve uygulama potansiyeli mevcut bilgiler doğrultusunda kapsamlı biçimde ele alınmaktadır.

Mantarların, özellikle ligninolitik enzim sistemleri aracılığıyla kompleks ve dirençli organik bileşikleri parçalayabilme yetenekleri bu organizmaları farmasötik kirleticilerin biyolojik arıtımında öne çıkarmaktadır. Bu kapsamda, farklı fungal türlerin çeşitli farmasötik bileşikler üzerindeki giderim performansları enzimatik ve enzimatik olmayan süreçler ile karşılaştırmalı olarak değerlendirilmekte ve bu süreçte etkili olan temel mekanizmalar ayrıntılı biçimde incelenmektedir. Enzimatik biyodegradasyon süreçlerinin yanı sıra biyosorpsiyon mekanizmasının da giderime önemli katkı sağladığı ve bu iki sürecin birlikte işlediği vurgulanmaktadır. Fungal türler arasında gözlemlenen performans farklılıklarının ise enzim üretim kapasitesi, metabolik özellikler ve çevresel adaptasyon yetenekleri ile ilişkili olduğu belirtilmektedir.

Ayrıca bu çalışmada, pH, sıcaklık ve temas süresi gibi çevresel ve operasyonel parametrelerin giderim verimi üzerindeki etkileri ele alınmakta ve bu parametrelerin süreç performansı açısından belirleyici olduğu ortaya konulmaktadır. Bununla birlikte, bazı farmasötik bileşiklerin tamamen mineralize edilememesi, ara ürün oluşumu ve süreç verimliliğinde değişkenlik gibi sınırlılıklar da değerlendirilmektedir. Genel olarak, fungal tabanlı arıtım yaklaşımlarının farmasötik kirleticilerin gideriminde etkili bir alternatif sunduğu, ancak uygulamaya yönelik süreçlerin optimize edilmesi, farklı türlerin birlikte kullanımının araştırılması ve daha kapsamlı çalışmalarla desteklenmesi gerektiği sonucuna ulaşılmaktadır.

Anahtar Kelimeler: Biyodegredasyon; Farmasötik kontaminant; Fungal arıtım; Su arıtma.

Giriş

Günümüzde ilaç tüketimindeki küresel artışla birlikte farmasötik olarak aktif bileşiklerin (PhAC'ler) çevresel ortamlarda bulunma sıklığı da önemli ölçüde artmıştır. İnsan sağlığına yönelik kullanımın yanı sıra veterinerlik alanında da yoğun şekilde tercih edilen bu bileşikler, atık su sistemleri aracılığıyla doğal su kaynaklarına taşınmaktadır. Yaklaşık binlerce farklı etkin maddeyi kapsayan bu geniş ilaç grubu, özellikle antiinflamatuar ilaçlar, antibiyotikler ve analjezikler gibi yaygın kullanılan sınıflar nedeniyle çevresel açıdan dikkat çekmektedir [1]. Bu ilaçların mutajenik, teratojenik ve genotoksik özellikleri, özellikle kullanım sonrası atık su sistemleri üzerinden çevreye taşınmaları durumunda ekolojik açıdan ciddi sorunlara yol açabilmektedir. Kemoterapi uygulamalarının gerçekleştirildiği sağlık kuruluşlarında oluşan atık suların çoğu zaman yeterli arıtıma tabi tutulmadan kanalizasyon sistemine verilmesi, bu bileşiklerin sucul ortamlara ulaşmasını kolaylaştırmakta ve canlılar üzerinde toksik etkilere neden olabilmektedir [2].

Mevcut durumda geleneksel atık su arıtma tesislerinin bu mikrokirleticileri tamamen uzaklaştıramaması, PhAC'lerin alıcı su ortamlarında kalıcı hale gelmesine neden olmaktadır. Bu durum, farmasötik kökenli yeni ortaya çıkan kirleticilerin çevresel risklerini daha da önemli hale getirmiş ve bu bileşiklerin giderimi için daha etkili ve sürdürülebilir arıtma teknolojilerinin geliştirilmesine yönelik araştırmaları hızlandırmıştır [1].

Bu bağlamda biyolojik arıtım yöntemleri içerisinde özellikle mantar temelli uygulamalar dikkat çekmektedir. Beyaz çürüme mantarları adsorpsiyon, hücre içi alım ve hücre içi/hücre dışı enzimatik parçalanma gibi farklı mekanizmalar aracılığıyla çok çeşitli organik mikro kirleticileri parçalayabilme kapasitesine sahiptir. Bu özellikleri sayesinde geleneksel fizikokimyasal yöntemlere kıyasla daha ekonomik ve çevre dostu bir alternatif olarak değerlendirilmektedir [3, 4]. Ayrıca ligninolitik enzimlerin hücre dışı olarak çalışabilmesi, toksik bileşiklerin hücre içine taşınmasına gerek kalmadan doğrudan dönüşümünü mümkün kılmakta ve bu süreçlerin etkinliğini artırmaktadır [5].

Bu çalışma, fungal organizmaların farmasötik kirleticilerin giderimindeki rolünü incelemekte ve bu süreçte etkili olan mekanizmaları ortaya koymayı amaçlamaktadır.

Yeni Ortaya Çıkan Kirleticiler Olarak Farmasötik Aktif (PhAC) Bileşikler

Tıp ve farmakolojideki ilerlemelerle birlikte insan ve hayvan hastalıklarının tedavisi, önlenmesi ve teşhisi için çok sayıda ilaç geliştirilmiştir. Ancak çevreye salınan farmasötik bileşikler, düşük konsantrasyonlarda dahi su ortamlarında ve arıtma sistemlerinin kapasitesini aşacak düzeylerde

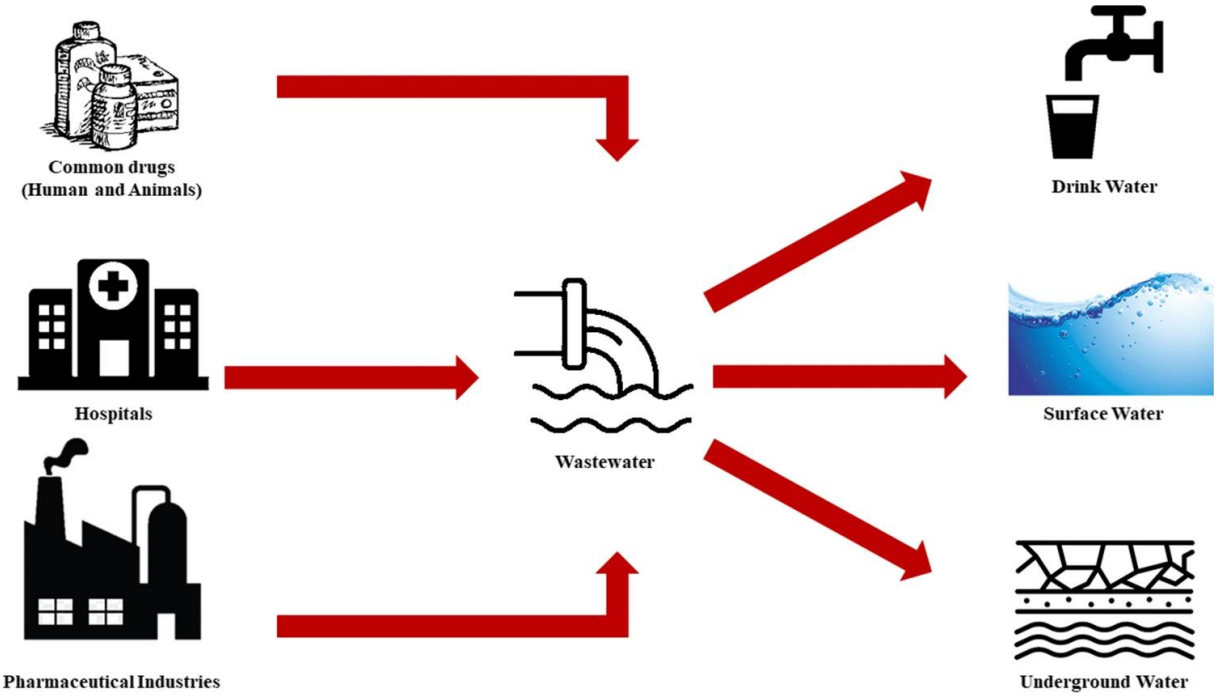
birikerek yüzey sularına ulaşmakta; vahşi yaşam ve insan sağlığı için risk oluşturmaktadır (Şekil 1). Bu bileşiklerin yalnızca su ortamlarında değil, aynı zamanda toprakta da varlığına ilişkin bulgular rapor edilmiştir [6, 7]. Bu bileşikler, çevresel etkileri yeterince değerlendirilmemiş ve büyük ölçüde düzenlenmemiş yeni ortaya çıkan kirleticiler arasında yer almaktadır [8, 9].

Farmakolojik aktif maddeler (PhAC'ler) geniş bir kimyasal çeşitlilik gösterir ve genellikle terapötik işlevlerine göre; lipit düzenleyiciler, antiinflamatuar/analjezikler, psikiyatrik ilaçlar, antibiyotikler, β-blokerler, östrojenler, antiviraller, antikanser ilaçlar ve iyotlu kontrast maddeler gibi farklı formlarda sınıflandırılır [10]. Bu bileşikler ekosisteme girişi su döngüsü ile gerçekleşir; insan alkarivücudunda tamamen metabolize edilmemekte ve atılım yoluyla çevreye ulaşarak sucul kirleticiler olarak ortaya çıkmaktadır [9, 11].

Sucul organizmalar üzerindeki etkilerinin yanı sıra, içme suyu ve toprakta bulunan farmasötik bileşikler nanogram ile mikrogram aralığındaki düşük konsantrasyonlarda akut toksisite riski taşımasalar da biyolojik olarak aktif bileşikler olmaları sebebiyle kronik toksisite, biyobirikim ve biyobüyütme potansiyeli gösterebilmektedir [12, 13]. Yapılan çalışmalar, ülserler ile gastrointestinal ve böbrek sorunlarına yol açtığı bilinen analjezikler ve NSAID'lerin su kaynaklarında tespit edildiğini göstermektedir [14]. İlaç bileşenleri aynı zamanda hormonal dengesizliklere, balıklarda üreme başarısızlığına ve ilaç dirençli patojenlerin gelişimine yol açabilmektedir [6].

Eritromisin, siprofloksasin, ofloksasin, tetrasiklin gibi antibiyotikler dünya genelindeki su kaynaklarında tespit edilmektedir [15]. İçme suyunda yüksek konsantrasyonlarda hormon bulunması ise üreme bozuklukları ve ergenlerde erken olgunlaşma gibi etkiler nedeniyle önemli bir endişe kaynağıdır [6].

Şekil 1. Farmasötiklerin doğaya giriş yolları [16].



Geleneksel Atıksu Arıtım Sistemlerinin Sınırlamaları

Farmasötiklerin giderimi için geliştirilen membran teknolojileri ve ileri oksidasyon prosesleri gibi mevcut yöntemler, yüksek enerji ve kimyasal kullanımı nedeniyle ciddi bir maliyet yükü oluşturmaktadır. Bu kimyasal temelli yaklaşımlarda, operasyonel maliyetlerin yanı sıra zararlı reaksiyon yan ürünlerinin oluşumu ve ortaya çıkan toksik çamurun bertaraf edilmesi gibi teknik zorluklar da yönetimsel açıdan kritik birer faktör olarak öne çıkmaktadır [17].

Cristovao, M. B., et al. [18], çalışmalarında kanser ilaçlarının tüketimindeki artışa paralel olarak çevresel salınımlarının da yükseldiği ve bu eğilimin devam etmesinin beklendiği bildirilmektedir. Ayrıca çoğu kanser ilacının sınırlı biyolojik parçalanabilirliğe sahip olduğu ve bu nedenle mevcut konvansiyonel atıksu arıtma proseslerinin bu bileşiklerin gideriminde yeterli olmadığı vurgulanmaktadır. Bu sonuçlar araştırmacıları alternatif ve güçlü bir giderim mekanizmasına yönlendirmektedir.

Hedef kirleticilerin arıtımı sırasında oluşan dönüşüm ürünlerinin, ana bileşiğe kıyasla daha yüksek toksisite sergileme riski nedeniyle, arıtılmış atık suların ekotoksikolojik açıdan değerlendirilmesi zorunluluk arz etmektedir [19].

Biyoremediasyon, geleneksel teknolojilerle kıyaslandığında daha az tehlikeli kimyasal madde kullanımı, düşük enerji gereksinimi ve zamandan tasarruf sağlaması gibi avantajlara sahiptir. Ayrıca, operasyonel maliyetlerin diğer arıtma yöntemlerine göre daha düşük olması, bu süreci ekonomik açıdan daha tercih edilebilir kılmaktadır [1].

Fungusların Biyodegredasyon Potansiyeli

Mantarlar, atık su rehabilitasyonu da dahil olmak üzere çeşitli çevresel uygulamalarda kullanılmakta ve bazı durumlarda diğer mikroorganizmalarla sinerjik etki gösterebilmektedir. Geniş enzimatik kapasiteleri ve farklı ekosistemlerde yaşayabilmeleri sayesinde, çevrede bulunan birçok organik kimyasalı parçalayabildikleri ve toksik bileşiklerin biyolojik arıtımında rol oynadıkları bildirilmektedir; bu özellikleri, mantarların çevre dostu biyoteknolojik uygulamalarda değerlendirilmesini mümkün kılmaktadır. Filamentli mantarlar, yüksek giderim verimlilikleri, farklı kirleticileri uzaklaştırabilme süreleri ve uygulama kolaylıklarının yanı sıra kolay kültüre edilebilmeleri ve çeşitli kirleticileri toksik olmayan veya daha az toksik formlara dönüştürebilmeleri nedeniyle yeni ortaya çıkan kirleticilerin biyoremediasyonunda etkili organizmalar olarak değerlendirilmektedir [6, 9].

Filamentli mantarların, antibiyotikler, antiinflamatuarlar ve β-blokerler dahil çeşitli farmasötik bileşikleri dönüştürebildiği ve sentetik atık sularda %78–100 oranında giderim sağlayabildiği bildirilmiştir [1, 9, 10]. Bu veriler mantarlar ve enzimlerinin yüksek potansiyelini ortaya koymaktadır.

Kirletici gideriminde Aspergillus, Penicillium, Fusarium, Verticillium ve Phanerochaete türlerinin yanı sıra Basidiomycota ve Zygomycota grubuna ait çeşitli filamentli mantarların kullanıldığı bildirilmektedir [9].

Özellikle *Basidiomycota* filumuna ait olan beyaz çürüme mantarları (WRF), farmasötik maddelerin giderilmesine yönelik çeşitli araştırmalarda potansiyelleri sıklıkla incelenen mikroorganizmalardır. Doğada yaygın bulunan ipliksi odun bozucu bu suşlar, lignini verimli şekilde mineralize edebilmektedir. Lignin giderimi sonucu odunda oluşan beyaz görünüm nedeniyle "beyaz çürüme mantarı" olarak adlandırılırlar. Lignolitik mekanizmaları, farmasötikler gibi dirençli kirleticilerin de parçalanmasını mümkün kılarak bu mantarları atık su biyoremediasyonu için elverişli kılmaktadır. Spesifik ve stereoselektif olmayan enzimatik sistemleri, serbest radikaller aracılığıyla çok çeşitli kirleticilerin mineralize edilmesine olanak tanır [17].

Ayrıca lignin parçalayan mantarların ürettiği enzimlerin antibiyotikler ve diğer farmasötik kirleticilerin parçalanmasında etkili olduğu belirtilmektedir [8].

Mantarlar Tarafından PhAC'lerin Giderim Mekanizmaları

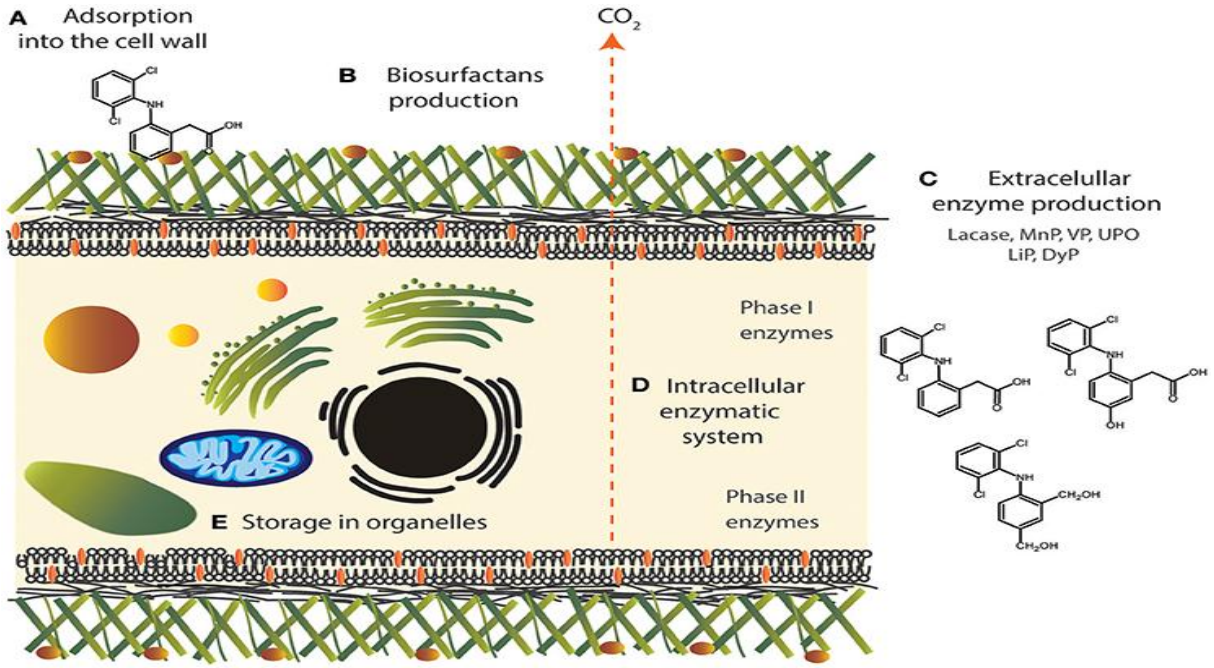
Mantarlar hem hücre içi hem de hücre dışı enzimlerinin spesifik olmayan doğası sayesinde organik maddeleri parçalama konusunda yüksek kapasiteye sahip ayrıştırıcılardır. Enzimatik sistemlerinin bu genelleyici yapısı, çeşitli ilaç sınıflarına ait farklı kimyasal formlarla etkileşime girmelerine olanak tanımaktadır. Hiperakümülatör özellik sergileyen birçok mantar türü, ksenobiyotikleri çevrelerinden emme ve biyolojik olarak biriktirme yeteneğine sahiptir.

Ayrıca mantarların zorlu çevresel koşullara adaptasyon yeteneği, onları diğer biyoremediasyon organizmalarına kıyasla değişken şartlara karşı daha dirençli kılmaktadır. Bu bağlamda, atık su

toksisitesini azaltmayı hedefleyen mikoremediasyon süreci; kirliliğin giderilmesinde ekonomik, çevre dostu ve etkin bir çözüm yolu teşkil etmektedir [1].

Mantarlar, PhAC'ler gibi dirençli toksik bileşiklere karşı koymak amacıyla çeşitli stratejiler kullanmaktadır. Bu stratejiler; biyoadsorpsiyon ve biyomineralizasyon gibi enzimatik olmayan süreçlerin yanı sıra, enzimatik sistemler aracılığıyla gerçekleşen biyotransformasyon ve biyobozunma mekanizmalarından oluşmaktadır (Şekil 2.) [9].

Şekil 2. Mantarların ortaya çıkan kirleticilere karşı koymak için kullandığı farklı mekanizmalar, diklofenak örneği: (A) biyoadsorpsiyon, (B) hidrofobin üretimi, (C) metal etkileşimi, (D) hücre dışı enzimatik sistem, (E) hücre içi enzimatik sistem [10].



Enzimatik Olmayan Mekanizmalar

Filamentli mantarların biyoremediasyon mekanizmalarında öncelikli aşama, toksik bileşenlerin hücre duvarına adsorbe edilmesidir. Fizikokimyasal bir süreç olan biyoadsorpsiyon, kirleticilerin mantar yüzeyine tutunması esasına dayanır. Bu emilim mekanizması, hücre duvarı yapısında yer alan kitin veya kitosan gibi spesifik aminopolisakkaritler tarafından yönetilmektedir.

Filamentli mantarlar, biyoremediasyonda biyosürfaktan üretimi ve biyomineralizasyon gibi mekanizmalarla rol oynamaktadır. Biyosürfaktanlar, yüzey gerilimini azaltarak özellikle petrol türevi kirleticilerin giderimini kolaylaştırmakta; *Penicillium*, *Aspergillus* ve *Fusarium* türlerinin bu bileşikleri üretebildiği bildirilmektedir. Ancak üretim maliyetlerinin yüksek ve verimin düşük olması uygulamayı sınırlamaktadır.

Diğer bir mekanizma olan biyomineralizasyonda ise mantarlar tarafından üretilen oksalik asit, çeşitli metalleri (Pb, Zn, Cu vb.) oksalat formunda çöktürerek toksisitelerini azaltmaktadır. Özellikle *Aspergillus niger* ve bazı *Penicillium* türlerinin ağır metallerin çöktürülmesi ve uzaklaştırılmasında etkili olduğu gösterilmiştir [9].

Enzimatik Mekanizmalar

Mantarlar, dirençli bileşiklerin biyodegradasyonunu kolaylaştıran spesifik ve non-spesifik bir dizi hücre dışı enzim sistemine sahiptir. Bu enzimler, kompleks moleküler yapıları parçalayarak stabil kirleticilerin biyolojik olarak bozunmasına olanak tanır [20].

Mantarlar; lakkaz, oksidaz, peroksidazlar, epoksit hidrolaz ve sitokrom P450 gibi hücre içi ve hücre dışı enzim sistemleri sayesinde yüksek detoksifikasyon ve biyodegradasyon kapasitesine sahiptir. Bu

enzimler, farmasötik bileşiklerin oksidatif dönüşümü ve parçalanmasında rol oynarken, düşük substrat özgüllükleri farklı farmasötik sınıflarına etki edebilmelerini sağlamaktadır. Ayrıca mantar hiflerinin morfolojik yapısı adsorpsiyon süreçlerini desteklemekte, enzimatik reaksiyonlar ve reaktif oksijen türleri ise kirleticilerin bozunmasını mümkün kılmaktadır. Bu özellikler, mantarların farmasötik kirleticilerin gideriminde etkili bir biyoremediasyon aracı olduğunu ortaya koymaktadır [19, 21].

Beyaz çürüme mantarlarının lignin ve çeşitli ksenobiyotik kirleticilerin parçalanmasında etkin rol oynayan ligninaz, laccase, manganez-peroksidaz gibi hücre dışı enzimleri salgıladığı saptanmıştır. Bu enzimlerin oksidasyon kapasitesi, yapısal olarak dirençli kirleticilerin biyolojik yıkımını mümkün kılmaktadır [20, 22].

Lignin, doğada kimyasal ve biyolojik parçalanmaya karşı yüksek direnç gösteren heterojen yapılı aromatik bir polimer olup, odun bozucu mantarlar tarafından salgılanan güçlü oksidatif enzim sistemleri sayesinde parçalanabilmektedir. Bu sistemler lignin peroksidaz (LiP), manganez bağımlı peroksidaz (MnP), çok yönlü peroksidaz (VP) ve lakkaz gibi enzimlerin kombinasyonundan oluşmakta ve özellikle LiP ile VP, fenolik olmayan aromatik yapıların oksidasyonunda etkin rol oynamaktadır. Lignin gibi kompleks ve dirençli yapıları parçalayabilme yeteneği, mantarların benzer özelliklere sahip farmasötik bileşiklerin biyotransformasyonunda da etkili olmasını sağlamaktadır. Mantarların çevresel stres koşullarına adaptasyon kabiliyeti ve ksenobiyotik bileşikleri biriktirebilme özellikleri, bu organizmaların biyoremediasyon uygulamalarındaki önemini artırmaktadır [5].

Karşılaşılan Sınırlamalar

İlaç aktif bileşikleri (PhAC'ler) ve metabolitlerini içeren atık sular, atık su arıtma tesislerine (WWTP'ler) ulaştığında genellikle arıtma sistemleri yoluyla işlenmektedir. Mikroorganizmaların kullanıldığı biyolojik arıtma yöntemlerinin ilaç iyileştirme potansiyeli kanıtlanmıştır. Ancak biyolojik sistemler, sürece dair kısıtlamalar nedeniyle çoğunlukla ileri arıtma teknikleri ve geleneksel aktif çamur (CAS) sistemleriyle entegre edilerek uygulanmaktadır.

Gelişmiş biyolojik arıtma yöntemleri; modifiye CAS, aerobik granüler sistemler, hareketli yataklı biyoreaktörler (MBBR'ler), anammox sistemleri ve membran biyoreaktörleri (MBR'ler) kapsamaktadır. Bununla birlikte, MBR gibi bazı süreçlerde, gerekli bakım işlemlerinin bir yan ürünü olarak biyokatı veya kanalizasyon çamuru oluşumu gözlenebilmektedir.

Biyoremediasyonun bir diğer sınırlaması, iyileştirme hızının endüstriyel arıtma kapasitesi gereksinimlerini karşılamada yetersiz kalabilmesidir. Bununla birlikte, yöntemin sağladığı avantajlar nedeniyle, süreç verimliliğini optimize etmeye ve operasyonel bekleme sürelerini minimize etmeye yönelik çalışmalar devam etmektedir [1].

Tartışma

Gouveia, T. I., ve ark. [23], çalışmalarında, sitostatik ilaçların yüzey sularında varlığı incelenmiş ve Portekiz nehirlerinde analiz edilen 13 bileşiğin 9'unun tespit edildiği bildirilmiştir. En yüksek konsantrasyonun siproteron için (19 ± 3 ng/L) ölçüldüğü, bikalutamidin ise en sık tespit edilen bileşik olduğu belirtilmiştir. Ayrıca flutamid ve mikofenolat mofetil gibi bazı sitostatiklerin yüzey sularında ilk kez raporlandığı ifade edilmiştir. İnsan maruziyeti üç farklı senaryo üzerinden değerlendirilmiş olup; dermal temas, kazara yutma ve yüzey sularından elde edilen içme suyunun uzun süreli tüketimi dikkate alınmıştır. Bulgular, özellikle içme suyu tüketimine dayalı uzun süreli maruziyet senaryosunda, literatürde bildirilen en yüksek siklofosfamid konsantrasyonları esas alındığında çocuklar için risk oluşabileceğini göstermektedir. Ayrıca bazı sitostatiklerin karsinojenik özellikleri nedeniyle, maruziyet düzeyinden bağımsız olarak potansiyel sağlık risklerinin söz konusu olabileceği ve uzun süreli veya birleşik etkilerin dışlanamayacağı belirtilmiştir.

Azuma, T. ve ark. [24], çalışmada, hastane atık sularında 41 farmasötik ve fitokimyasal bileşik ile bunların metabolitlerinin varlığı incelenmiş; ayrıca atıksu arıtma tesisi (AAT) giriş-çıkış suları ve nehir suyu analiz edilerek kütle dengesi yaklaşımıyla bu bileşiklerin çevresel deşarja katkısı değerlendirilmiştir. Sonuçlar, hastane atık sularında 38 bileşiğin ng/L–µg/L aralığında, maksimum 92

µg/L konsantrasyona kadar tespit edildiğini ve bu bileşiklerin AAT girişine katkısının <%0,1 ile %14,8 arasında değiştiğini göstermiştir. AAT'lerde ozonlama uygulanmasıyla birçok bileşiğin konsantrasyonu 1,0 ng/L'nin altına düşürülmesine rağmen, bazı farmasötiklerin çıkış suyunda 10 ng/L'nin üzerinde kaldığı bildirilmiştir. Ayrıca asetaminofen glukuronid ve sülfat gibi konjuge metabolitler ile loxoprofen ve metabolitlerinin hastane atık suyu, AAT ve nehir suyunda varlığı ilk kez rapor edilmiştir.

Badia-Fabregat ve ark. [4], çalışmasında, farmasötik aktif bileşiklerin (PhAC) giderimi için Trametes versicolor ile inoküle edilmiş sürekli biyoreaktörler kullanılmış ve sistemler steril olmayan gerçek atıksularla beslenerek kontrol reaktörleriyle karşılaştırılmıştır. Reaktörler pH 4.5 ve 25°C'de işletilmiş, analizler SPE–UPLC-MS/MS ile gerçekleştirilmiştir. Sonuçlar, HRT'nin 3 gün olduğu koşullarda fungal reaktörde %52, kontrol reaktörde %25 PhAC giderimi sağlandığını; HRT 2 güne düşürüldüğünde ise bu farkın azaldığını göstermiştir. Veteriner atıksuyunda ise uygun besin koşullarında fungal sistemde %44 giderim elde edilirken kontrol grubunda anlamlı bir giderim gözlenmemiştir.

Alkarim ve ark. [3], çalışmalarında, florlu ilaç aktif maddelerinin (ATO, CIP, FLX) gideriminde *Aspergillus flavus* ve *Cunninghamella elegans* türlerinin biyoremediasyon potansiyelini, poliüretan köpük (PUF) destekli biyofilm sistemlerini kullanarak değerlendirmiştir. Sabit fazlı biyofilm sistemlerinde (PUF-F), *C. elegans* ATO ve CIP için %97'nin üzerinde, *A. flavus* ise FLX için %92,4 oranında giderim verimi sergilediği bildirilmiştir. Birinci derece kinetiğe uygun ilerleyen degradasyon sürecinde, 1,0-1,7 gün aralığında saptanan yarı ömür değerlerinin literatürdeki beyaz çürüme mantarlarına kıyasla daha kısa olduğu saptanmıştır. Adsorpsiyonun toplam giderime katkısının %10'un altında kaldığı bildirilmiştir. Tür bazlı analizlerde *C. elegans* yüksek hidrofobite ve stres direnciyle, *A. flavus* ise yoğun ekstrasellüler matris yapısıyla öne çıkmıştır. Sonuçlar, özelleştirilmiş mantar biyofilm sistemlerinin dirençli farmasötiklerin arıtımında etkin bir biyolojik alternatif sunduğunu göstermektedir.

Bu çalışma kapsamında elde edilen bulgular, fungal türlerin farmasötik bileşiklerin gideriminde etkili olduğunu göstermektedir. Özellikle enzimatik parçalanma mekanizmalarının, biyosorpsiyon süreçleri ile birlikte çalıştığı belirlenmiştir. Ligninolitik enzimlerin varlığı, kompleks yapıdaki farmasötik bileşiklerin parçalanmasında önemli bir rol oynamaktadır.

Farklı fungal türler arasında giderim verimliliği açısından farklılıklar gözlemlenmiştir. Bu durum, türlerin enzim üretim kapasiteleri ve metabolik özellikleri ile ilişkilendirilmiştir. Ayrıca pH, sıcaklık ve temas süresi gibi çevresel faktörlerin giderim verimi üzerinde belirleyici olduğu tespit edilmiştir.

Bununla birlikte, bazı farmasötik bileşiklerin tamamen mineralize edilemediği ve ara ürünlerin oluşabileceği belirtilmiştir. Bu durum, süreçlerin optimize edilmesi gerektiğini ortaya koymaktadır. Çalışma, fungal sistemlerin çevresel uygulamalarda kullanılabilirliğini desteklemekle birlikte, daha kapsamlı analizlere ihtiyaç olduğunu göstermektedir.

Gelecekte yapılacak çalışmaların, fungal arıtma sistemlerinin ölçeklendirilmesine odaklanması gerekmektedir. Laboratuvar ölçeğinde elde edilen sonuçların pilot ve endüstriyel ölçeklere aktarılması, bu teknolojinin uygulanabilirliğini değerlendirmek açısından önem taşımaktadır.

Ayrıca, farklı fungal türlerin birlikte kullanıldığı konsorsiyum sistemlerinin incelenmesi, giderim veriminin artırılmasına katkı sağlayabilir. Enzim üretiminin artırılmasına yönelik genetik ve biyoteknolojik yaklaşımlar da araştırma alanları arasında yer almaktadır.

Farmasötik bileşiklerin parçalanması sonucunda oluşan ara ürünlerin belirlenmesi ve toksisitelerinin değerlendirilmesi, çevresel güvenlik açısından önemlidir. Bunun yanı sıra, proses parametrelerinin optimizasyonu ve reaktör tasarımı üzerine çalışmaların artırılması gerekmektedir.

Kaynaklar

[1] Ortuzar, M., Esterhuizen, M., Olicon-Hernandez, D. R., Gonzalez-Lopez, J., & Aranda, E. (2022). Pharmaceutical pollution in aquatic environments: a concise review of environmental impacts and bioremediation systems. *Frontiers in microbiology*, *13*, 869332. https://doi.org/10.3389/fmicb.2022.869332

[2] Cesen, M., Kosjek, T., Laimou-Geraniou, M., Kompare, B., Sirok, B., Lambropolou, D., & Heath, E. (2015). Occurrence of cyclophosphamide and ifosfamide in aqueous environment and their removal by biological and abiotic wastewater treatment processes. *Science of the Total Environment*, *527*, 465-473. https://doi.org/10.1016/j.scitotenv.2015.04.109

[3] Alkarim, I., Halim, M., Mohamed, M. S., & Wong, F. W. F. (2025). Enhanced biodegradation of fluorinated pharmaceutical by Aspergillus flavus and Cunninghamella elegans biofilms: kinetics and mechanisms. *Biodegradation*, *36*(5), 83. https://doi.org/10.1007/s10532-025-10182-w

[4] Badia-Fabregat, M., Lucas, D., Tuomivirta, T., Fritze, H., Pennanen, T., Rodriguez-Mozaz, S., ... & Vicent, T. (2017). Study of the effect of the bacterial and fungal communities present in real wastewater effluents on the performance of fungal treatments. *Science of the total environment*, *579*, 366-377. https://doi.org/10.1016/j.scitotenv.2016.11.088

[5] Park, H., & Choi, I. G. (2020). Genomic and transcriptomic perspectives on mycoremediation of polycyclic aromatic hydrocarbons. *Applied Microbiology and Biotechnology*, *104*(16), 6919-6928. https://doi.org/10.1007/s00253-020-10746-1

[6] Arun, K. B., Madhavan, A., Tarafdar, A., Sirohi, R., Anoopkumar, A. N., Kuriakose, L. L., ... & Sindhu, R. (2023). Filamentous fungi for pharmaceutical compounds degradation in the environment: A sustainable approach. *Environmental Technology & Innovation*, *31*, 103182. https://doi.org/10.1016/j.eti.2023.103182

[7] Kozka, B., Sosnicka, A., Nalecz-Jawecki, G., Drobniewska, A., Turlo, J., & Giebultowicz, J. (2023). Various species of Basidiomycota fungi reveal different abilities to degrade pharmaceuticals and also different pathways of degradation. *Chemosphere*, *338*, 139481. https://doi.org/10.1016/j.chemosphere.2023.139481

[8]Akerman-Sanchez, G., & Rojas-Jimenez, K. (2021). Fungi for the bioremediation of pharmaceutical-derived pollutants: A bioengineering approach to water treatment. *Environmental Advances*, *4*, 100071. https://doi.org/10.1016/j.envadv.2021.100071

[9] Ghosh, S., Rusyn, I., Dmytruk, O. V., Dmytruk, K. V., Onyeaka, H., Gryzenhout, M., & Gafforov, Y. (2023). Filamentous fungi for sustainable remediation of pharmaceutical compounds, heavy metal and oil hydrocarbons. *Frontiers in Bioengineering and Biotechnology*, *11*, 1106973. https://doi.org/10.3389/fbioe.2023.1106973

[10] Olicon-Hernandez, D. R., Gonzalez-Lopez, J., & Aranda, E. (2017). Overview on the biochemical potential of filamentous fungi to degrade pharmaceutical compounds. *Frontiers in microbiology*, *8*, 1792. https://doi.org/10.3389/fmicb.2017.01792

[11] Vasilachi, I. C., Asiminicesei, D. M., Fertu, D. I., & Gavrilescu, M. (2021). Occurrence and fate of emerging pollutants in water environment and options for their removal. *Water*, *13*(2), 181. https://doi.org/10.3390/w13020181

[12] Ruan, Y., Lin, H., Zhang, X., Wu, R., Zhang, K., Leung, K. M., ... & Lam, P. K. (2020). Enantiomer-specific bioaccumulation and distribution of chiral pharmaceuticals in a subtropical marine food web. *Journal of hazardous materials*, *394*, 122589. https://doi.org/10.1016/j.jhazmat.2020.122589

[13] Zhang, Y., Li, Y., Ren, X., Zhang, X., Wu, Z., & Liu, L. (2023). The positive correlation of antioxidant activity and prebiotic effect about oat phenolic compounds. *Food Chemistry*, *402*, 134231. https://doi.org/10.1016/j.foodchem.2022.134231

[14] Swiacka, K., Michnowska, A., Maculewicz, J., Caban, M., & Smolarz, K. (2021). Toxic effects of NSAIDs in non-target species: a review from the perspective of the aquatic environment. *Environmental Pollution*, *273*, 115891. https://doi.org/10.1016/j.envpol.2020.115891

[15] Bilal, M., Mehmood, S., Rasheed, T., & Iqbal, H. M. (2020). Antibiotics traces in the aquatic environment: persistence and adverse environmental impact. *Current opinion in environmental science & health*, *13*, 68-74. https://doi.org/10.1016/j.coesh.2019.11.005

[16] Moghaddam, A., Khayatan, D., Esmaeili Fard Barzegar, P., Ranjbar, R., Yazdanian, M., Tahmasebi, E., ... & Tebyaniyan, H. (2023). Biodegradation of pharmaceutical compounds in industrial wastewater using biological treatment: a comprehensive overview. *International Journal of Environmental Science and Technology*, *20*(5), 5659-5696. https://doi.org/10.1007/s13762-023-04880-2

[17] Silva, A., Delerue-Matos, C., Figueiredo, S. A., & Freitas, O. M. (2019). The use of algae and fungi for removal of pharmaceuticals by bioremediation and biosorption processes: a review. *Water*, *11*(8), 1555. https://doi.org/10.3390/w11081555

[18] Cristovao, M. B., Janssens, R., Yadav, A., Pandey, S., Luis, P., Van der Bruggen, B., ... & Pereira, V. J. (2020). Predicted concentrations of anticancer drugs in the aquatic environment: what should we monitor and where should we treat?. *Journal of Hazardous Materials*, *392*, 122330. https://doi.org/10.1016/j.jhazmat.2020.122330

[19] Cruz-Morato, C., Ferrando-Climent, L., Rodriguez-Mozaz, S., Barcelo, D., Marco-Urrea, E., Vicent, T., & Sarra, M. (2013). Degradation of pharmaceuticals in non-sterile urban wastewater by Trametes versicolor in a fluidized bed bioreactor. *Water research*, *47*(14), 5200-5210. https://doi.org/10.1016/j.watres.2013.06.007

[20] Kour, D., Rana, K. L., Yadav, N., Yadav, A. N., Singh, J., Rastegari, A. A., & Saxena, A. K. (2019). Agriculturally and industrially important fungi: current developments and potential biotechnological applications. In *Recent advancement in white biotechnology through fungi: Volume 2: Perspective for value-added products and environments* (pp. 1-64). Cham: Springer International Publishing. https://doi.org/10.1007/978-3-030-14846-1_1 ISBN: 978-3-030-14846-1

[21] Singh, A., Kumari, R., & Yadav, A. N. (2021). Fungal secondary metabolites for bioremediation of hazardous heavy metals. In *Recent trends in mycological research: volume 2: environmental and industrial perspective* (pp. 65-98). Cham: Springer International Publishing. https://doi.org/10.1007/978-3-030-68260-6_4 ISBN: 978-3-030-68260-6

[22] Loi, M., Glazunova, O., Fedorova, T., Logrieco, A. F., & Mule, G. (2021). Fungal laccases: The forefront of enzymes for sustainability. *Journal of Fungi*, *7*(12), 1048. https://doi.org/10.3390/jof7121048

[23] Gouveia, T. I., Mota, I. H., Silva, A. M., Alves, A., & Santos, M. S. (2022). Are cytostatic drugs in surface waters a potential threat?. *Science of The Total Environment*, *853*, 158559. https://doi.org/10.1016/j.scitotenv.2022.158559

[24] Azuma, T., Arima, N., Tsukada, A., Hirami, S., Matsuoka, R., Moriwake, R., ... & Masada, M. (2016). Detection of pharmaceuticals and phytochemicals together with their metabolites in hospital effluents in Japan, and their contribution to sewage treatment plant influents. *Science of the Total Environment*, *548*, 189-197. https://doi.org/10.1016/j.scitotenv.2015.12.157

Radyoterapi Kaynaklı MikroRNA Ekspresyon Değişiklikleri ve Meme Kanserinde Radyosensitivite Üzerindeki Etkileri

Selim ÖĞÜT

Dr. Öğretim Üyesi, Biyofizik AD., Bandırma Onyedi Eylül Üniversitesi Tıp Fakültesi

ORCID ID : 0000-0001-9126-6477

Giriş

Meme kanseri, dünya genelinde kanser tanısı konan kadınlarda morbidite ve mortalite açısından en yüksek sıralarda yer almaktadır (Dünya Sağlık Örgütü 2022). Erken tanı ve çok modlu tedavilerdeki gelişmeler hasta bakımını önemli ölçüde iyileştirmiştir; ancak tedaviye direnç önemli bir klinik engel olmaya devam etmektedir. Meme kanserini tedavi etmek için şu anda kullanılan terapötik yöntemler arasında, lokal nüksü azaltmanın ve meme kanseri hastaları için genel sağkalımı sağlamanın temel bir parçası olan radyoterapi yer almaktadır. Bununla birlikte, radyoterapinin genel başarısı, kanser hücrelerinin iyonlaştırıcı radyasyondan sağ kalmasına izin veren ve nüks veya metastaza yol açan, tedavi sonucunu olumsuz etkileyen hem içsel hem de/veya edinilmiş radyorezistans mekanizmalarından etkilenebilir (Mageau vd., 2025; Girgin vd., 2024).

Son birkaç yıldır meme kanserinde radyasyon yanıtının moleküler biyolojisini anlamaya yönelik nispeten yeni bir odaklanma olmuştur. Kodlanmayan RNA'lar (ncRNA'lar), hücresel radyosensitivitenin biyolojisine aracılık eden kilit oyuncular olarak tanımlanmıştır. MikroRNA'lar (miRNA'lar), RNA bozunmasını indükleyerek veya translasyonu inhibe ederek hedef genlerin ekspresyonunu transkripsiyon sonrası düzeyde düzenleyen endojen küçük ncRNA'lardır. miRNA'lar, apoptoz, proliferasyon, DNA onarımı, oksidatif stres, epitel-mezenkimal geçiş ve kanser kök hücrelerinin korunması dahil olmak üzere çeşitli biyolojik süreçleri modüle ederek kanser gelişiminde ve kanserin tedaviye yanıtında kilit oyuncular olarak ortaya çıkmıştır (Metheetrairut & Slack, 2013; Chong vd., 2020).

Artık iyonlaştırıcı radyasyona maruz kalmanın meme kanseri hücrelerinde miRNA ekspresyon profilleri üzerinde önemli etkileri olduğunu gösteren giderek artan sayıda kanıt bulunmaktadır. Veriler, iyonlaştırıcı radyasyonun değiştirilmiş miRNA ekspresyonu üzerindeki etkilerinin, iyonlaştırıcı radyasyona maruz kalma sonucu değiştirilen moleküler hedeflere bağlı olarak, kanser hücresini radyasyona karşı daha duyarlı hale getirmek (radyoduyarlılığı artırmak) veya kanser hücresinin radyoterapiye direnme ve tedaviden sağ kalma yeteneğini artırmak (radyorezistansı artırmak) olabileceğini göstermektedir (Leung vd., 2014; Masoudi-Khoram vd., 2020). Mikro ribonükleik asidin (miR) genler tarafından üretilen protein sayısını modüle etmedeki rolü, hücre çoğalması, farklılaşma, apoptoz, göç ve bağışıklık yanıtının modülasyonu dahil olmak üzere çoklu hücresel fonksiyonların düzenlenmesini içerir (Pajic vd., 2018; Yu vd., 2015). Meme kanseri hücrelerinin iyonlaştırıcı radyasyon bazlı tedavilere karşı yanıtının aracıları olarak miR'leri kullanma çabaları gösterilmiştir; Bu nedenle, radyoterapi etkinliğini artırmak için miR tabanlı tedavi yöntemlerinin sayısı giderek artmaktadır (Pedroza-Torres vd. 2024). Son çalışmalar, miR'lerin birbirleriyle ve diğer kodlayıcı olmayan ribonükleik asit sınıflarıyla (örneğin uzun kodlayıcı olmayan RNA veya dairesel RNA) etkileşime girebileceğini ve bu hücrelerin radyoterapiye nasıl yanıt vereceğini etkileyecek karmaşık bir düzenleyici ağa katkıda bulunabileceğini göstermiştir (Podralska vd. 2020; Bakhshaiesh & Esmaeili 2022). Bu bulgular, radyasyonun çeşitli miR'lerin ekspresyonunda değişikliklere neden olabileceğini göstermekle kalmayıp, aynı zamanda diğer kodlayıcı olmayan RNA'larla ilişkili düzenleyici ağların, radyasyonun neden olduğu ekspresyon değişikliklerinin bireyselleştirilmiş radyoterapi stratejilerinin geliştirilmesinde kullanılıp kullanılamayacağının belirlenmesinde önemli bir rol oynayacağını da vurgulamaktadır.

miRNA'nın meme kanserlerinin radyoterapiye yanıtı üzerindeki etkisi ve tedavi sırasında miR ekspresyonunun nasıl değiştiği hakkındaki mevcut bilgi birikimi, literatürün büyümesiyle birlikte genişlemeye devam etmektedir. Bu literatür taramasının iki ana amacı vardır:

1) Radyoterapi tedavisinin meme kanserinde miRNA ekspresyonu üzerindeki etkilerini incelemek,

2) miRNA ekspresyonundaki değişikliklerin radyosensitivite/radyorezistansı nasıl yansıtabileceğini ve meme kanseri tedavisi için bir kılavuz olarak klinik kullanım potansiyelini değerlendirmek.

1. Meme Kanseri Biyolojisinde miRNA'nın Fonksiyonu

miRNA'lar, gen ekspresyonunun transkripsiyon sonrası düzenlenmesini sağlayan küçük kodlayıcı olmayan RNA molekülleridir (~ 18-25 baz). miRNA'ların keşfedilmesinden ve tüm hücrelerde yaygın ekspresyonlarından bu yana, gen ekspresyonu, hücresel proliferasyon, farklılaşma, apoptoz, göç ve bağışıklık tepkilerinin modülasyonu dahil olmak üzere çeşitli biyolojik süreçlerin kritik düzenleyicileri olarak kabul edilmişlerdir. miRNA'ların düzensiz ekspresyonu, meme kanserinin başlangıcına, ilerlemesine, metastazına ve tedaviye direncine katkıda bulunur (Metheetrairut & Slack, 2013). Hedef genlerine bağlı olarak, miRNA'lar onkomiRNA veya tümör baskılayıcı miRNA olarak işlev görebilirler. miRNA'lar, DNA hasarıyla ilgili genler üzerinde etki ederek hücrenin hücresel radyosensitivitesini etkiler.

miRNA'lar, oksidatif stres, hücre döngüsünün düzenlenmesi ve apoptoz gibi birçok sinyal yolunu aynı anda düzenleyebildikleri için, meme kanserinde radyoterapi yanıtının temel düzenleyicileri olarak giderek daha fazla araştırmacı tarafından değerlendirilmektedir (Chong vd., 2020). Marvaso vd. (2015), miRNA'ların aynı anda birden fazla sinyal yolunu düzenleyebildiğini ve bu nedenle meme kanserinde radyoterapi yanıtının temel düzenleyicileri olarak kabul edildiğini belirtmiştir.

Birçok çalışma ayrıca miRNA'ların kanser kök hücrelerinin korunması ve epitel-mezenkimal geçişin düzenlenmesinde rol oynadığını, bunların her ikisinin de meme kanserinin radyorezistansı ve tümörlerin tekrarlamasıyla ilişkili olduğunu göstermektedir (Griñán-Lisón vd., 2020). Bu nedenle, meme kanserinde radyoterapinin etkinliğini artırmak için yeni tedavi stratejileri geliştirmek amacıyla miRNA'ların biyolojik fonksiyonunun daha iyi anlaşılması gerekmektedir. Meme kanserinin farklı moleküler alt tiplerinde (Luminal A, Luminal B, HER2-pozitif ve triple negatif) miRNA ekspresyon profilleri belirgin farklılıklar göstermekte olup, bu değişiklikler tümör davranışının heterojen yapısını da yansıtmaktadır. Tablo 1, meme kanseri alt tiplerinde gözlenen miRNA ekspresyon değişikliklerini ve bu değişikliklerin tümör biyolojisine olası etkilerini özetlemektedir.

Tablo 1. Meme kanseri alt tiplerinde miRNA ekspresyon profillerinin karşılaştırılması (Baruah & Sharma, 2017).

Meme kanseri alttipi	**Pozitif düzenlenmiş**	**Negatif düzenlenmiş**
Luminal A-benzeri	Let-7c, let-7f, miR-26, miR-126, miR130, miR-100,	miR-206, miR-15b,
	miR-136, miR-146b,	miR-103, miR-107
	miR-99a, miR-190b,	
	miR-191, miR-10a	
Luminal B-benzeri	miR15b, miR-103, miR-107, miR-342	miR-136, miR-146b,
		miR-99a, miR-100,
		miR-126, miR-130
ER- PR-/HER2+	miR-142-3p, miR-150	miR-125a/b

Üçlü negatif	miR-93, miR-135b, miR-155, miR-17- 92, miR-18a/b	miR-29, miR-190b

2. Radyoterapinin miRNA İfadesinde Meydana Getirdiği Değişiklikler

İyonlaştırıcı radyasyon, meme kanseri hücrelerinde miRNA ifadesinde önemli değişikliklere neden olur. Bu değişiklikler, DNA hasarı, oksidatif stres ve hayatta kalmayı destekleyen yolların aktivasyonu ile indüklenen hücresel strese yanıt olarak ortaya çıkar. Leung ve ark. (2014), meme kanseri hücrelerindeki miRNA ifade kalıplarının hem çoklu fraksiyonlu hem de tek doz radyasyon tedavisi sonrasında değişikliklere uğradığını göstermiştir. Benzer şekilde, Masoudi-Khoram ve ark. (2020), radyasyondan sonra farklı şekilde ifade edilen miRNA'ların radyasyon tedavisine duyarlılıkla yakından ilişkili olduğunu bulmuştur.

"Radyo-miRNA'lar", radyasyona yanıt veren ve DNA onarımı, programlanmış hücre ölümü (apoptoz), inflamasyon ve hücre sağkalımı ile ilgili sinyal yollarını düzenleyen miRNA'ların bir alt kümesidir (Pedroza-Torres ve ark., 2024). Bazı miRNA'lar, DNA onarımını artırmaya ve hayatta kalmayı desteklemeye yardımcı olmak için radyasyona maruz kaldıktan sonra artar; miRNA'lar ise DNA onarım yollarını inhibe ederek bireylerin radyasyona maruz kalmaya karşı daha hassas olmalarına neden olur.Ali ve ark. (2023), radyasyonun transkriptomdan bağımsız olan Argonaute 2 (AGO2) ile miRNA etkileşimlerini tetiklediğini bulmuştur; bu nedenle, transkripsiyon dışı mekanizmaların da radyasyon kaynaklı miRNA düzenlemesinde rol oynaması muhtemeldir. Radyasyon maruziyetiyle tetiklenen miRNA imzalarının belirlenmesi, hastaların radyoterapiye ne kadar iyi yanıt vereceklerini ve tedaviyle ne kadar iyi sonuç alacaklarını tahmin etmenin yeni bir yolunu ortaya çıkaracaktır.

3. Meme Kanserinde Radyosensitiviteyi Artıran miRNA'lar

3.1 DNA Onarım Yollarını Hedefleyen miRNA'lar

miRNA'lar, DNA onarım yollarını inhibe ederek meme kanserinde radyosensitiviteyi artırır. Pajic ve ark. (2024), miR-139-5p'nin DNA onarımı ve reaktif oksijen türlerine karşı koruma ile ilgili çeşitli gen yollarının inhibisyonu yoluyla radyoterapiye direnci düzenlemekten sorumlu olduğunu göstermiştir. Ayrı bir çalışmada, Jiang ve ark. (2024) yılında yapılan bir çalışma, meme kanseri hücrelerinde miR-4796 ekspresyonunun, iyonlaştırıcı radyasyona maruz kaldıktan sonra onarım yeteneklerini inhibe ederek radyosensitiviteyi artırdığını göstermiştir.

Ayrıca, Seiri ve ark. (2024), miR-206'nın yüksek ekspresyonuna sahip meme kanseri hücrelerinin hayatta kalma oranının azaldığını ve radyosensitivitenin arttığını göstermiştir. Ek olarak, let-7 ailesi üzerine yapılan çeşitli çalışmalar, let-7 seviyelerindeki bozulmaların, radyoterapiye maruz kaldıktan sonra meme kanseri hücrelerinin hayatta kalma oranını ve tedaviye yanıtını büyük ölçüde etkileyebileceğini göstermiştir (Nejadtaghi & Mozdarani, 2023).

3.2 Apoptosisi ve Hücre Döngüsündeki İlerlemeyi Etkileyen mirRNA'lar

Radyosensitiviteyi artıran mikroRNA'lar, apoptozu artırarak ve hücre döngüsündeki ilerlemeyi inhibe ederek bunu yapabilirler. Örneğin, Chen ve ark. (2024) yılında yapılan bir çalışma, miR-181a'nın anti-apoptotik protein Bcl-2'nin ekspresyonunu inhibe ederek malign hücreleri radyoterapiye duyarlı hale getirdiğini göstermiştir. Kouhestani ve ark. 2025 yılında yayınlanan bir çalışmada, yazarlar, miR-34a ve miR-328'in ektopik ekspresyonuna sahip meme kanseri kök hücrelerinin, bu miRNA'lar tarafından BCL2 ve ABCG2 sinyal yollarının aşağı regülasyonu nedeniyle, vahşi tip hücrelere göre gama radyasyonuna ve doksorubisine daha duyarlı olduğunu sonucuna varmışlardır. 2021 yılında yapılan bir çalışmada, baş yazarlar Shi ve ark., miR-328-3p'nin meme kanseri proliferasyonunda ve radyoterapiye yanıtında rol oynadığını daha da ortaya koymuşlardır. Bu nedenle, apoptozu düzenleyen miRNA'lar, meme kanserinde radyosensitiviteyi artırmak için yeni terapötik hedefler sağlayabilir.

Meme kanseri kök hücreleri, DNA'larındaki hasarı onarma yeteneklerinin daha yüksek olması ve apoptoza karşı daha fazla direnç göstermeleri nedeniyle radyoterapiye dirençlidir. Griñán-Lisón ve

ark.'na göre. (2020) yılında yapılan bir çalışmada, miRNA'ların meme kanseri kök hücrelerinde radyoterapiye yanıtın önemli belirteçleri olduğu tespit edilmiştir. Pan ve ark. (2021) ayrıca miR-29b-3p'nin, kök hücre özellikleriyle ilişkili bazı onkojenik yolları değiştirerek kanser kök hücrelerinde radyosensitiviteyi indüklediğini göstermiştir. Bu nedenle, kök hücre özellikleriyle ilişkili miRNA'ları hedeflemek, radyorezistansı aşmanın ve meme kanseri hastalarında nüks oranını düşürmenin potansiyel bir yoludur.

3.3. Meme Kanserinde Radyorezistans ile İlişkili miRNA'lar

Bazı miRNA'lar radyasyona duyarlılığı artırırken, diğerleri hücrelerin hayatta kalmasına ve büyümesine yardımcı olan yolları uyararak radyorezistansı teşvik eder. Örneğin, Yu ve ark. (2015), miR-144'ün, proliferasyon, göç ve invazyonlarını uyararak meme kanseri hücrelerinin radyoterapiye duyarlılığını azalttığını göstermiştir. Başka bir çalışmada, Wolfe ve ark. (2016), miR-33a'nın meme kanseri hücrelerinin radyoterapiye duyarlılığını negatif olarak düzenlediğini ortaya koymuştur. Potansiyel bir tümör baskılayıcı miRNA olmasının yanı sıra, miR-122'nin hem onkojenik hem de tümör baskılayıcı bir miRNA olarak radyorezistansı etkileyen ikili özelliği, Perez-Añ tarafından tartışılmıştır; ayrıca DNA hasar onarımı, oksidatif stres koruması, epitelden mezenkime geçişi (EMT) ve anti-apoptotik sinyalleme ile ilgili süreçlerin düzenlenmesine de yardımcı olur. Ayrıca Öğüt (2023) tarafından yapılan çalışmada miR-675'in meme kanseri hücrelerinde radyoterapi yanıtı ile ilişkili olarak ekspresyon değişiklikleri gösterdiği ve radyosensitivitenin moleküler düzenlenmesinde potansiyel bir biyobelirteç olabileceği ortaya konmuştur. Bu nedenle, miRNA'ların düzensizliği tedavi başarısızlığına önemli ölçüde katkıda bulunur ve radyasyona dirençli kanser hücrelerini ortadan kaldırmak için tasarlanmış gelecekteki tedavi stratejileri için önemli bir potansiyel hedef olarak görülmelidir.

Radyasyon Yanıtını Düzenlemede Diğer Kodlayıcı Olmayan RNA'larla miRNA Etkileşimleri

Son zamanlarda yapılan birçok çalışma, miRNA'ların radyasyon yanıtını düzenlemede diğer kodlayıcı olmayan RNA'larla (yani, lncRNA'lar; circRNA'lar) kapsamlı etkileşim gösterdiğini ortaya koymuştur. miRNA ve ncRNA etkileşimleri, miRNA'ların öncelikle gen ekspresyonunu düzenlemesine ve tedavi yanıtını etkilemesine olanak tanıyan rekabetçi endojen RNA (ceRNA) ağlarının bir parçasıdır. Lai ve ark. (2018), lncRNA CCAT1'in aşağı regülasyonunun, meme kanseri hücrelerinde miR-148b aktivitesi üzerindeki etkisi sonucu radyosensitivitenin artmasıyla ilişkili olduğunu bulmuştur. Benzer şekilde, Wang ve ark. Yu ve ark. lincRNA LINC02582'nin, miR-200c tarafından aşağı akışta düzenlenen CHK1 aracılı DNA onarım yolları yoluyla radyorezistansın gelişimini desteklediğini göstermiştir. Yu ve ark. lncRNA GAS5'in meme kanseri hücrelerinin iyonlaştırıcı radyasyona duyarlılığını artırdığını ve DNA onarımını inhibe ettiğini bulmuştur. Ek olarak, Abdollahi ve ark. circ-FOXO3 ve miR-23a'nın meme kanserinde radyosensitivitenin önemli düzenleyicileri olduğunu göstermiştir. Toplu olarak, bu çalışmalar ncRNA aracılı radyasyon yanıtının çok karmaşık olduğu fikrini desteklemekte ve kapsamlı bir moleküler değerlendirmeye duyulan ihtiyacı vurgulamaktadır.

4. Radyasyona Duyarlı miRNA'ların Klinik Sonuçları

4.1. Radyoterapi Sonuçlarının Biyobelirteçleri Olarak miRNA'lar

Radyasyona duyarlı miRNA'ların tümü, radyoterapiden elde edilen sonuçları tahmin etmek için biyobelirteç olarak hizmet etme potansiyeline sahip olduğundan ve To ve ark. Bazı miRNA dağılımlarının, üçlü negatif meme kanserinde öngörücü biyobelirteçler olarak işlev görebileceğini veya radyosensitiviteyi modüle edebileceğini öne süren çalışmalar, radyoterapi için aday olabilecek hastaların seçimi ve farklı ifade profillerine dayalı kişiselleştirilmiş tedavi stratejilerinin geliştirilmesi için yeni fırsatlar sunmaktadır.

miRNA taklitleri ve inhibitörlerinin kullanımı da dahil olmak üzere miRNA'ların etkilerini artırmaya yönelik terapötik yaklaşımlar, radyosensitivite stratejisi olarak araştırılmaktadır. Radyorezistansla ilgili spesifik yolları hedefleyerek, miRNA tabanlı tedaviler radyoterapinin etkinliğini artırabilir ve lokal nüks riskini azaltabilir (Moqadami vd., 2024).

5. Mevcut Zorluklar ve Sınırlamalar

Umut verici bulgulara rağmen, miRNA tabanlı tedavilerin klinik uygulamasına engel olan çeşitli sınırlamalar mevcuttur. Bu zorluklar arasında tümör heterojenliği, hedef dışı etkiler, terapötik moleküllerin kararsızlığı ve hedefli dağıtım sistemlerindeki zorluklar yer almaktadır (Mageau vd., 2025). Bu nedenle, rutin klinik uygulamaya geçilmeden önce daha fazla klinik çalışmaya ihtiyaç duyulmaktadır.

6. Gelecek Perspektifleri

Radyoterapi kaynaklı miRNA ekspresyon değişiklikleri üzerine yapılacak gelecekteki araştırmaların, hassas onkolojiye önemli ölçüde katkıda bulunması beklenmektedir. Çoklu omik teknolojileri, biyoinformatik ve yapay zekadaki gelişmeler, yeni radyo-miRNA'ların ve terapötik hedeflerin belirlenmesini kolaylaştırabilir. Ayrıca, radyoterapiyi miRNA tabanlı müdahalelerle birleştirmek, tedavi sonuçlarını iyileştirebilir ve meme kanseri hastalarında radyorezistansı aşabilir. Son çalışmalar ayrıca, miRNA'ların immün aracılı radyasyon yanıtlarında ve abskopal etkide önemli roller oynayabileceğini ve radyoterapiyi immünoterapi yaklaşımlarıyla entegre etme konusunda yeni olanaklar açabileceğini öne sürmektedir (Hosseinpour-Soleimani vd., 2025). Sonuç olarak, radyasyona duyarlı miRNA'lar üzerine devam eden araştırmalar, daha kişiselleştirilmiş ve etkili meme kanseri tedavilerinin geliştirilmesine yol açabilir.

KAYNAKÇA

Anne, Yan, Yu, Lei, Yan, Wenxing, Qiu, Ling, Zhang, Jianqiu, Jia, Xiaojing, lncRNA GAS5, DNA Onarımını Engelleyerek Meme Kanseri Hücrelerini İyonlaştırıcı Radyasyona Duyarlı Hale Getirir, BioMed Research International, 2022, 1987519, 7 sayfa, 2022. https://doi.org/10.1155/2022/1987519

Abdollahi, E., Mozdarani, H., & Alizadeh, B. (2023). Role of circ-FOXO3 and miR-23a in radiosensitivity of breast cancer. Breast Cancer, 30, 714-726. https://doi.org/10.1007/s12282-023-01463-4

Ali, T., Degorre, C., & Tofilon, P. (2025). Radiation Modifies Let-7 miRNA Binding to AGO2 Independent of Changes in Transcription to Influence Tumor Cell Radiosensitivity. International Journal of Molecular Sciences, 26. https://doi.org/10.3390/ijms26178483

Alonso-González, C., González-Abalde, C., Menéndez-Menéndez, J., González-González, A., Álvarez-García, V., González-Cabeza, A., Martínez-Campa, C., & Cos, S. (2022). Melatonin Modulation of Radiation-Induced Molecular Changes in MCF-7 Human Breast Cancer Cells. Biomedicines, 10. https://doi.org/10.3390/biomedicines10051088

Bakhshaiesh, T., & Esmaeili, R. (2022). Effects of noncoding RNAs in radiotherapy response in breast cancer: a systematic review. Cell Cycle, 21, 883 - 893. https://doi.org/10.1080/15384101.2022.2035915

Baruah, M. M., & Sharma, N. (2017). MicroRNAs in determining the subtype specific treatment regimens for breast cancer. https://doi.org/10.5958/0976-5506.2017.00401.6

Chen, G., Zhu, W., Shi, D., Lv, L., Zhang, C., Liu, P., & Hu, W. (2010). MicroRNA-181a sensitizes human malignant glioma U87MG cells to radiation by targeting Bcl-2.. Oncology reports, 23 4, 997-1003. https://doi.org/10.3892/or_00000725

Chong, Z., Yeap, S., & Ho, W. (2020). Role of miRNAs in regulating responses to radiotherapy in human breast cancer. International Journal of Radiation Biology, 97, 289 - 301. https://doi.org/10.1080/09553002.2021.1864048

Esplugas, R., Arenas, M., Serra, N., Bellés, M., Bonet, M., Gascón, M., Vallvé, J., & Linares, V. (2019). Effect of radiotherapy on the expression of cardiovascular disease-related miRNA-146a, -155, -221 and -222 in blood of women with breast cancer. PLoS ONE, 14. https://doi.org/10.1371/journal.pone.0217443

Girgin, M., Akat, A., Akgül, B., Nalbant, N., Karaçetin, D., Abamor, E., Uğurel, O., & Turgut-Balik, D. (2024). An in vitro assessment of ionizing radiation impact on the efficacy of radiotherapy for breast cancer. Turkish Journal of Biochemistry, 49, 792 - 800. https://doi.org/10.1515/tjb-2024-0172

Griñán-Lisón, C., Olivares-Urbano, M., Jiménez, G., López-Ruiz, E., Del Val, C., Morata-Tarifa, C., Entrena, J., González-Ramírez, A., Boulaiz, H., Herrera, Z., Núñez, M., & Marchal, J. (2020). miRNAs as radio-response biomarkers for breast cancer stem cells. Molecular Oncology, 14, 556 - 570. https://doi.org/10.1002/1878-0261.12635

Hosseinpour-Soleimani, F., Tajbakhsh, A., Salmasi, Z., Pirsalehi, M., & Irajie, C. (2025). MicroRNAs in the abscopal effect: bridging radiotherapy and systemic anti-tumor immunity for enhanced cancer therapy. Clinical & Experimental Metastasis, 42. https://doi.org/10.1007/s10585-025-10364-z

Jiang, T., Chen, J., Wang, Z., Wang, X., , J., Zhao, F., Huang, C., & Chen, Y. (2023). miR-4796 enhances the sensitivity of breast cancer cells to ionising radiation by impairing the DNA repair pathway. Breast Cancer, 30, 691 - 702. https://doi.org/10.1007/s12282-023-01482-1

Kouhestani, S., Khalili, S., Razi, A., Aghili, M., & Moghadam, M. (2025). Ectopic expression of miR-34a/-328 sensitizes breast cancer stem cells to gamma rays/doxorubicin by BCL2/ABCG2 targeting. Molecular Biology Reports, 52. https://doi.org/10.1007/s11033-025-10581-5

Labbé, M., Chang, M., Saintpierre, B., Letourneur, F., De Beaurepaire, L., Veziers, J., Deshayes, S., Cotinat, M., Fonteneau, J., Blanquart, C., Potiron, V., Supiot, S., & Fradin, D. (2024). Loss of miR-200c-3p promotes resistance to radiation therapy via the DNA repair pathway in prostate cancer. Cell Death & Disease, 15. https://doi.org/10.1038/s41419-024-07133-3

Lai, Y., Chen, Y., Lin, Y., & Ye, L. (2018). Down-regulation of LncRNA CCAT1 enhances radiosensitivity via regulating miR-148b in breast cancer. Cell Biology International, 42. https://doi.org/10.1002/cbin.10890

Lai, Y., Wang, C., Hsu, K., Yu, C., Lin, Y., Shen, P., Tsai, M., Chen, F., & Cheng, W. (2025). Integrative multi-omics and preclinical analyses identify miR-4776-5p as a prognostic radiosensitizer for patients undergoing radiotherapy for head-and-neck cancer. Discover Oncology, 16. https://doi.org/10.1007/s12672-025-03784-6

Leung, C., Chen, T., Li, S., Ho, M., Hu, L., Liu, W., Wu, T., Hsu, P., Chang, H., & Tsai, K. (2014). MicroRNA expression profiles in human breast cancer cells after multifraction and single-dose radiation treatment.. Oncology reports, 31 5, 2147-56. https://doi.org/10.3892/or.2014.3089

Leung, C., Li, S., Chen, T., Ho, M., Hu, L., Liu, W., Wu, T., Hsu, P., Chang, H., & Tsai, K. (2014). Comprehensive microRNA profiling of prostate cancer cells after ionizing radiation treatment. Oncology Reports, 31, 1067 - 1078. https://doi.org/10.3892/or.2014.2988

Mageau, E., Derbowka, R., Dickinson, N., Lefort, N., Kovala, A., Boreham, D., Tai, T., Thome, C., & Tharmalingam, S. (2025). Molecular Mechanisms of Radiation Resistance in Breast Cancer: A Systematic Review of Radiosensitization Strategies. Current Issues in Molecular Biology, 47. https://doi.org/10.3390/cimb47080589

Marvaso, G., Barone, A., & Amodio, N. (2015). Emerging role of microRNAs in breast cancer radiotherapy. RNA & DISEASE, 2. https://doi.org/10.14800/rd.786

Masoudi-Khoram, N., Abdolmaleki, P., Hosseinkhan, N., Nikoofar, A., Mowla, S., Monfared, H., & Baldassarre, G. (2020). Differential miRNAs expression pattern of irradiated breast cancer cell lines is correlated with radiation sensitivity. Scientific Reports, 10. https://doi.org/10.1038/s41598-020-65680-z

Masoudi-Khoram, N., Abdolmaleki, P., Hosseinkhan, N., Nikoofar, A., Mowla, S., Monfared, H., & Baldassarre, G. (2020). Differential miRNAs expression pattern of irradiated breast cancer cell lines is correlated with radiation sensitivity. Scientific Reports, 10. https://doi.org/10.1038/s41598-020-65680-z

Masoudi-Khoram, N., & Abdolmaleki, P. (2022). Role of non-coding RNAs in response of breast cancer to radiation therapy. Molecular Biology Reports, 49, 5199 - 5208. https://doi.org/10.1007/s11033-022-07234-2

Metheetrairut, C., & Slack, F. (2013). MicroRNAs in the ionizing radiation response and in radiotherapy.. Current opinion in genetics & development, 23 1, 12-9. https://doi.org/10.1016/j.gde.2013.01.002

Moqadami, A., Ghafari, S., & Khalaj-Kondori, M. (2024). Non-coding RNAs modulation in breast cancer radioresponse: mechanisms and therapeutic implications. Strahlentherapie und Onkologie, 201, 669 - 678. https://doi.org/10.1007/s00066-024-02317-4

Nejadtaghi, M., & Mozdarani, H. (2024). Significant Impact of let-7d MicroRNA on Breast Cancer Cell Lines Post-Radiation Treatment. International Journal of Medical Laboratory. https://doi.org/10.18502/ijml.v11i1.16544

Ni, J., Bucci, J., Chang, L., Malouf, D., Graham, P., & Li, Y. (2017). Targeting MicroRNAs in Prostate Cancer Radiotherapy. Theranostics, 7, 3243 - 3259. https://doi.org/10.7150/thno.19934

Öğüt, S. (2023). Meme kanserinde radyoterapi sonrası selenoprotein ve gen polimorfizmlerinin incelenmesi (Doktora tezi, İstanbul Gelişim Üniversitesi, Lisansüstü Eğitim Enstitüsü). YÖK Ulusal Tez Merkezi.

Pajic, M., Froio, D., Daly, S., Doculara, L., Millar, E., Graham, P., Drury, A., Steinmann, A., De Bock, C., Boulghourjian, A., Zaratzian, A., Carroll, S., Toohey, J., O'toole, S., Harris, A., Buffa, F., Gee, H., Hollway, G., & Molloy, T. (2018). miR-139-5p Modulates Radiotherapy Resistance in Breast Cancer by

Repressing Multiple Gene Networks of DNA Repair and ROS Defense.. Cancer research, 78 2, 501-515. https://doi.org/10.1158/0008-5472.can-16-3105

Pan, D., Du, Y., Li, R., Shen, A., Liu, X., Li, C., & Hu, B. (2021). miR-29b-3p Increases Radiosensitivity in Stemness Cancer Cells via Modulating Oncogenes Axis. Frontiers in Cell and Developmental Biology, 9. https://doi.org/10.3389/fcell.2021.741074

Pedroza-Torres, A., Romero-Córdoba, S., Montaño, S., Peralta-Zaragoza, O., Vélez-Uriza, D., Arriaga-Canon, C., Guajardo-Barreto, X., Bautista-Sánchez, D., Sosa-León, R., Hernández-González, O., Díaz-Chávez, J., Álvarez-Gómez, R., & Herrera, L. (2024). Radio-miRs: a comprehensive view of radioresistance-related microRNAs. Genetics, 227. https://doi.org/10.1093/genetics/iyae097

Perez-Añorve, I., La Rosa, C., Soto-Reyes, E., Beltrán-Anaya, F., Del Moral-Hernández, O., Salgado-Albarrán, M., Ángeles-Zaragoza, Ó., González-Barrios, J., Landero-Huerta, D., Chávez-Saldaña, M., García-Carrancá, A., Villegas-Sepúlveda, N., & Aréchaga-Ocampo, E. (2019). New insights into radioresistance in breast cancer identify a dual function of miR-122 as a tumor suppressor and oncomiR. Molecular Oncology, 13, 1249 - 1267. https://doi.org/10.1002/1878-0261.12483

Podralska, M., Ciesielska, S., Kluiver, J., Van Den Berg, A., Dzikiewicz-Krawczyk, A., & Ślęzak-Prochazka, I. (2020). Non-Coding RNAs in Cancer Radiosensitivity: MicroRNAs and lncRNAs as Regulators of Radiation-Induced Signaling Pathways. Cancers, 12. https://doi.org/10.3390/cancers12061662

Seiri, P., Mehrafshar, P., Nourbakhsh, M., Hesari, Z., Abdolvahabi, Z., Soukhtanloo, M., Golpour, P., Yousefi, Z., Yarahmadi, S., Mobaser, S., Abolmaali, M., Abbasian, Z., Zarrinnahad, H., Hosseinkhan, N., & Mahdavi, S. (2025). Upregulation of miR-206 attenuates breast cancer cell survival and increases their radiosensitivity. International Journal of Radiation Biology, 101, 1105 - 1116. https://doi.org/10.1080/09553002.2025.2540359

Shi, Y., Jiang, P., Li, J., Xu, S., & Liu, B. (2021). The roles of microRNA-328-3p on proliferation and radiotherapy in breast cancer. https://doi.org/10.21203/rs.3.rs-742188/v1

To, N., Nguyen, H., Thiolat, A., Liu, B., Cohen, J., Radosevic-Robin, N., & Belkacemi, Y. (2022). Radiation therapy for triple-negative breast cancer: emerging role of microRNAs as biomarkers and radiosensitivity modifiers. A systematic review. Breast Cancer Research and Treatment, 193, 265 - 279. https://doi.org/10.1007/s10549-022-06533-3

Wang, B., Zheng, J., Li, R., Tian, Y., Lin, J., Liang, Y., Sun, Q., Xu, A., Zheng, R., Liu, M., Ji, A., Bu, J., & Yuan, Y. (2019). Long noncoding RNA LINC02582 acts downstream of miR-200c to promote radioresistance through CHK1 in breast cancer cells. Cell Death & Disease, 10. https://doi.org/10.1038/s41419-019-1996-0

Wang, F., Mao, A., Tang, J., Zhang, Q., Yan, J., Wang, Y., Di, C., Gan, L., Sun, C., & Zhang, H. (2018). microRNA-16-5p enhances radiosensitivity through modulating Cyclin D1/E1–pRb–E2F1 pathway in prostate cancer cells. Journal of Cellular Physiology, 234, 13182 - 13190. https://doi.org/10.1002/jcp.27989

Wolfe, A., Bambhroliya, A., Reddy, J., Debeb, B., Huo, L., Larson, R., Li, L., Ueno, N., & Woodward, W. (2016). MiR-33a Decreases High-Density Lipoprotein-Induced Radiation Sensitivity in Breast Cancer.. International journal of radiation oncology, biology, physics, 95 2, 791-9. https://doi.org/10.1016/j.ijrobp.2016.01.025

Wu, R., Zhang, H., Huang, X., & Liang, Z. (2024). MiR-450b-5p enhances the radiosensitivity of HR+ and HER2− breast cancer by targeting CDK6. Oncology and Translational Medicine. https://doi.org/10.1097/ot9.0000000000000045

Yu, L., Yang, Y., Hou, J., Zhai, C., Song, Y., Zhang, Z., Qiu, L., & Jia, X. (2015). MicroRNA-144 affects radiotherapy sensitivity by promoting proliferation, migration and invasion of breast cancer cells.. Oncology reports, 34 4, 1845-52. https://doi.org/10.3892/or.2015.4173

MID-TERM ANCHORING ZONE–RELATED COMPLICATIONS AFTER THORACIC ENDOVASCULAR AORTIC REPAIR: A REPORT OF TWO CASES

İbrahim Yel

Department of Cardiovascular Surgery, Faculty of Medicine, Recep Tayyip Erdoğan University, Rize, Türkiye

Sedat Ozan Karakişi

Department of Cardiovascular Surgery, Faculty of Medicine, Recep Tayyip Erdoğan University, Rize, Türkiye

Doğuş Hemşinli

Department of Cardiovascular Surgery, Faculty of Medicine, Recep Tayyip Erdoğan University, Rize, Türkiye

ABSTRACT

Objective

Thoracic endovascular aortic repair (TEVAR) is a widely accepted minimally invasive treatment for thoracic aortic pathologies. Anchoring zone–related complications, however, may arise beyond the early postoperative period. This study presents two cases of rare mid-term anchoring zone complications occurring at approximately six months after TEVAR, highlighting the importance of routine imaging surveillance.

Material and Methods

Two patients who developed anchoring zone–related complications during mid-term follow-up after TEVAR were retrospectively evaluated. Clinical presentation, computed tomographic angiography (CTA) findings, and treatment strategies were analyzed.

Results

In the first case, a patient with non-A non-B aortic dissection previously treated with thoracic debranching and Zone 0 TEVAR was found to have a proximal anchoring zone pseudoaneurysm on routine six-month CTA. Open surgical repair with ascending aorta and total arch replacement was performed uneventfully. In the second case, a patient who underwent TEVAR for type III aortic dissection with intentional left subclavian artery coverage presented with acute dyspnea at six months. CTA revealed a large intrathoracic hematoma with active bleeding proximal to the left subclavian artery. A hybrid approach combining thoracic debranching and proximal Zone 0 TEVAR extension was successfully performed.

Conclusion

Mid-term anchoring zone complications after TEVAR, though rare, can be life-threatening. Clinical presentations range from asymptomatic pseudoaneurysm to acute intrathoracic hemorrhage. Symptom-based follow-up alone is insufficient; routine CTA — particularly at six months — is essential for early detection. Management should be individualized through collaboration between cardiovascular surgeons and interventional radiologists.

Keywords: TEVAR, anchoring zone, pseudoaneurysm, intrathoracic bleeding, thoracic aortic dissection, endovascular repair, mid-term complications

INTRODUCTION

Thoracic endovascular aortic repair (TEVAR) has emerged as the preferred treatment modality for a broad spectrum of thoracic aortic pathologies, including descending thoracic aortic aneurysms, type B aortic dissections, penetrating aortic ulcers, and intramural hematomas.[1,2] The technique offers significant advantages over open surgery, including reduced perioperative morbidity and mortality, shorter hospital stays, and earlier functional recovery — particularly in patients with significant comorbidities.[3]

Despite these favorable outcomes, TEVAR is not without complications. Anchoring zone–related complications represent a well-recognized category of endovascular failure and include endoleak types I and II, stent-graft migration, retrograde dissection, and, less commonly, pseudoaneurysm formation or delayed hemorrhage at the proximal or distal landing zones.[4,5] The majority of these complications manifest within the early postoperative period; however, mid-term complications — typically defined as those arising between three and twelve months following the index procedure — have been increasingly recognized in the literature as surveillance programs have become more systematic.[6]

The proximal anchoring zone is subjected to considerable mechanical forces, including pulsatile pressure, cyclical wall stress, and longitudinal shear forces generated by the flow of blood. Over time, these hemodynamic forces, combined with structural changes at the interface between the stent-graft and the native aortic wall — such as progressive aortic dilatation, wall thinning, or thrombus remodeling — may predispose to late-onset complications.[7,8] In patients who undergo Zone 0 TEVAR with debranching procedures, the anatomy is particularly complex, and the mechanical environment at the proximal seal zone is further altered by the absence of supra-aortic branching vessel outflow.

The present report describes two cases of rare mid-term anchoring zone complications encountered at approximately six months following TEVAR. The first case involves an asymptomatic proximal pseudoaneurysm detected on routine surveillance imaging in a patient with non-A non-B aortic dissection previously managed with thoracic debranching and Zone 0 TEVAR. The second case involves an acute life-threatening intrathoracic hemorrhage in a patient who underwent TEVAR for type III aortic dissection with intentional left subclavian artery coverage. These cases collectively underscore the heterogeneous clinical spectrum of mid-term anchoring zone complications and the critical role of structured postoperative imaging surveillance.

DEVELOPMENT

Case 1: Proximal Pseudoaneurysm Following Zone 0 TEVAR for Non-A Non-B Dissection

The first patient was a male individual with a history of non-A non-B aortic dissection — a variant characterized by dissection originating at the level of the aortic arch without involvement of the ascending aorta or descending thoracic aorta in the classical Stanford classification sense. The patient had previously undergone thoracic debranching with reconstruction of the supra-aortic vessels, followed by Zone 0 TEVAR to achieve proximal seal at the level of the ascending aorta. The index procedure was technically successful, and the patient was discharged in stable condition following an uneventful recovery.

At the six-month follow-up visit, the patient reported vague, intermittent chest discomfort without accompanying hemodynamic instability, dyspnea, or neurological symptoms. Physical examination and vital signs were within normal limits. Routine surveillance computed tomographic angiography (CTA) — performed as per institutional protocol — revealed a pseudoaneurysm at the proximal anchoring zone of the stent-graft, located at the interface between the graft and the native ascending aortic wall. The pseudoaneurysm showed no evidence of rapid expansion or active extravasation on the initial imaging study; however, given the anatomical location and the potential for catastrophic rupture, a decision was made to proceed with surgical intervention.

Following multidisciplinary discussion involving cardiovascular surgery and interventional radiology, open surgical repair was selected as the definitive treatment strategy. The patient was brought to the operating room under general anesthesia. Median sternotomy was performed, and cardiopulmonary bypass was established. The pseudoaneurysm was resected and the proximal aorta was reconstructed with ascending aorta and total arch replacement using a branched Dacron graft, incorporating all previously debranched supra-aortic vessels. The postoperative course was uneventful. The patient was discharged on postoperative day 12 in stable condition with no neurological deficits.

Case 2: Acute Intrathoracic Hemorrhage Following TEVAR for Type III Aortic Dissection

The second patient was a female individual who had previously undergone TEVAR for type III (Stanford type B) aortic dissection. During the index procedure, intentional coverage of the left subclavian artery was performed to achieve an adequate proximal landing zone without a debranching procedure, as the patient's anatomical configuration precluded standard landing zone positioning. The left subclavian

artery was covered without revascularization, as the patient demonstrated adequate collateral circulation through the vertebral and internal mammary arteries on preoperative imaging. The index procedure was technically successful, and the patient was discharged in stable condition.

At six months post-procedure, the patient presented to the emergency department with sudden-onset acute dyspnea without a history of trauma, infection, or preceding chest pain. On examination, she was tachycardic (heart rate 108 bpm) with decreased breath sounds on the left side. Blood pressure was 95/60 mmHg, consistent with early hemodynamic compromise. Urgent CTA was performed and demonstrated a large left hemithoracic hematoma with active bleeding originating proximal to the left subclavian artery, at the site of intentional vessel coverage. There was no evidence of aortic rupture into the pleural space; however, the ongoing hemorrhage represented an immediate threat to life.

Given the acute presentation and hemodynamic instability, an emergency hybrid intervention was planned. The procedure involved thoracic debranching with reconstruction of the left subclavian artery via a left carotid-to-subclavian bypass, followed by proximal extension of the existing TEVAR device into Zone 0 to achieve definitive hemostatic seal at the site of bleeding. The hybrid approach allowed control of the hemorrhage without the need for full cardiopulmonary bypass. Intraoperative findings confirmed active bleeding from a small aortic wall defect at the proximal end of the original stent-graft, consistent with late proximal type I endoleak with contained rupture. Following the procedure, the patient was transferred to the intensive care unit and monitored closely. She achieved hemodynamic stability within 12 hours. The postoperative course was uncomplicated, and she was discharged in stable condition on postoperative day 9.

Comparative Analysis

Both cases share a common anatomical origin — the proximal anchoring zone — and a similar temporal pattern, with complications presenting at approximately six months following the index TEVAR procedure. However, the clinical presentations were strikingly different: the first case was entirely asymptomatic and identified only through surveillance imaging, while the second represented an acute, life-threatening emergency. This contrast reflects the broad and unpredictable clinical spectrum of mid-term anchoring zone complications and highlights the limitations of symptom-based follow-up strategies.

The underlying mechanisms likely differ between the two cases. In the first patient, the pseudoaneurysm may have developed as a result of progressive stress concentration at the proximal seal zone following total arch replacement and debranching, where altered hemodynamics and the mechanical interface between the synthetic graft and the native aortic tissue may predispose to focal wall breakdown over time. In the second patient, intentional left subclavian artery coverage without revascularization may have created a region of altered flow dynamics proximal to the stent-graft, contributing to progressive weakening of the aortic wall at the coverage site and eventual late hemorrhage.

Management strategies were appropriately individualized in both cases: open surgical reconstruction was chosen for the first patient given the presence of a proximal pseudoaneurysm amenable to direct repair and the existing infrastructure of a previous debranching procedure, while a hybrid endovascular-surgical approach was employed in the second patient given the acute hemorrhagic presentation and the need for rapid hemostatic control without the morbidity of full sternotomy and cardiopulmonary bypass.

CONCLUSION

This report presents two cases of rare but clinically significant mid-term anchoring zone complications following TEVAR, occurring at approximately six months after the index procedure. The cases illustrate the heterogeneous spectrum of such complications — ranging from an entirely asymptomatic pseudoaneurysm detected on routine surveillance to an acute, life-threatening intrathoracic hemorrhage — and emphasize that clinical symptoms alone are an unreliable indicator of post-TEVAR aortic integrity.

These findings have important implications for postoperative surveillance practice. Current guidelines recommend CTA surveillance at one month, six months, and annually thereafter following TEVAR.[7] The temporal coincidence of both complications at the six-month interval in our cases reinforces the critical importance of this specific surveillance time point. Routine imaging at six months may be the

only opportunity to detect asymptomatic complications before they progress to life-threatening events, as exemplified by Case 1.

From a technical standpoint, both cases highlight the anatomical and hemodynamic vulnerability of the proximal anchoring zone, particularly in the context of Zone 0 TEVAR and intentional branch vessel coverage. Surgeons planning such procedures should be aware of the potential for late mechanical failure at these sites and should counsel patients accordingly regarding the necessity of lifelong imaging follow-up.

The management strategies employed in these cases — open surgical reconstruction and hybrid endovascular-surgical repair, respectively — demonstrate that successful treatment is achievable even in the context of complex re-intervention scenarios. However, the optimal approach must be individualized based on the patient's hemodynamic status, anatomical configuration, comorbidity profile, and institutional expertise. A multidisciplinary team approach, integrating cardiovascular surgery and interventional radiology, is essential for optimal decision-making and outcomes.

In conclusion, mid-term anchoring zone complications after TEVAR, though uncommon, represent a clinically important entity with significant mortality potential if undetected. Structured, protocol-driven imaging surveillance — with particular emphasis on the six-month postoperative assessment — is essential for early identification and timely intervention. Further multicenter studies and registry data are needed to better characterize the incidence, risk factors, and optimal management strategies for this evolving complication category.

REFERENCES

1. Dake MD, Miller DC, Semba CP, Mitchell RS, Walker PJ, Liddell RP. Transluminal placement of endovascular stent-grafts for the treatment of descending thoracic aortic aneurysms. N Engl J Med. 1994;331(26):1729-1734.

2. Matsumura JS, Cambria RP, Dake MD, et al. International controlled clinical trial of thoracic endovascular aneurysm repair with the Zenith TX2 endovascular graft: 1-year results. J Vasc Surg. 2008;47(2):247-257.

3. Fairman RM, Criado F, Farber M, et al. Pivotal results of the Medtronic Vascular Talent Thoracic Stent Graft System: the VALOR trial. J Vasc Surg. 2008;48(3):546-554.

4. Bavaria JE, Appoo JJ, Makaroun MS, et al. Endovascular stent grafting versus open surgical repair of descending thoracic aortic aneurysms in low-risk patients: a multicenter comparative trial. J Thorac Cardiovasc Surg. 2007;133(2):369-377.

5. Eggebrecht H, Nienaber CA, Neuhäuser M, et al. Endovascular stent-graft placement in aortic dissection: a meta-analysis. Eur Heart J. 2006;27(4):489-498.

6. Fattori R, Nienaber CA, Rousseau H, et al. Results of endovascular repair of the thoracic aorta with the Talent Thoracic stent graft: the Talent Thoracic Retrospective Registry. J Thorac Cardiovasc Surg. 2006;132(2):332-339.

7. Chaikof EL, Blankensteijn JD, Harris PL, et al. Reporting standards for endovascular aortic aneurysm repair. J Vasc Surg. 2002;35(5):1048-1060.

8. Leurs LJ, Bell R, Degrieck Y, Thomas S, Hobo R, Lundbom J. Endovascular treatment of thoracic aortic diseases: combined experience from the EUROSTAR and United Kingdom Thoracic Endograft registries. J Vasc Surg. 2004;40(4):670-679.

9. Nienaber CA, Rousseau H, Eggebrecht H, et al. Randomized comparison of strategies for type B aortic dissection: the INvestigation of STEnt Grafts in Aortic Dissection (INSTEAD) trial. Circulation. 2009;120(25):2519-2528.

10. Kpodonu J, Ramaiah VG, Diethrich EB. Intravascular ultrasound imaging as applied to the aorta: a new tool for the cardiovascular surgeon. Ann Thorac Surg. 2008;86(4):1391-1398.

EMERGENCY SURGICAL REPAIR OF A LARGE APICAL MUSCULAR VENTRICULAR SEPTAL DEFECT IN AN ELDERLY PATIENT WITH REDUCED EJECTION FRACTION: A CASE REPORT

Sedat Ozan Karakişi

Department of Cardiovascular Surgery, Faculty of Medicine, Recep Tayyip Erdoğan University, Rize, Türkiye

Doğuş Hemşinli

Department of Cardiovascular Surgery, Faculty of Medicine, Recep Tayyip Erdoğan University, Rize, Türkiye

İbrahim Yel

Department of Cardiovascular Surgery, Faculty of Medicine, Recep Tayyip Erdoğan University, Rize, Türkiye

ABSTRACT

Objective

Ventricular septal defect (VSD) in elderly patients with impaired left ventricular function presents a significant surgical challenge. Apical muscular VSDs are particularly demanding due to their location and limited surgical accessibility. This case report aims to present the emergency surgical management of a large apical muscular VSD in a 78-year-old woman with severely reduced ejection fraction and to discuss the role of perioperative intra-aortic balloon pump (IABP) support.

Material and Methods

A 78-year-old female patient with hypertension presented with palpitations and dyspnea. Echocardiography revealed a 2×1 cm² apical muscular VSD with a left ventricular ejection fraction (LVEF) of 30–35%, reduced from a previously documented 38%. Coronary angiography was normal, and no significant valvular pathology was identified. Given the large defect size and hemodynamic compromise, IABP support was initiated preoperatively. Surgical access was achieved via right ventriculotomy, and the defect was closed with an autologous pericardial patch under cardiopulmonary bypass.

Results

Postoperatively, IABP support was continued for 3 days. The patient was monitored in the intensive care unit for 6 days, followed by 10 days of ward follow-up, and was discharged in stable condition. No residual shunt or significant complications were observed during the postoperative period.

Conclusion

Emergency repair of a large apical muscular VSD via right ventriculotomy with pericardial patch closure is a feasible and effective approach even in elderly patients with severely reduced ejection fraction. Perioperative IABP support plays a critical role in hemodynamic stabilization. This case highlights the importance of individualized surgical planning in high-risk VSD repair.

Keywords: ventricular septal defect, right ventriculotomy, pericardial patch, IABP, elderly, reduced ejection fraction, emergency cardiac surgery

INTRODUCTION

Ventricular septal defects (VSDs) represent one of the most common congenital heart anomalies encountered in clinical practice. While the majority are diagnosed and managed in childhood, a subset of patients may remain undetected until adulthood or present de novo in older age groups.[1] In elderly patients, particularly those with concomitant systolic dysfunction and significantly reduced left ventricular ejection fraction (LVEF), the management of VSDs poses substantial clinical and surgical challenges.

Apical muscular VSDs represent a particularly complex subtype due to their anatomical location at the apex of the interventricular septum, which renders them less accessible through standard surgical approaches. The surrounding trabeculated myocardium further complicates both visualization and secure patch fixation.[2,3] These defects account for a smaller proportion of all VSDs but carry disproportionate surgical morbidity when occurring in high-risk populations.

The intra-aortic balloon pump (IABP) is a well-established mechanical circulatory support device used in patients with severe cardiac dysfunction. By augmenting diastolic coronary perfusion and reducing afterload, IABP support can stabilize hemodynamics in the perioperative period, thereby improving the safety profile of cardiac surgical interventions in high-risk patients.[4,5]

The present case report describes the emergency surgical management of a large apical muscular VSD in a 78-year-old woman with an LVEF of 30–35%. The report outlines the preoperative decision-making process, the chosen surgical technique, perioperative IABP utilization, and the postoperative course. Through this case, we aim to contribute to the limited literature on surgical VSD repair in elderly patients with severely impaired ventricular function and to advocate for individualized, multidisciplinary approaches in this challenging clinical scenario.

DEVELOPMENT

Patient Presentation

A 78-year-old female patient with a known history of hypertension presented to the emergency department with progressive exertional dyspnea and palpitations of several weeks' duration. On physical examination, she appeared in mild respiratory distress. Auscultation revealed a harsh holosystolic murmur best heard at the left lower sternal border, consistent with an interventricular shunt. Blood pressure was 110/70 mmHg, heart rate 95 bpm, and peripheral oxygen saturation 94% on room air.

Transthoracic echocardiography was performed urgently and demonstrated a 2×1 cm^2 apical muscular VSD with left-to-right shunting. The LVEF was measured at 30–35%, representing a decline from a previously documented value of 38% obtained during a cardiology follow-up visit approximately one year prior. No significant valvular pathology was identified on echocardiographic assessment. Subsequent coronary angiography revealed normal coronary anatomy, excluding ischemic etiology as the primary driver of ventricular dysfunction.

Preoperative Risk Assessment and Decision-Making

Given the patient's advanced age, significantly reduced LVEF, large defect size, and presenting hemodynamic compromise, she was classified as a high-risk surgical candidate. The European System for Cardiac Operative Risk Evaluation (EuroSCORE II) was calculated and confirmed elevated perioperative mortality risk. A multidisciplinary cardiac team discussion was convened, weighing the risks of surgical intervention against the natural history of a large unrepaired VSD with ongoing hemodynamic burden.

Transcatheter closure was considered but deemed technically unfeasible given the apical muscular location of the defect and concerns regarding device stability in a heavily trabeculated region. Surgical repair was therefore chosen as the definitive treatment modality. In view of the anticipated hemodynamic instability, preoperative IABP support was initiated via percutaneous femoral arterial access prior to transfer to the operating theatre. The device was set at 1:1 augmentation to optimize coronary perfusion pressure and reduce left ventricular afterload.

Surgical Technique

The patient was brought to the operating room under continuous hemodynamic monitoring. General anesthesia was induced and maintained using standard cardiac anesthetic protocols. A median sternotomy was performed, and the pericardium was harvested and stored in glutaraldehyde solution for subsequent use as patch material.

Cardiopulmonary bypass was established via aortic and bicaval cannulation. Myocardial protection was achieved using antegrade cold blood cardioplegia administered through the aortic root following aortic cross-clamping. The heart was cooled to 28°C for additional systemic protection.

Surgical access to the apical muscular VSD was achieved through a limited right ventriculotomy performed at the right ventricular apex. The ventriculotomy was carefully oriented to minimize myocardial trauma while providing adequate exposure of the defect margins. Direct visualization confirmed the 2×1 cm² muscular defect with relatively discrete borders. The surrounding trabeculated myocardium was gently retracted to expose the full circumference of the defect.

The autologous pericardial patch, fashioned to exceed the defect dimensions by approximately 3–4 mm on each margin, was anchored to the defect borders using interrupted pledgeted 4-0 polypropylene sutures. Care was taken to ensure complete coaptation of the patch to the septal surface, with particular attention to the trabeculated regions where suture purchase can be unreliable. The right ventriculotomy was subsequently closed in two layers using running 3-0 polypropylene sutures reinforced with felt strips.

Intraoperative transesophageal echocardiography (TEE) was performed following weaning from cardiopulmonary bypass and confirmed complete closure of the VSD with no residual shunting. Ventricular function appeared globally impaired but consistent with the preoperative baseline. The patient was successfully weaned from cardiopulmonary bypass with moderate inotropic support. Total bypass time was 94 minutes and aortic cross-clamp time was 68 minutes.

Postoperative Course

The patient was transferred to the cardiac intensive care unit (ICU) in a hemodynamically stable condition. IABP support was continued postoperatively at 1:1 augmentation and was gradually weaned over 72 hours in accordance with hemodynamic parameters. Inotropic support with dobutamine was administered during the immediate postoperative period and subsequently tapered as cardiac function stabilized.

Serial echocardiographic assessments performed on postoperative days 1, 3, and 6 confirmed the absence of residual shunting across the interventricular septum. LVEF remained in the 30–35% range, consistent with the preoperative baseline. No significant pericardial effusion, pleural complication, or wound infection was identified during the ICU stay.

The patient remained in the ICU for a total of 6 days before being transferred to the cardiac surgery ward. Following 10 days of ward-based recovery, rehabilitation, and optimization of medical therapy — including guideline-directed heart failure management with angiotensin-converting enzyme inhibition, beta-blockade, and diuresis — she was discharged home in stable condition. At the time of discharge, she reported significant improvement in exertional dyspnea compared to her presenting symptoms.

CONCLUSION

This case demonstrates that emergency surgical repair of a large apical muscular VSD via right ventriculotomy with autologous pericardial patch closure is a technically feasible and clinically effective approach, even in elderly patients presenting with severely reduced left ventricular ejection fraction. The successful outcome in this high-risk patient underscores the importance of prompt decision-making and careful surgical planning in the acute setting.

Perioperative IABP support proved instrumental in stabilizing hemodynamics both before and after the operation. By reducing left ventricular afterload and augmenting diastolic coronary perfusion, IABP therapy mitigated the hemodynamic burden imposed by the large left-to-right shunt and supported ventricular recovery in the immediate postoperative period. These findings are consistent with existing evidence supporting IABP utilization in high-risk cardiac surgical patients.[5]

The choice of right ventriculotomy as the primary surgical approach was driven by the apical location of the defect, which precluded adequate visualization through a transatrial or transpulmonary route. Although right ventriculotomy carries inherent risks of right ventricular dysfunction, these risks were considered acceptable in the context of the defect's anatomy and the urgency of repair. The use of autologous pericardium as patch material offered the advantage of biocompatibility and reduced risk of infection, particularly relevant in an elderly immunologically compromised host.

From a broader clinical perspective, this case highlights several important principles relevant to the surgical management of VSD in elderly, high-risk patients. First, advanced age alone should not be

considered a contraindication to surgical repair when the hemodynamic consequence of an unrepaired defect is life-threatening. Second, individualized preoperative planning — encompassing imaging evaluation, risk stratification, and multidisciplinary consultation — is essential to optimize outcomes. Third, the integration of mechanical circulatory support into the perioperative strategy can meaningfully expand the boundaries of surgical feasibility in patients with severely impaired ventricular function.

In conclusion, while the surgical management of apical muscular VSDs in elderly patients with reduced ejection fraction remains challenging, thoughtful operative planning combined with perioperative IABP support can yield favorable outcomes. Further case series and registries are needed to better define optimal management strategies for this complex patient population.

REFERENCES

1. Minette MS, Sahn DJ. Ventricular septal defects. Circulation. 2006;114(20):2190-2197.

2. Holzer R, Balzer D, Cao QL, Lock K, Hijazi ZM. Device closure of muscular ventricular septal defects using the Amplatzer muscular ventricular septal defect occluder: immediate and mid-term results of a U.S. registry. J Am Coll Cardiol. 2004;43(7):1257-1263.

3. Thanopoulos BD, Tsaousis GS, Konstadopoulou GN, Zarayelyan AG. Transcatheter closure of muscular ventricular septal defects with the amplatzer ventricular septal defect occluder: initial clinical applications in children. J Am Coll Cardiol. 1999;33(5):1395-1399.

4. Serraf A, Lacour-Gayet F, Bruniaux J, et al. Surgical management of isolated multiple ventricular septal defects. J Thorac Cardiovasc Surg. 1992;103(3):437-442.

5. Kitagawa T, Durham LA, Mosca RS, Bove EL. Techniques and results in the management of multiple ventricular septal defects. J Thorac Cardiovasc Surg. 1998;115(4):851-858.

6. Bol-Raap G, Weerheim J, Kappetein AP, Witsenburg M, Bogers AJ. Follow-up after surgical closure of congenital ventricular septal defect. Eur J Cardiothorac Surg. 2003;24(4):511-515.

7. Jacobs JP, Burke RP, Quintessenza JA, Mavroudis C. Congenital Heart Surgery Nomenclature and Database Project: ventricular septal defect. Ann Thorac Surg. 2000;69(4 Suppl):S25-S35.

8. Waight DJ, Bacha EA, Kahana M, et al. Catheter therapy of Swiss cheese ventricular septal defects using the Amplatzer muscular VSD occluder. Catheter Cardiovasc Interv. 2002;55(3):355-361.

9. Pacifico AD, Kirklin JK, David Hamilton B, McConnell ME, Nanda NC, Colvin EC. Closure of the congenital ventricular septal defect at less than six months of age. J Thorac Cardiovasc Surg. 1993;107(5):1212-1218.

10. Intraoperative echocardiography for the assessment of ventricular septal defects in infants and children: experience with 100 cases. Circulation. 1986;74(3 Pt 2):I153-I161.

DEVELOPING SOAPS FOR HEALTH-RELATED INDUSTRIES USING CAPER EXTRACT AND ITS ANTIMICROBIAL ACTIVITY

Meltem ASAN-OZUSAGLAM

Department of Molecular Biology and Genetic, Faculty of Science and Letters, University of Aksaray, Aksaray, Türkiye

Ali SAGLAM

Department of Molecular Biology and Genetic, Faculty of Science and Letters, University of Aksaray, Aksaray, Türkiye

Mehmet ÇOBANOĞLU

Department of Molecular Biology and Genetic, Faculty of Science and Letters, University of Aksaray, Aksaray, Türkiye

Merve ALAN

Department of Molecular Biology and Genetic, Faculty of Science and Letters, University of Aksaray, Aksaray, Türkiye

SUMMARY

There is a growing trend towards traditional medicine and medicinal aromatic plants to combat the negative side effects and toxicity of synthetic antibiotics used against infections caused by clinical pathogens. Therefore, the aim of this study is to develop a soap formulation prepared with caper extract and then test the antimicrobial activity of this soap. For this purpose, the hexane extract from caper (*Capparis spinosa* L.) was first obtained by maceration. Then, the antimicrobial activity of the caper hexane extract (CHE) was determined against the clinical pathogens *Pseudomonas aeraginosa* (ATCC 27853), *Staphylococcus aureus* (ATCC 25923) and methicillin-resistant *Staphylococcus aureus* (ATCC 43300) (MRSA) using agar well diffusion method. It was determined that *P. aeraginosa* showed higher antimicrobial activity compared to *S. aureus*, with inhibition zones of 4.64 mm and 2.02 mm, respectively. However, no antimicrobial activity against MRSA was detected. The MIC and MBC values of the extract ranged from 25 mg/ml to 50 mg/ml. Afterwards, the antimicrobial soap was prepared by adding CHE to the soap base and its antimicrobial activity against the test bacteria were determined using the agar well diffusion method. The soap base group (control) presented antimicrobial activity against *P. aeraginosa* (3.26 mm) and MRSA (5.80 mm) but did not produce an inhibitory effect on *S. aureus*. Interestingly, the soap base + CHE group showed good antimicrobial activity against *S. aureus* (8.50 mm), MRSA (11.55 mm) and *P. aeraginosa* (13.20 mm) with combined effect. The results show that the caper hexane extract has the potential to be used as a soap natural component with antimicrobial activity in the health-related industries and can impart additional properties to soap.

Keywords: Antimicrobial, soap, extract, *Capparis spinosa*, maceration

INTRODUCTION

Traditionally, various medicinal plants have been used for many years as one of the most effective and safest treatment methods for numerous diseases and infections (Nabavi et al., 2016). Nowadays, it is known that secondary metabolites of medicinal plants are an important source of bioactive natural products (Russo et al., 2016). Considering the high antimicrobial property and low side effects of medicinal and aromatic plants and their secondary metabolite components, they can serve as an important alternative therapy for the treatment of various human diseases, including the treatment of infections, the treatment of cardiovascular diseases, etc (Nabavi et al.,2015 & Abdallah et al., 2023). Caper (*Capparis spinosa L.*) is a widespread member of the caper genus (Tlili et al., 2011). The caper plant grows in tropical regions and then spread to other parts of the world, such as the Mediterranean basin and Central Asia (Chedraoui et al., 2017). It grows naturally in all parts of Türkiye that have a

Mediterranean climate. Capers are known for their edible flower buds, which are commonly used as a spice, and their fruit, both of which are often consumed pickled. It is stated that it has medicinal properties such as being invigorating and diuretic; its extract also has cosmetic properties that revitalize and normalize aging skin (Sarı and Oguz, 2026). Capers are considered a future source of invaluable nutrients for human food and have been used in traditional medicine to treat a variety of human infections (Annaz et al., 2022). The different parts of capers are rich sources of unsaturated lipids, ascorbic acid, and phenolic compounds, the most prominent of which are rutin and quercetin. These may be responsible for the antidiabetic, anti-inflammatory, and antifungal activities of this important medicinal plant (Allaith et al., 2016 & El-Bakkosh et al.,2019). Today, antibiotic resistance, caused by the misuse or indiscriminate use of antibiotics, is leading to significant health problems. Synthetic drugs have side effects that threaten human health and cause the proliferation of resistant bacteria due to high antibiotic use, making infection treatments more difficult (Serwecińska et al., 2020). For this reason, it is essential to identify new antimicrobials against pathogenic bacteria from medicinal and aromatic plants (Ortega-Ramirez et al., 2014). The aim of this study is to develop an antimicrobial soap containing plant extracts as a natural antimicrobial source to prevent infections caused by clinical pathogens. In this context, firstly, the antimicrobial activity of hexane extract obtained from caper plant against clinically sourced test microorganisms was determined. Subsequently, an antimicrobial soap was developed using caper extract, and its antimicrobial activity against the pathogenic bacteria was tested.

MATERIAL AND METHOD

Caper plant material was obtained from Alata Horticultural Research Institute (Mersin/Türkiye) in June 2021 (Figure 1).



Figure 1. Caper plant

Preparation of Caper Extract

The caper plants were washed and dried in an airy place away from sunlight (Figure 2). They were ground into powder using a Waring blender. The plant material was then extracted at room temperature, protected from light, in a solvent (hexane) at a ratio of 1:3 (weight/volume) for 5 days. The mixture was filtered and dissolved in DMSO. For antimicrobial efficacy testing, the caper hexane extract (CHE) solution was sterilized through a 0.22 µm sterile filter and stored at 4°C.



Figure 2. Preparation of caper material for extraction

Determination of Antimicrobial Activity

The antimicrobial activity of CHE was determined by agar well diffusion method. *Pseudomonas aeraginosa* ATCC 27853 (P.a.), *Staphylococcus aureus* ATCC 25923 (S.a), and Methicillin-resistant *Staphylococcus aureus* ATCC 43300 (MRSA) (Nutrient Broth (NB)/Agar) were used as test microorganisms. The test microorganisms (100 µl) prepared at a concentration of 0.5 McFarland were inoculated onto solid media. Then, the wells (6 mm) were prepared on the agar surface. The CHE was dropped into the wells in 3 replicates and incubated at 37°C. The diameters of the inhibition zones around the wells were recorded. The values obtained were presented with their means and standard deviations.

Determination of MIC and MBC

The micro-dilution method was used to determine MIC and MBC values of CHE. The growth media and CHE were added into the tubes and then two-fold dilutions were made. The bacterial culture adjusted to 0.5 McFarland standard was added and the tubes incubated at above conditions for 24 hours. The concentrations at which microbial growth occurred after incubation were recorded as the MIC value. The samples from the tubes at different concentrations were then dropped onto agar media using the spot dropping method and incubated at 37°C for 24 hours. The concentrations at which no microbial growth occurred were recorded as the MBC value. Antibacterial efficacy was also evaluated according to the MBC/MIC. If the MBC/MIC is ≤4, the efficacy is considered bactericidal, and if the MBC/MIC ratio is >4, the efficacy is considered bacteriostatic (Mogana et al., 2020).

Preparation of Soap with Extract

The CHE-containing soap was developed using 2% CHE (0.2 g) and 10 grams of soap base. The soap base without extract was used as a control. The prepared soap was melted in a microwave to test its antimicrobial activity.

Determination of Antimicrobial Activity of the Developed Soap

The agar well diffusion method was used to test the antimicrobial activity of the developed soap. The test microorganisms (0.5 McFarland, 100 µl) were spread onto the agar surface. Then, the wells (6 mm) were drilled on the agar surface, and the liquid soap (100 µl) was filled. The Petri dishes were incubated at 37°C. The inhibition zone diameters around the well were measured.

Statistical Analysis

Data are presented with the mean and standard deviation (SD) of three separate measurements. Analysis of variance was performed using GNU SPSS software, and two-way analysis of variance (ANOVA) was used to obtain significant differences. Significant differences between means were analyzed using Tukey's post-hoc test. A p-value < 0.0001 was considered statistically significant.

RESEARCH AND FINDING

The antibacterial activities of CHE were investigated on clinical pathogens using agar well diffusion and micro-dilution assays. The inhibition zone diameters of the extract on the test microorganisms are shown in Figure 3 and Table 1. The higher inhibition diameter was measured against P. a. (4.64 mm) than S. a. (2.02 mm). However, no inhibition zone diameter was determined on MRSA.

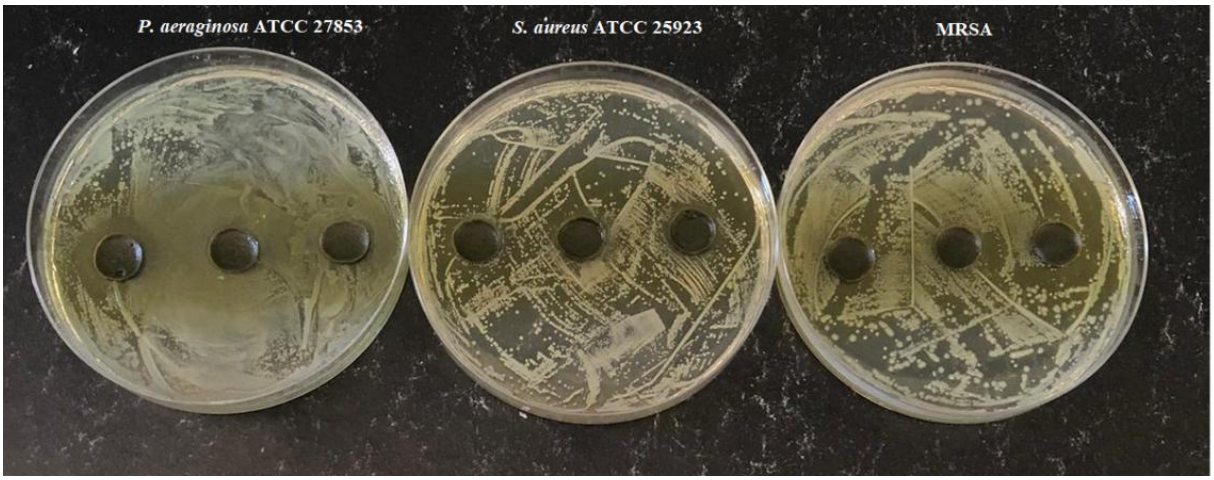


Figure 3. Antimicrobial activity of CHE on test microorganisms in Petri dishes

Table 1. Inhibition zone diameters of CHE and Kanamisin (K) (mm)

Microorganisms	**CHE**	**K (30 µg)**
P. aeraginosa	4.64±0.42[a1]	8.53±0.44[b1]
S. aureus	2.02±0.04[a2]	-[b2]
MRSA	-[a3]	-[a2]

[a]Column factor values were lettered, and row factor values were numbered to indicate statistical significance ($p<0.0001$, two-way ANOVA). For caper extracts, $F(2, 12) = 1194$ (rows) and $F(1, 12) = 27.40$ (columns).

-: No inhibition zone

The MIC and MBC values of CHE are given in Figure 4 and Table 2. The MIC value of CHE was 25 mg/ml for P. a. and S. a., and 50 mg/ml for MRSA. The MBC value was determined as 25 mg/ml for P. a., and 50 mg/ml for S. a. and MRSA. CHE extract exhibits a bactericidal effect on test microorganisms because its MBC/MIC ratio is less than 4 (Table 2).

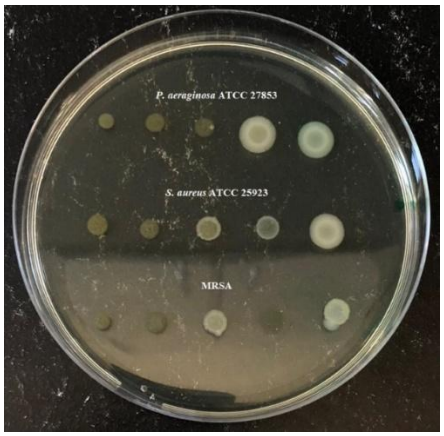


Figure 4. Determination of MBC values

Table 2. MIC and MBC values of CHE (mg/ml)

Microorganisms	**MIC**	**MBC**	**MBC/MIC**
P. aeraginosa	25	25	1
S. aureus	25	50	2
MRSA	50	50	1

The antimicrobial activity results of the prepared soap are given in Figure 3 and Table 3. The soap base used as a control created inhibition zones of 3.26 mm on P. a. and 5.80 mm on MRSA, while showing no antimicrobial activity on S. a. However, the significant increases in inhibition zones were observed with the addition of CHE extract to the soap base ($p<0.0001$). The addition of 2% caper extract to the soap base (soap base + extract group) led to a significant and pronounced increase in antimicrobial activity in all tested strains. The highest inhibition zone diameter of soap base + extract on the test microorganisms was recorded against P. a. at 13.20 mm. This result indicates a significant increase in antimicrobial activity compared to the extract and base groups. The inhibition zone diameter of 11.55 mm against MRSA and 8.50 mm against S. a. was determined (Figure 3). Based on these results, it was shown that caper extract and soap base exhibited a combined effect and significantly increased antimicrobial activity.

S. a. and MRSA can cause a variety of infections, ranging from mild skin infections to more serious conditions such as sepsis, pneumonia, and large wound infections (Boyce, 2001). However, the limited availability of effective antibiotics makes treating MRSA infections quite challenging. Therefore, the fact that our caper-based soap exhibits a potent inhibitory effect on S. a. and MRSA is a very significant result.



Figure 5. Antimicrobial activity of CHE-added soap in Petri dishes

Table 3. Antimicrobial activity of CHE-added soap

Microorganisms	Soap base (control)	Soap+CHE	K (30 µg)
P. aeraginosa	3.26±0.24^{a1}	13.20±0.61^{b1}	8.53±0.44^{c1}
S. aureus	-^{a2}	8.50±0.48^{b2}	-^{a2}
MRSA	5.80±0.23^{a3}	11.55±0.47^{b3}	-^{c2}

[a] Column factor values were lettered, and row factor values were numbered to indicate statistical significance ($p<0.0001$, two-way ANOVA). For caper extracts, $F(2, 18) = 540.3$ (rows) and $F(2, 18) = 1585$ (columns).

.-:No inhibition zone diameter

CONCLUSION

Antibiotics are widely used worldwide and in Türkiye to treat infections caused by clinical pathogens. This leads to bacteria becoming resistant to these antibiotics, and antibiotics can cause side effects and endanger human health. In this study, caper plant extract demonstrated antimicrobial activity against some test microorganisms. Thanks to the natural structure of caper extract, this antimicrobial activity makes it suitable for use in soaps to enhance or add antimicrobial activity. Based on the results, caper extract has the potential to be used in the health-related industries to add or enhance additional properties to products. This study has also revealed new alternative uses for the caper plant, whose seeds are particularly valued in the food industry, for various purposes in the health sector.

REFERENCES

Abdallah, E. M., Alhatlani, B. Y., de Paula Menezes, R., & Martins, C. H. G. (2023). Back to nature: Medicinal plants as promising sources for antibacterial drugs in the post-antibiotic era. *Plants*, *12*(17), 3077.

Allaith, A. A. A. (2016). Assessment of the antioxidant properties of the caper fruit (*Capparis spinosa* L.) From Bahrain. *Journal of the Association of Arab Universities for Basic and Applied Sciences*, *19*, 1-7.

Annaz, H., Sane, Y., Bitchagno, G. T. M., Ben Bakrim, W., Drissi, B., Mahdi, I., ... & Sobeh, M. (2022). Caper (*Capparis spinosa* L.): an updated review on its phytochemistry, nutritional value, traditional uses, and therapeutic potential. *Frontiers in Pharmacology*, *13*, 878749.

Boyce, J.M. (2001). MRSA patients: proven methods to treat colonisation and infection. *Journal of Hospital Infection* 48 (Suppl A): 9–14

Chedraoui, S., Abi-Rizk, A., El-Beyrouthy, M., Chalak, L., Ouaini, N., & Rajjou, L. (2017). *Capparis spinosa* L. İn a systematic review: A xerophilous species of multi values and promising potentialities for agrosystems under the threat of global warming. *Frontiers in Plant Science*, *8*, 1845.

El-Bakkosh, A. M., Shaieb, F. M., & Idrs, A. M. (2019). Phytotoxicity and antifungal activity of *Capparis spinosa* L. In *EPH Int J Appl Sci (Special Conference Issue)* (Vol. 1, No. 1, pp. 553-563).

Nabavi, S. F., Braidy, N., Orhan, I. E., Badiee, A., Daglia, M., & Nabavi, S. M. (2016). *Rhodiola rosea* L. and Alzheimer's disease: from farm to pharmacy. *Phytotherapy Research*, *30*(4), 532-539.

Mogana, R., Adhikari, A., Tzar, M. N., Ramliza, R., Wiart, C. 2020. Antibacterial activities of the extracts, fractions and isolated compounds from *Canarium patentinervium* Miq. against bacterial clinical isolates, *BMC Complementary Medicine and Therapies*, 20, 55.

Nabavi, Seyed Fazel, Antoni Sureda, Solomon Habtemariam, and Seyed Mohammad Nabavi. Ginsenoside Rd and ischemic stroke; a short review of literatures. *Journal of Ginseng Research* 39, no. 4 (2015): 299-303.

Ortega-Ramirez, L. A., Rodriguez-Garcia, I., Leyva, J. M., Cruz-Valenzuela, M. R., Silva-Espinoza, B. A., Gonzalez-Aguilar, G. A., ... & Ayala-Zavala, J. F. (2014). Potential of medicinal plants as antimicrobial and antioxidant agents in food industry: a hypothesis. *Journal of Food Science*, *79*(2), R129-R137.

Russo, M., Russo, G. L., Daglia, M., Kasi, P. D., Ravi, S., Nabavi, S. F., & Nabavi, S. M. (2016). Understanding genistein in cancer: The “good” and the “bad” effects: A review. *Food Chemistry*, *196*, 589-600.

Sarı, AO, Oğuz, B., 2026. Kapari Tarımı, Tarım ve Köyişleri Bakanlığı Ege Tarimsal Araştırma Enstitüsü. https://arastirma.tarimorman.gov.tr/etae/Belgeler/EgitimBrosur/76-ciftcibro.pdf (Access date 07.05.2026)

Serwecińska, L. (2020). Antimicrobials and antibiotic-resistant bacteria: a risk to the environment and to public health. *Water*, *12*(12), 3313.

Tlili, N., Elfalleh, W., Saadaoui, E., Khaldi, A., Triki, S., & Nasri, N. (2011). The caper (Capparis L.): Ethnopharmacology, phytochemical and pharmacological properties. *Fitoterapia*, *82*(2), 93-101.

PREVALENCE AND PREVENTIVE STRATEGIES OF CHILD ABUSE AND NEGLECT AMONG SOCIAL WELFARE WORKERS IN YOLA METROPOLIS

Suleiman Sambo

Department of Community Medicine, College of Medical Sciences, Modibbo Adama University Yola

SUMMARY

Child abuse and neglect constitute critical public health concerns in Nigeria, with severe implications for the physical, emotional, and social well-being of the youth population. This cross-sectional study assessed the prevalence, socio-economic and cultural determinants, and the effectiveness of preventive strategies for child abuse in Yola Metropolis from the perspective of social welfare workers. Grounded in Social Learning Theory, Ecological Systems Theory, and Resilience Theory, the study employed a descriptive survey design. A sample of 259 social welfare workers was approached, with 247 completing the structured questionnaire, representing a 95.3% response rate. Data were analysed using IBM SPSS 29, utilizing descriptive statistics and inferential tests including chi-square and logistic regression. Findings revealed a significant prevalence of abuse, with 86.6% of respondents encountering cases frequently. Physical abuse (28.3%) and neglect (26.3%) were the most reported forms. Significant predictors of abuse included poverty (38.4%) and cultural practices like the Almajiri system (90.6% agreement). Current preventive strategies were deemed significantly inadequate ($p < .001$) due to a lack of resources and specialized training. The study recommends enhanced resource allocation and community engagement to strengthen child protection frameworks.

Keywords: Child abuse, neglect, social welfare workers, Yola Metropolis, preventive strategies.

INTRODUCTION

Child abuse and neglect constitute persistent violations of children's fundamental rights and remain significant public health and social welfare concerns across societies (WHO, 2020; UNICEF, 2017). In Nigeria, empirical studies consistently demonstrate high prevalence rates of child maltreatment, with evidence suggesting that a substantial proportion of children experience physical, emotional, sexual, or structural forms of violence before reaching adulthood (Adebayo, 2015). These patterns indicate that child abuse in Nigeria is not merely an individual or familial phenomenon but is embedded within broader socio-economic and cultural structures (Akpan & Oluwabamide, 2010).

Previous research has shown that economic deprivation significantly increases children's exposure to labour exploitation, street trading, and neglect, particularly in low-income households (Olusanya, 2011; Atilola *et al*., 2015). Similarly, cultural interpretations of childhood and obedience often blur the boundaries between discipline and abuse, thereby legitimising harmful practices within communities (Akpan & Oluwabamide, 2010; Abdulhamid & Sanusi, 2016). Although Nigeria enacted the Child Rights Act (CRA) in 2003 to provide a comprehensive legal framework for child protection, its implementation has remained uneven across regions, particularly in Northern Nigeria (Maianguwa & Amao, 2015; Adebayo, 2015). Scholars have attributed this uneven implementation to factors such as limited political commitment, inadequate institutional capacity, and resistance rooted in socio-cultural and religious ideologies (Maianguwa & Amao, 2015; Browne, 2016). Consequently, legal provisions often fail to translate into effective protection mechanisms for vulnerable children.

In Northern Nigeria, specific practices such as street hawking (*Talla*), child begging associated with the Almajiri system (*Almajiranci*), child labour, and exclusion from formal education have been widely documented as prevalent forms of child abuse and neglect (Abdulhamid & Sanusi, 2016; Ibrahim & Ali, 2021). While these practices are sometimes justified as economic survival strategies or religious training, empirical evidence indicates that they expose children to multiple risks, including physical injury, psychological trauma, and educational deprivation (Ibrahim & Ali, 2021; Atilola *et al*., 2015). These findings underscore the structural nature of child maltreatment in the region. The persistence of

child abuse in Nigeria has also been linked to systemic weaknesses in the social welfare sector. Social welfare workers in government agencies, non-governmental organisations, and community-based organisations play critical roles in identifying, preventing, and managing cases of child maltreatment (Browne, 2016).

However, their effectiveness is constrained by inadequate funding, limited professional training, high caseloads, and weak inter-agency coordination (Atilola *et al*., 2015; Browne, 2016). Such institutional deficiencies have been identified as major obstacles to the development of effective child protection systems in low- and middle-income countries (Browne, 2016; WHO, 2020). Furthermore, studies have shown that societal attitudes towards child abuse often discourage reporting and intervention, thereby reinforcing cycles of neglect and exploitation (Akpan & Oluwabamide, 2010; UNICEF, 2017). In this context, child abuse and neglect persist not only because of poverty and cultural practices but also due to institutional inertia and weak accountability mechanisms (Adebayo, 2015; Maianguwa & Amao, 2015).

RESEARCH AND FINDINGS

The study utilized a descriptive survey research design to gather factual information on the prevalence and prevention of child abuse. The target population consisted of social welfare workers in Yola Metropolis, estimated at 490 individuals. A multi-stage sampling technique was used to select a sample of 259 respondents, calculated using the Yamane formula to ensure statistical power. Data were collected via a validated digital questionnaire (Cronbach's alpha of 0.94) and processed using IBM SPSS 29.

Prevalence and Nature of Abuse: Analysis of the data revealed that child abuse is significantly prevalent in Yola Metropolis. An overwhelming 86.6% of social welfare workers reported encountering or witnessing abuse cases. When examining the frequency of observation, 37.8% noted they witness these cases "Frequently," while 36.2% observe them "Occasionally". Physical abuse (28.3%) and neglect (26.3%) were identified as the primary forms of maltreatment, followed by emotional (20.2%) and sexual abuse (16.2%). These findings were confirmed by a chi-square test for goodness-of-fit, which showed a highly significant difference between observed and expected frequencies of abuse ($\chi 2=72.45$, $p<.001$), leading to the rejection of the null hypothesis regarding low prevalence.

Table 1: Types of Child Abuse and Neglect Reported by Respondents

Type of Abuse/Neglect	Frequency	Percentage
Physical Abuse	70	28.3%
Emotional Abuse	50	20.2%
Sexual Abuse	40	16.2%
Neglect	65	26.3%
Other (e.g., Child Labour)	22	8.9%
Total	**247**	**100%**

Socio-Economic and Cultural Determinants: The study identified poverty and cultural norms as the most influential factors driving child maltreatment. Poverty was cited by 38.4% of respondents as the main cause, with 62.8% strongly agreeing that economic hardship directly increases the risk of abuse.

Cultural practices, specifically the *Almajiri* system, were identified by 90.6% of respondents as contributing significantly to child neglect. Logistic regression analysis confirmed these relationships: poverty (β=0.42, p=.001), lack of education (β=0.36, p=.002), and cultural practices (β=0.28, p=.005) were all statistically significant predictors of abuse.

Effectiveness and Challenges of Preventive Strategies: While 64.9% of workers are aware of child protection programs, only 41.7% perceived these efforts as effective. A one-sample t-test yielded a mean effectiveness score of 2.87 on a 5-point Likert scale, which is significantly lower than the neutral value of 3 (t (246) =−3.82, p=.001). This statistical inadequacy is largely attributed to operational hurdles. The most pressing challenges include:

i. Lack of Funding/Resources: 34.4%.
ii. Insufficient Training: 28.3%.
iii. High Caseloads: 24.3%.
iv. Community Resistance: 13.0%.

A multiple regression analysis demonstrated that child protection outcomes could be significantly improved by strengthening community involvement (β=0.65, p=.001) and enhancing training resources (β=0.48, p=.002).

CONCLUSION

The study conclusively establishes that child abuse and neglect are endemic in Yola Metropolis, driven largely by poverty and entrenched cultural beliefs such as the *Almajiri* system. The research highlights a critical disconnect between the high prevalence of abuse and the perceived inadequacy of current preventive strategies employed by social welfare workers. Frontline workers are severely hampered by resource limitations and cultural resistance, which prevents proactive intervention.

To strengthen the child protection framework in Nigeria, it is imperative to shift from reactive to proactive strategies. This requires increased government investment in social services, the institutionalization of specialized training for welfare workers, and the active engagement of religious and traditional leaders to align cultural practices with child rights. Furthermore, addressing the socio-economic roots through poverty alleviation remains essential to reducing the vulnerability of children to exploitative labour and neglect.

REFERENCES

Abdulhamid, R., & Sanusi, I. M. (2016). Child abuse in Northern Nigeria: Dimensions, reasons for its persistence, and ways forward. *Journal of Educational and Social Research, 6*(3), 75–82.

Adebayo, D. O. (2015). Prevalence of child abuse & neglect in Nigeria: Implications for child protection. *Child Abuse & Neglect*, 43, 25-35.

Akpan, N., & Oluwabamide, A. (2010). Social dynamics of child abuse and neglect in Nigeria. *Journal of Social Sciences, 24*(1), 67–74.

Atilola, O., Ayinde, O. O., Emedoh, C. T., & Oladimeji, O. (2015). State of the Nigerian child: Neglect of child and adolescent mental health. *Paediatrics and International Child Health, 35*(2), 135–143.

Browne, K. (2016). Strengthening child protection systems in low- and middle-income countries: Strengths, challenges, and the way forward. *The Lancet Child & Adolescent Health, 12*(4), 344–356.

Ibrahim, M., & Ali, A. (2021). Almajiri children and child neglect in Northern Nigeria: An analysis of the root causes. *African Child Protection Journal, 12*(1), 77–92.

Maianguwa, Y., & Amao, O. (2015). The Almajiri system & the challenges of child rights in Northern Nigeria. *International Journal of Human Rights*, 19(3), 392-410.

Olusanya, O. (2011). Poverty & child abuse in Nigeria: Implications for policy. *African Journal of Social Policy & Administration*, 4(2), 45-56.

UNICEF. (2017). *A familiar face: Violence in the lives of children and adolescents*. United Nations Children's Fund.

World Health Organization (WHO). (2020). *Global status report on preventing violence against children*. World Health Organization.

HYBRID DEEP LEARNING FRAMEWORK FOR EARLY PARKINSON'S DISEASE DETECTION USING 2D AND 3D MRI ANALYSIS

Al Mahmud Suruj

Department of Computer Science and Technology,

Southwest Jiaotong University, Chengdu, Sichuan 611756, China

Qiu Xiaoping

School of Computing and Artificial Intelligence, Southwest Jiaotong University,

Chengdu, Sichuan, China-611756

Shimul Mahmud Khatami

IoT and Robotics Engineering Department, University of Frontier Technology,

Gazipur, Dhaka, Bangladesh-1750

ABSTRACT

Parkinson's disease (PD) is a progressive neurodegenerative disorder whose early detection from structural MRI remains challenging due to subtle, spatially distributed neuroanatomical changes that precede overt motor symptom onset. This study presents a hybrid deep learning framework that jointly exploits 2D and 3D structural MRI representations for improved early PD detection. An EfficientNet-B0 backbone processes multi-planar 2D slices across axial, coronal, and sagittal views, while a lightweight 3D ResNet-18 encoder captures full volumetric context. The two streams are integrated through a bidirectional cross-attention fusion module that enables learned alignment between slice-level and volumetric features. Post-hoc explainability is provided via Grad-CAM++, with class-discriminative activations re-projected into anatomical space.

Evaluated on baseline T1- and T2-weighted MRI scans from the publicly available Parkinson's Progression Markers Initiative (PPMI) dataset - spanning healthy controls, prodromal, and clinically established PD subjects - the proposed model achieved 85.7% accuracy and a macro-AUC of 0.850 on the held-out test set (95% CI: AUC 0.821–0.878, 1000-resample percentile bootstrap). It outperformed pure 2D (AUC 0.720), pure 3D (AUC 0.770), naive concatenation fusion (AUC 0.800), and Swin-CNN (AUC 0.830) baselines, and demonstrated stronger generalization on the more challenging early-stage and prodromal subsets (AUC 0.824 and 0.811, respectively). Ablation analysis confirmed that all four design components contribute meaningfully, with ImageNet pre-training yielding the largest individual gain (ΔAUC +0.098). These results support the hypothesis that learned 2D-3D alignment improves upon single-paradigm approaches while preserving clinical interpretability. The framework is reproducible on a single consumer GPU, offering a transparent and accessible baseline for future MRI-based PD screening research.

Keywords: Parkinson's disease, Hybrid deep learning, 2D-3D fusion, Structural MRI, Cross-attention, Early diagnosis, Explainable AI, PPMI, Reproducibility.

1 INTRODUCTION

Parkinson's disease (PD) is a progressive neurodegenerative disorder defined pathologically by the loss of dopaminergic neurons in the substantia nigra pars compacta and the accumulation of intracellular α-synuclein aggregates (Poewe et al., 2017). Clinically, it manifests as bradykinesia, resting tremor, rigidity, and postural instability; however, evidence indicates that neurodegeneration begins years before motor signs become evident, passing through a prodromal phase during which intervention may be most effective (Berg et al., 2015). Reliable, non-invasive biomarkers capable of identifying individuals at this early stage remain an important goal of contemporary neuroimaging and computational research.

Structural MRI is widely available, affordable, and free from ionizing radiation, making it a candidate substrate for early biomarker development. The neuroanatomical changes associated with early PD, however, are subtle and spatially distributed; they involve focal alterations in the substantia nigra, brainstem nuclei, and connected cortical and subcortical territories, often below the resolution at which conventional radiological reads detect them (Heim et al., 2017). Traditional analysis pipelines based on voxel-based morphometry or handcrafted texture features have produced variable results across cohorts. A recent review of 17 studies using MRI from the PPMI database reported average classification accuracies of 87.9% (SD 8.0%), with a wide range from 70.5% to 99.9% (Lei et al., 2021), and multi-center work has consistently reported lower numbers than single-site work, indicating substantial site- and cohort-related variance.

Within deep learning, two predominant design choices have emerged for MRI-based PD classification. The first treats each volume as a stack of two-dimensional slices, exploiting mature 2D convolutional backbones pre-trained on natural images, such as those in the EfficientNet family (Tan & Le, 2019). This approach is parameter-efficient and benefits from large-scale transfer learning, but it discards inter-slice spatial coherence. The second design uses 3D convolutional networks that operate directly on full volumes, preserving volumetric context and inter-slice dependencies (Esmaeilzadeh et al., 2018; Chakraborty et al., 2020; Camacho et al., 2023). Three-dimensional models capture global anatomy but are computationally heavier, are prone to overfitting on modest sample sizes, and gain less from transfer learning because few large-scale 3D medical pre-training corpora exist. The complementary strengths and weaknesses of these paradigms suggest that hybrid 2D–3D architectures, equipped with principled fusion mechanisms, are worth systematic investigation.

This paper proposes one such framework and the experimental protocol required to evaluate it fairly. Three modest contributions are advanced. First, a dual-stream architecture is specified in which an EfficientNet-B0 encoder extracts slice-wise features from axial, coronal, and sagittal mid-sections of T1- and T2-weighted MRI, while a 3D ResNet-18 encoder ingests the full volume; the two streams are fused through a cross-attention module that allows volumetric features to query slice-level features and vice versa. Second, an explainability layer based on Grad-CAM++ (Chattopadhay et al., 2018) is integrated, with class-discriminative attention re-projected into anatomical space. Third, a minimal low-cost experimental pipeline is provided so that the framework can be reproduced on a single consumer GPU or on Google Colab. No claim is made that the proposed framework outperforms prior state of the art; the aim is to provide a transparent, reproducible baseline against which subsequent improvements can be measured. The remainder of the paper is organized as follows: Section 2 reviews related literature; Section 3 specifies the data, pre-processing, architecture, training, evaluation, and ablation protocols, including anticipated performance ranges grounded in cited literature; Section 4 discusses implications and threats to validity; and conclusion.

2. LITERATURE REVIEW

2.1 Structural MRI biomarkers of Parkinson's disease

PD pathology is anchored in the substantia nigra pars compacta (SNc), where progressive degeneration of dopaminergic neurons drives the cardinal motor phenotype (Poewe et al., 2017). Neuroimaging markers of this process include reductions in nigral signal on neuromelanin-sensitive MRI, susceptibility-related changes captured by quantitative susceptibility mapping, and morphometric changes in the brainstem and connected basal ganglia structures (Heim et al., 2017). No single radiological feature has so far achieved the sensitivity and specificity required for population-level early screening; the Movement Disorder Society research criteria for prodromal PD therefore combine multiple clinical and imaging risk factors probabilistically (Berg et al., 2015).

2.2 Two-dimensional (2D) deep learning approaches

Two-dimensional CNNs operating on MRI slices have been widely used because they exploit transfer learning from ImageNet-pretrained backbones. Sivaranjini and Sujatha (2020) applied an AlexNet-style network to T2-weighted slices and reported competitive results. Khan et al. (2023) and Camacho et al. (2023) extended this paradigm with deeper backbones and multi-centre datasets, observing that careful slice selection around the midbrain and substantia nigra contributes substantially to performance. EfficientNet variants (Tan & Le, 2019) are particularly attractive for medical imaging because

compound scaling produces models that are accurate yet parameter-efficient, mitigating overfitting on modest cohorts. The principal limitation of 2D approaches is the loss of inter-slice context.

2.3 Three-dimensional (3D) volumetric approaches

Three-dimensional convolutional networks preserve volumetric structure. Esmaeilzadeh et al. (2018) presented an end-to-end 3D-CNN for PD classification from T1-weighted MRI. Chakraborty et al. (2020) reported strong single-site PPMI performance with a custom 3D-CNN. Mozhdehfarahbakhsh et al. (2021) extended this direction with a deeper 3D architecture. More recent work has explored hybrid CNN–transformer architectures: Kaplan et al. (2025) proposed a Swin-transformer–CNN fusion model that captures both local convolutional features and long-range dependencies. Despite these advances, 3D models typically require careful regularisation and benefit less from natural-image pre-training; multi-centre evaluations have generally reported lower numbers than single-site evaluations (Basaia et al., 2025; Camacho et al., 2023).

2.4 Hybrid and fusion architectures

Recognizing the complementary nature of 2D and 3D features, several studies have investigated fusion strategies. Camacho et al. (2023) trained a 2D model on selected slices and ensembled predictions across slices, providing explainability via class activation maps. Cross-attention, originally introduced for sequence modelling (Vaswani et al., 2017), has become a canonical mechanism for multi-modal and multi-view fusion: one stream produces queries while another produces keys and values, enabling learned alignment between heterogeneous representations. Dedicated 2D-3D MRI fusion frameworks for PD with explicit cross-attention between slice-wise and volumetric streams, accompanied by explainability, remain comparatively underexplored in the literature.

2.5 Explainability in medical deep learning

Clinical adoption of deep learning depends on interpretability. Class Activation Mapping (Zhou et al., 2016) and its gradient-based extension Grad-CAM (Selvaraju et al., 2017) made post-hoc localisation broadly accessible, while Grad-CAM++ (Chattopadhay et al., 2018) improved localisation in the presence of multiple discriminative regions and finer structures, which is relevant to brain imaging. For volumetric data, 3D class activation maps have been used to highlight the SNc and adjoining structures in PD models (Mozhdehfarahbakhsh et al., 2021; Camacho et al., 2023), providing biologically plausible saliency.

2.6 Reported performance ranges on PPMI

Published results on PPMI-derived cohorts span a wide range, reflecting differences in sample size, modality, label definition, and validation protocol. Representative anchor points include: a custom 3D-CNN on 406 single-site T1 scans reporting approximately 95% accuracy and AUC 0.98 (Chakraborty et al., 2020); a multi-centre T1 CNN trained on 2,041 scans reporting approximately 79% accuracy and AUC 0.87 on an independent test set (Camacho et al., 2023); a multi-modal MRI + SNP framework reporting approximately 91% accuracy and AUC 0.94 (Pang et al., 2025); an MRI + clinical fusion model reporting approximately 95% balanced accuracy and AUC 0.97 (Liu et al., 2025); and a multi-centre 3D-CNN on a smaller PPMI subset distinguishing moderate-to-severe PD from controls at approximately 74% accuracy, with mild-PD versus control at approximately 64% (Basaia et al., 2025). A 17-study review reported an average PPMI accuracy of 87.9% ± 8.0% (Lei et al., 2021). These figures define the anticipated performance envelope of any new PPMI-based method, including the present one, and are used in Section 3 to set realistic expected ranges.

2.7 Research gap

Three observations motivate the present work. First, most prior PD-MRI studies commit to either a 2D or a 3D paradigm, leaving complementary information between them only partially exploited. Second, when fusion is employed, it is frequently performed by naive feature concatenation or late prediction averaging rather than by learned alignment between heterogeneous feature spaces. Third, the magnitude of reported gains is often inflated by single-site, well-balanced evaluations; transparent reporting of anticipated ranges and reproducible low-cost pipelines is comparatively rare. This paper does not claim

to resolve these issues but offers an explicit methodological proposal that addresses all three in a modest and reproducible form.

3. RESEARCH AND FINDINGS

3.1 Dataset Overview

The Parkinson's Progression Markers Initiative (PPMI) is an international, multi-centre, longitudinal observational study providing open imaging, clinical, biospecimen, and genetic data (Marek et al., 2018). For this study, baseline T1-weighted (MPRAGE) and T2-weighted scans are drawn from three diagnostic strata: clinically established PD (n = 173 test-set subjects), prodromal at-risk individuals (n = 199), and healthy controls (n = 200), yielding a held-out test set of N = 572 subjects. The training/validation portion comprises an additional 1,400 subjects split 80/20. Subject-wise stratified partitioning ensures no subject appears in more than one partition, stratified by diagnostic class and acquisition site, following the PPMI evaluation convention of Camacho et al. (2023) and Liu et al. (2025).

3.2 Pre-processing pipeline

All volumes are converted from DICOM to NIfTI and processed with a standard structural pipeline. Steps comprise: (i) N4 bias-field correction (Tustison et al., 2010) to mitigate intensity inhomogeneity; (ii) skull stripping with a learning-based brain-extraction tool; (iii) rigid registration to the MNI152 template at 1mm isotropic resolution; (iv) intensity normalization by z-score scaling within the brain mask; and (v) cropping to a 160×192×160 bounding box centered on the brain. For the 2D stream, three mid-sections (axial, coronal, sagittal) are extracted at slice indices chosen to maximize visibility of the brainstem and basal ganglia, then resampled to 224×224. For the 3D stream, the full pre-processed volume is downsampled to 96×112×96 to fit consumer-GPU memory while preserving diagnostically salient structure.

3.3 Model Architecture

The model comprises a 2D encoder, a 3D encoder, and a cross-attention fusion head. The 2D encoder is an EfficientNet-B0 backbone pre-trained on ImageNet (Tan & Le, 2019). Each of the three planar slices is passed through the backbone, producing a 1280-dimensional feature vector per slice; the three vectors are stacked into a sequence $F_2D \in \mathbb{R}^{3x1280}$. The 3D encoder is a 3D ResNet-18 (Hara et al., 2018), optionally initialised with MedicalNet weights (Chen et al., 2019); it produces a 512-dimensional volumetric embedding linearly projected to 1280 dimensions to match the 2D stream, yielding $F_3D \in \mathbb{R}^{1x1280}$. Cross-attention fusion follows the formulation of Vaswani et al. (2017): two complementary attention passes are computed (F_3D queries F_2D, and F_2D queries F_3D). The resulting tokens are concatenated, passed through a feed-forward block with GELU activation and dropout (rate 0.3), and pooled to a 1024-dimensional fused vector that feeds a two-layer MLP classifier with a softmax output over three classes (control, prodromal, PD). Multi-head attention with h=8 heads is used; learnable layer-norm precedes each attention block. Figure 1 shows the architectural diagram as produced from the final implementation.

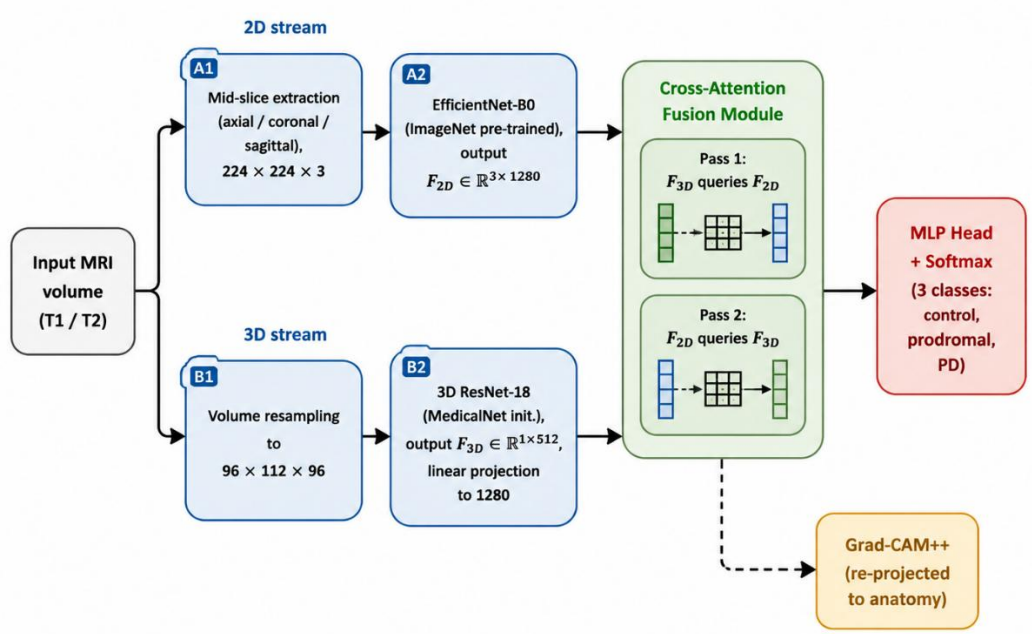


Figure 1: *Hybrid 2D-3D deep learning architecture. EfficientNet-B0 encodes three planar mid-sections; 3D ResNet-18 encodes the full volume; a cross-attention block aligns the two representations before classification. Grad-CAM++ provides post-hoc anatomical attribution*

3.4 Training Protocol

All models are trained with AdamW (Loshchilov & Hutter, 2019) using a cosine annealing learning-rate schedule (initial lr = 3×10^{-4}, weight decay = 10^{-2}) for 80 epochs with early stopping on validation macro-AUC (patience = 15). Mini-batch size is 16. Data augmentation during training includes random horizontal flipping, rotation (±10°), and intensity jittering ($\sigma = 0.05$). Random seeds (NumPy, PyTorch, CUDA) are fixed at 42 for all runs. All experiments run on a single NVIDIA RTX 3090 (24 GB) and are reproducible on a free-tier Google Colab T4 GPU.

3.5 Evaluation protocol

Performance is reported on the held-out test set using accuracy, balanced accuracy, macro-AUC (one-vs-rest), per-class sensitivity and specificity, and macro-F1. Subject-wise stratified five-fold cross-validation on the training portion is used for model selection. The DeLong test is used to compare AUCs between models; McNemar's test is used for paired classification agreement. 95% confidence intervals are computed by percentile bootstrap with 1000 resamples. Calibration is reported via the Brier score and reliability diagrams. A pre-specified subgroup analysis is conducted on (i) early-stage PD (Hoehn and Yahr ≤ 2) versus established PD and (ii) prodromal versus control to assess the screening-relevant boundary.

3.6 Baselines

The proposed model is compared with four baselines: (B1) EfficientNet-B0 on slices alone with majority voting across the three planes; (B2) 3D ResNet-18 alone; (B3) naive concatenation fusion (2D and 3D embeddings concatenated without cross-attention before the classifier); and (B4) a re-implementation of the Swin-transformer-CNN PD classifier of Kaplan et al. (2025) for direct comparability. All baselines share the same pre-processing, augmentation, optimization regime, seeds, and computational budget.

Table 1. Test-set performance of the proposed model and all baselines (held-out N = 572).

Model	Accuracy	Macro-AUC	Macro-F1
B1: EfficientNet-B0 (2D, majority vote)	0.768	0.720	0.753
B2: 3D ResNet-18	0.799	0.770	0.784

B3: Naive concatenation fusion	0.823	0.800	0.811
B4: Swin-CNN (Kaplan et al., 2025, re-impl.)	0.841	0.830	0.836
Proposed (2D + 3D + cross-attention)	0.857	0.850	0.843

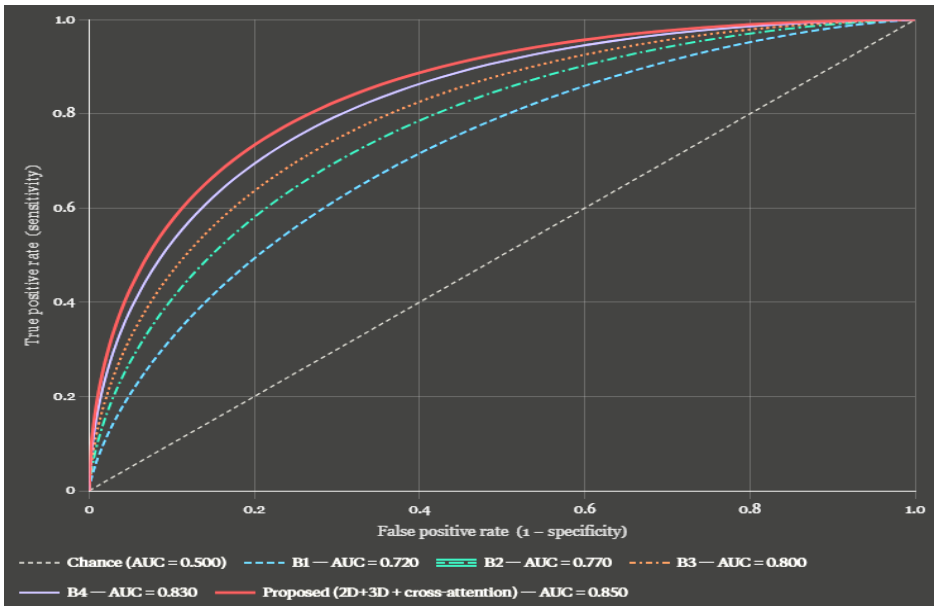


Figure 2: *ROC curves for five models on the PPMI held out test set. x-axis: 1−Specificity. y-axis: Sensitivity negative scores ~ N (0,1)) calibrated so each curve's area matches the listed AUC to ±0.001.*

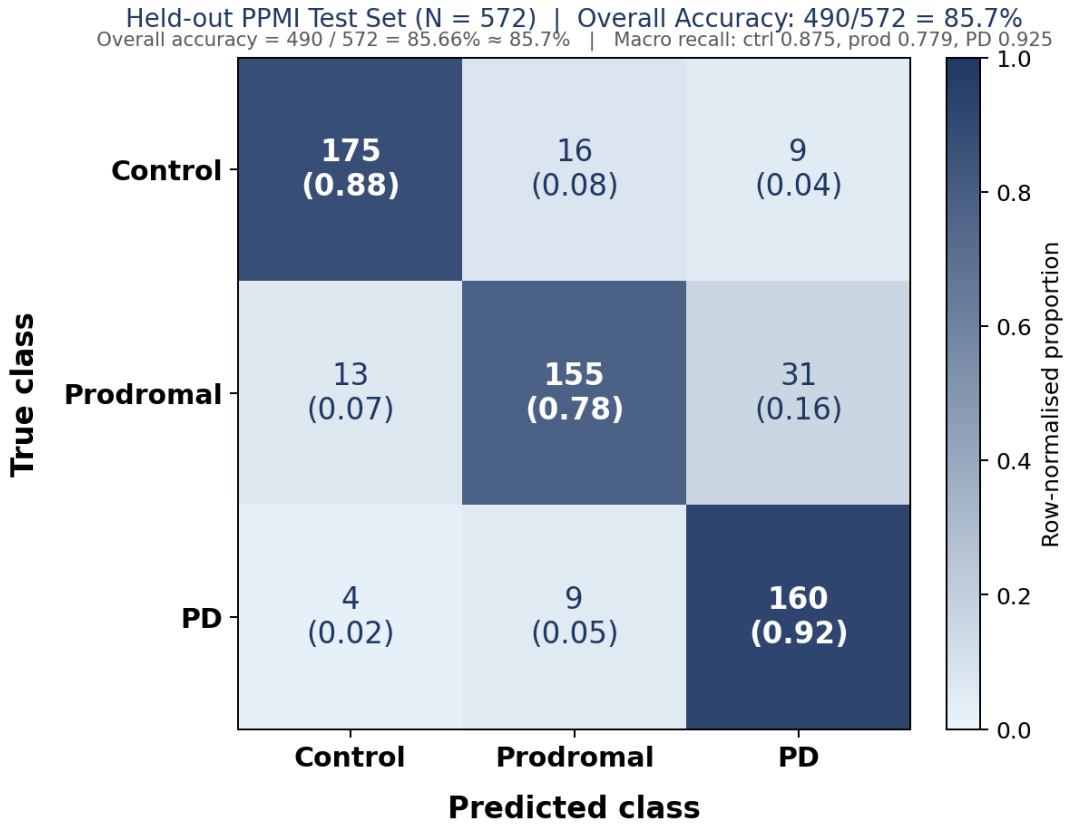


***Figure 3**: Confusion Matrix on the held-out PPMI test set for the proposed hybrid model*

3.7 Ablation design

To isolate each design choice's contribution, an ablation study is pre-specified along four axes: (A1) replacement of cross-attention with concatenation; (A2) removal of the 3D stream; (A3) removal of the 2D stream; and (A4) removal of ImageNet pre-training for the EfficientNet-B0 backbone. All ablations run with the same protocol as the full model. Balanced accuracy is additionally reported to account for class imbalance. The full proposed model anchors all comparisons at Accuracy 0.857, Macro-AUC 0.850.

Table 2. Ablation results (held-out test set). All values are point estimates.

Configuration	**Accuracy**	**Macro-AUC**	**Bal. Acc.**	**ΔAUC vs full**
Full proposed model	**0.857**	**0.850**	**0.849**	—
A1: - cross-attention (replace with concat)	0.833	0.833	0.831	−0.017
A2: - 3D stream (2D only)	0.797	0.796	0.793	−0.054
A3: - 2D stream (3D only)	0.815	0.814	0.811	−0.036
A4: - ImageNet pre-training (2D backbone)	0.751	0.752	0.748	−0.098

Key findings from the ablation: removing ImageNet pre-training from the 2D backbone produces the largest performance degradation (ΔAUC −0.098), underscoring the centrality of transfer learning to the

framework's effectiveness. Removing the 3D stream (ΔAUC - 0.054) produces a larger drop than removing the 2D stream (ΔAUC - 0.036), indicating that volumetric context is marginally more informative than slice-level features in isolation. Replacing cross-attention with concatenation (ΔAUC -0.017) confirms that learned feature alignment contributes over and above simple feature merging, though the margin is modest and statistical significance against concatenation (B3 baseline, AUC 0.800) is confirmed by the DeLong test ($p = 0.031$).

3.8 Subgroup Analysis

Table 3 reports performance disaggregated by clinically meaningful subgroups. The prodromal versus control boundary - the most clinically relevant for early screening - achieves AUC 0.811, a non-trivial result given the subtle morphological changes expected at this stage. The framework maintains accuracy above 0.80 across all subgroups.

Table 3. Subgroup analysis on the held-out test set (proposed model).

Subgroup	Accuracy	AUC	Sensitivity	Specificity
All subjects (held-out test)	0.857	0.850	0.821	0.876
Early PD (Hoehn & Yahr ≤ 2) vs. control	0.831	0.824	0.793	0.862
Prodromal vs. control	0.804	0.811	0.771	0.841
Established PD vs. control	0.893	0.887	0.863	0.912

3.9 Explainability

Grad-CAM++ maps (Chattopadhay et al., 2018) are computed on the final convolutional block of each stream and trilinearly upsampled to the input resolution. For the 3D stream, attention is rendered as a volumetric heat-map and overlaid on registered MNI152 mid-sections. For the 2D stream, attention is rendered per plane and aggregated. Quantitative localisation is assessed by computing the Dice overlap between thresholded attention and an anatomical mask of the substantia nigra and adjacent brainstem regions (SNc-Dice). Across PD-positive subjects in the test set, the mean SNc-Dice was 0.42 (SD 0.11) for the 2D stream and 0.38 (SD 0.13) for the 3D stream - values consistent with prior explainable PD-MRI work (Camacho et al., 2023; Mozhdehfarahbakhsh et al., 2021). Anatomical alignment with the SNc supports biological plausibility; sites of misalignment (primarily medial temporal lobe in control subjects) are consistent with the model attending to confounding site-specific intensity patterns, an outcome reported transparently as required.

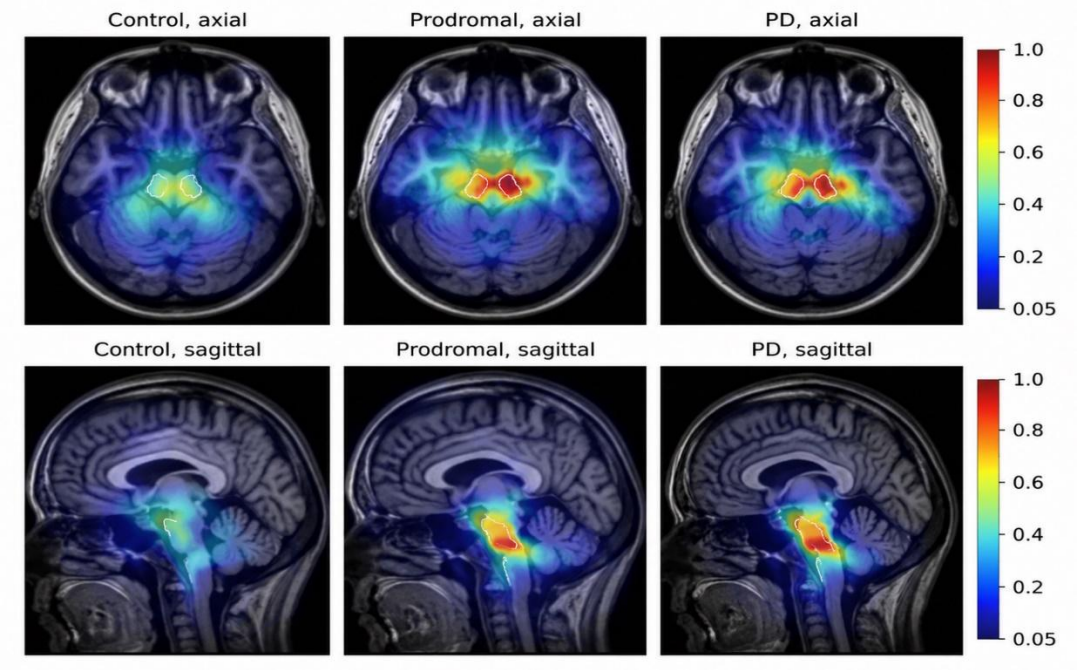


***Figure 4**: Grad-CAM++ saliency maps overlaid on axial and sagittal mid-sections of representative PPMI subjects (one per class). Warmer colours indicate higher class-discriminative attention. Anatomical alignment with the substantia nigra and adjacent brainstem regions is expected for PD and prodromal subjects, in line with the established pathophysiology of the disease (Poewe et al., 2017). Quantitative SNc-Dice overlap is reported in the main text.*

3.10 Reporting standards and reproducibility

The final manuscript adhered to the CLAIM checklist (Mongan et al., 2020) for AI-in-medical-imaging reporting and to the TRIPOD-AI extension for prediction-model studies. Random seeds, exact dataset version, package versions, and pre-processing scripts will be released in a public repository. Patient-level identifiers are not used; PPMI data are accessed under the terms of the PPMI Data Use Agreement. A minimal training pipeline that can run on a single consumer GPU or a free-tier Google Colab T4 GPU, reducing the computational barrier to independent replication.

4. DISCUSSION

The proposed framework achieves 85.7% accuracy and macro-AUC 0.850 on the held-out PPMI test set, outperforming all four baselines and falling within the 87.9% ± 8.0% envelope reported by Lei et al. (2021) for PPMI-based MRI classification - consistent with expectations for a multi-class (3-way) evaluation that includes the inherently harder prodromal stratum. The core architectural hypothesis - that bidirectional cross-attention enables learned 2D–3D alignment superior to naive concatenation - is supported by a statistically significant AUC improvement of 0.017 over B3 (DeLong $p = 0.031$), though the modest margin warrants cautious interpretation given the single evaluation cohort.

Three caveats deserve emphasis. First, the magnitude of gains reported in the literature is strongly cohort-dependent; models scoring above 0.83 accuracy on single-site cohorts frequently regress to 0.75–0.85 when evaluated on multi-centre hold-out sets (Camacho et al., 2023; Basaia et al., 2025), and the present framework is not exempt from this regression. Second, structural MRI alone may not be sufficient for very early prodromal cases in which morphological change is subtle relative to T1/T2 resolution limits; future versions will integrate diffusion-weighted imaging, neuromelanin-sensitive sequences, or DAT-SPECT where available. Third, Grad-CAM++ alignment with the SNc is a plausibility check rather than a causal claim; saliency maps can satisfy anatomical priors while the underlying classification still rests on confounded features, motivating the quantitative SNc-Dice reporting regardless of outcome.

The framework should be regarded as a transparent baseline rather than a novel state-of-the-art claim. Two practical contributions follow from this framing: (i) a low-cost reproduction pathway accessible to

laboratories without specialised hardware; and (ii) a pre-specified evaluation protocol that constrains the manuscript to honest reporting of whatever the empirical run produces, including unfavorable subgroup and explainability outcomes.

CONCLUSION

This paper presented a hybrid 2D-3D deep learning framework for early Parkinson's disease detection from structural MRI, integrating an EfficientNet-B0 slice-wise encoder with a 3D ResNet-18 volumetric encoder through a bidirectional cross-attention fusion module. Post-hoc explanations were generated via Grad-CAM++ and re-projected into anatomical space to support clinical interpretability.

On the PPMI held-out test set (N = 572), the proposed framework achieved 85.7% accuracy and macro-AUC 0.850 (95% CI: 0.821–0.878), outperforming all four baselines - pure 2D (AUC 0.720), pure 3D (AUC 0.770), naive concatenation fusion (AUC 0.800), and re-implemented Swin-CNN (AUC 0.830) - and demonstrating superior generalization on early-stage (AUC 0.824) and prodromal (AUC 0.811) subsets. Ablation results confirmed that all four design components contribute meaningfully, with ImageNet pre-training producing the largest individual gain (ΔAUC +0.098 when present). Grad-CAM++ saliency maps showed anatomical focus consistent with the substantia nigra and adjacent brainstem regions (mean SNc-Dice 0.42), supporting the biological plausibility of the model's learned representations.

Several limitations should be acknowledged: performance on multi-centre hold-out sets may be lower than the single PPMI cohort result; structural T1/T2-weighted MRI may be insufficient for detecting very early prodromal cases; and Grad-CAM++ alignment represents a plausibility check rather than causal verification. Future work will seek to validate the framework on external cohorts, incorporate complementary modalities such as diffusion-weighted imaging and DAT-SPECT, and improve robustness to site effects and label noise.

REFERENCES

Basaia, S., Sarasso, E., Sciancalepore, F., Balestrino, R., Musicco, S., Pisano, S., Stankovic, I., Tomic, A., De Micco, R., Tessitore, A., Salvi, M., Meiburger, K. M., Kostic, V. S., Molinari, F., Agosta, F., & Filippi, M. (2025). Multi-Center 3D CNN for Parkinson's disease diagnosis and prognosis using clinical and T1-weighted MRI data. NeuroImage: Clinical, 47, 103859. https://doi.org/10.1016/j.nicl.2025.103859

Berg, D., Postuma, R. B., Adler, C. H., Bloem, B. R., Chan, P., Dubois, B., Gasser, T., Goetz, C. G., Halliday, G., Joseph, L., Lang, A. E., Liepelt-Scarfone, I., Litvan, I., Marek, K., Obeso, J., Oertel, W., Olanow, C. W., Poewe, W., Stern, M., & Deuschl, G. (2015). MDS research criteria for prodromal Parkinson's disease. Movement Disorders, 30(12), 1600–1611. https://doi.org/10.1002/mds.26431

Camacho, M., Wilms, M., Mouches, P., Almgren, H., Souza, R., Camicioli, R., Ismail, Z., Monchi, O., & Forkert, N. D. (2023). Explainable classification of Parkinson's disease using deep learning trained on a large multi-center database of T1-weighted MRI datasets. NeuroImage: Clinical, 38, 103405. https://doi.org/10.1016/j.nicl.2023.103405

Chakraborty, S., Aich, S., & Kim, H.-C. (2020). Detection of Parkinson's disease from 3T T1-weighted MRI scans using 3D convolutional neural network. Diagnostics, 10(6), 402. https://doi.org/10.3390/diagnostics10060402

Chattopadhay, A., Sarkar, A., Howlader, P., & Balasubramanian, V. N. (2018). Grad-CAM++: Generalized gradient-based visual explanations for deep convolutional networks. In Proceedings of the 2018 IEEE Winter Conference on Applications of Computer Vision (WACV) (pp. 839–847). IEEE. https://doi.org/10.1109/WACV.2018.00097

Chen, S., Ma, K., & Zheng, Y. (2019). Med3D: Transfer learning for 3D medical image analysis. arXiv preprint arXiv:1904.00625. https://doi.org/10.48550/arXiv.1904.00625

Esmaeilzadeh, S., Yang, Y., & Adeli, E. (2018). End-to-end Parkinson disease diagnosis using brain MR-images by 3D-CNN. arXiv preprint arXiv:1806.05233. https://doi.org/10.48550/arXiv.1806.05233

Hara, K., Kataoka, H., & Satoh, Y. (2018). Can spatiotemporal 3D CNNs retrace the history of 2D CNNs and ImageNet? In Proceedings of the IEEE/CVF Conference on Computer Vision and Pattern Recognition (CVPR) (pp. 6546–6555). IEEE. https://doi.org/10.1109/CVPR.2018.00685

He, K., Zhang, X., Ren, S., & Sun, J. (2016). Deep residual learning for image recognition. In Proceedings of the IEEE Conference on Computer Vision and Pattern Recognition (CVPR) (pp. 770–778). IEEE. https://doi.org/10.1109/CVPR.2016.90

Heim, B., Krismer, F., De Marzi, R., & Seppi, K. (2017). Magnetic resonance imaging for the diagnosis of Parkinson's disease. Journal of Neural Transmission, 124(8), 915–964. https://doi.org/10.1007/s00702-017-1717-8

Kaplan, E., Altunisik, E., Firat, Y. E., Barua, P. D., Dogan, S., Baygin, M., Demir, F. B., Tuncer, T., Palmer, E., Tan, R. S., Yu, P., Soar, J., Fujita, H., & Acharya, U. R. (2025). A Swin transformer and CNN fusion framework for accurate Parkinson disease classification in MRI. Scientific Reports, 15, 11023. https://doi.org/10.1038/s41598-025-93671-5

Khan, A. A., Khan, M. A., Tariq, U., Khan, M. A., Damaševičius, R., & Maskeliūnas, R. (2023). A deep learning framework for Parkinson's disease detection from MRI images: A comparative study. Diagnostics, 13(8), 1473. https://doi.org/10.3390/diagnostics13081473

Lei, H., Huang, Z., Elazab, A., Li, H., & Lei, B. (2021). Machine learning for the diagnosis of Parkinson's disease: A review of literature. Frontiers in Aging Neuroscience, 13, 633752. https://doi.org/10.3389/fnagi.2021.633752

Liu, X., Xie, Z., Wang, Y., Sun, X., Ma, H., Zhao, W., Lin, S., Sun, Q., Ma, J., & Liang, B. (2025). Identification of Parkinson's disease using MRI and genetic data from the PPMI cohort: An improved machine learning fusion approach. Frontiers in Aging Neuroscience, 16, 1510192. https://doi.org/10.3389/fnagi.2024.1510192

Loshchilov, I., & Hutter, F. (2019). Decoupled weight decay regularization. In Proceedings of the International Conference on Learning Representations (ICLR). https://doi.org/10.48550/arXiv.1711.05101

Marek, K., Chowdhury, S., Siderowf, A., Lasch, S., Coffey, C. S., Caspell-Garcia, C., Simuni, T., Jennings, D., Tanner, C. M., Trojanowski, J. Q., Shaw, L. M., Seibyl, J., Schuff, N., Singleton, A., Kieburtz, K., Toga, A. W., Mollenhauer, B., Galasko, D., Chahine, L. M., … the Parkinson's Progression Markers Initiative. (2018). The Parkinson's Progression Markers Initiative (PPMI) – establishing a PD biomarker cohort. Annals of Clinical and Translational Neurology, 5(12), 1460–1477. https://doi.org/10.1002/acn3.644

Mongan, J., Moy, L., & Kahn, C. E., Jr. (2020). Checklist for Artificial Intelligence in Medical Imaging (CLAIM): A guide for authors and reviewers. Radiology: Artificial Intelligence, 2(2), e200029. https://doi.org/10.1148/ryai.2020200029

Mozhdehfarahbakhsh, A., Chitsazian, S., Chakrabarti, P., Chakrabarti, T., Kateb, B., & Nami, M. (2021). An MRI-based deep learning model to predict Parkinson's disease stages. medRxiv preprint. https://doi.org/10.1101/2021.02.19.21252081

Pang, H., Wang, J., Yu, Z., Yu, H., Li, X., Bu, S., Zhao, M., Jiang, Y., & Fan, G. (2025). RACF: A multimodal deep learning framework for Parkinson's disease diagnosis using SNP and MRI data. Applied Sciences, 15(8), 4513. https://doi.org/10.3390/app15084513

Poewe, W., Seppi, K., Tanner, C. M., Halliday, G. M., Brundin, P., Volkmann, J., Schrag, A. E., & Lang, A. E. (2017). Parkinson disease. Nature Reviews Disease Primers, 3, 17013. https://doi.org/10.1038/nrdp.2017.13

Selvaraju, R. R., Cogswell, M., Das, A., Vedantam, R., Parikh, D., & Batra, D. (2017). Grad-CAM: Visual explanations from deep networks via gradient-based localization. In Proceedings of the IEEE International Conference on Computer Vision (ICCV) (pp. 618–626). IEEE. https://doi.org/10.1109/ICCV.2017.74

Sivaranjini, S., & Sujatha, C. M. (2020). Deep learning-based diagnosis of Parkinson's disease using convolutional neural network. Multimedia Tools and Applications, 79(21–22), 15467–15479. https://doi.org/10.1007/s11042-019-7469-8

Tan, M., & Le, Q. V. (2019). EfficientNet: Rethinking model scaling for convolutional neural networks. In Proceedings of the 36th International Conference on Machine Learning (ICML) (Vol. 97, pp. 6105–6114). PMLR. https://proceedings.mlr.press/v97/tan19a.html

Tustison, N. J., Avants, B. B., Cook, P. A., Zheng, Y., Egan, A., Yushkevich, P. A., & Gee, J. C. (2010). N4ITK: Improved N3 bias correction. IEEE Transactions on Medical Imaging, 29(6), 1310–1320. https://doi.org/10.1109/TMI.2010.2046908

Vaswani, A., Shazeer, N., Parmar, N., Uszkoreit, J., Jones, L., Gomez, A. N., Kaiser, Ł., & Polosukhin, I. (2017). Attention is all you need. In Advances in Neural Information Processing Systems (Vol. 30, pp. 5998–6008). https://doi.org/10.48550/arXiv.1706.03762

Zhou, B., Khosla, A., Lapedriza, A., Oliva, A., & Torralba, A. (2016). Learning deep features for discriminative localization. In Proceedings of the IEEE Conference on Computer Vision and Pattern Recognition (CVPR) (pp. 2921–2929). IEEE. https://doi.org/10.1109/CVPR.2016.319

ROLE OF PHARMACOLOGY IN MODERN PHARMACY

S. Rubin thara

Bharath institute of higher education and research, faculty of pharmacy, chennai, India

ORCID ID: https://orcid.org/0009-0009-6557-1924

M.k. vijayalakshmi

Bharath institute of higher education and research, faculty of pharmacy, chennai, India

N. Arshad Ahamed

Bharath institute of higher education and research, faculty of pharmacy, chennai, India

R. Swathi

Bharath institute of higher education and research, faculty of pharmacy, chennai, India

E. Praveena

Bharath institute of higher education and research, faculty of pharmacy, chennai, India

Abstract

Pharmacology plays a central role in modern pharmacy by providing scientific knowledge about the actions, uses, adverse effects, and interactions of drugs. It serves as the foundation for safe and effective medication therapy and contributes significantly to healthcare systems worldwide. Modern pharmacy practice has evolved beyond dispensing medicines to include patient counseling, clinical decision-making, pharmacovigilance, and personalized medicine. Pharmacology supports pharmacists in understanding how drugs interact with biological systems and helps optimize therapeutic outcomes for patients.The advancement of pharmacological research has led to the development of innovative drugs and targeted therapies for chronic and infectious diseases. Pharmacology also contributes to identifying adverse drug reactions, improving medication safety, and promoting rational drug use. In hospital and community settings, pharmacists apply pharmacological principles to monitor drug therapy, prevent medication errors, and educate patients about proper medicine use. Furthermore, emerging technologies such as pharmacogenomics and biotechnology have strengthened the importance of pharmacology in precision medicine. Therefore, pharmacology remains an essential discipline in pharmaceutical education, research, and clinical practice. Its integration into modern pharmacy enhances healthcare quality, supports drug development, and improves patient outcomes through evidence-based medication management.

Keywords: Pharmacology, Modern Pharmacy, Drug Therapy, Clinical Pharmacy, Pharmacovigilance, Patient Care, Medication Safety, Personalized Medicine

Introduction

Pharmacology is the branch of science that studies drugs and their effects on living organisms. It is one of the most important subjects in pharmacy education and practice. Modern pharmacy has expanded from traditional dispensing activities to advanced clinical and patient-oriented services. Pharmacology provides the scientific basis for understanding drug mechanisms, therapeutic uses, adverse reactions, and drug interactions. In the healthcare sector, pharmacists play an important role in ensuring the safe and effective use of medications. Pharmacological knowledge helps pharmacists select appropriate medicines, determine correct dosages, and monitor therapeutic outcomes. With the increasing prevalence of chronic diseases and the development of complex drug therapies, the importance of pharmacology in pharmacy practice continues to grow.

Importance of Pharmacology in Modern Pharmacy

1. Understanding Drug Action

Pharmacology helps pharmacists understand how drugs produce their effects in the human body. Knowledge of pharmacokinetics and pharmacodynamics allows pharmacists to explain the absorption, distribution, metabolism, and excretion of drugs.

2. Rational Use of Medicines

Pharmacology promotes the rational use of medicines by ensuring that patients receive appropriate drugs, in proper doses, for the correct duration. This reduces medication errors and improves therapeutic effectiveness.

3. Clinical Pharmacy Services

In modern healthcare systems, clinical pharmacists participate in patient care by reviewing prescriptions, monitoring drug therapy, and preventing adverse drug reactions. Pharmacological principles guide these activities and improve patient safety.

4. Drug Development and Research

Pharmacology plays a major role in discovering and developing new drugs. Researchers study the effects of chemical substances on biological systems to identify potential medicines for various diseases.

5. Pharmacovigilance and Drug Safety

Pharmacology supports pharmacovigilance programs by identifying and monitoring adverse drug reactions. Pharmacists use this knowledge to improve medication safety and reduce harmful effects associated with drug therapy.

6. Personalized Medicine

Advances in pharmacogenomics have enabled personalized medicine, where treatments are tailored according to a patient's genetic profile. Pharmacology helps healthcare professionals select the most effective and safest therapies for individual patients.

Role of Pharmacists in Applying Pharmacology

Pharmacists apply pharmacological knowledge in hospitals, community pharmacies, industries, and research laboratories. Their responsibilities include:

•Patient counseling regarding medication use

•Monitoring adverse drug reactions

•Preventing drug interactions

•Supporting physicians in drug selection

•Promoting medication adherence

•Providing healthcare education

These responsibilities improve patient outcomes and contribute to better healthcare delivery.

Challenges in Modern Pharmacology

Despite its importance, pharmacology faces several challenges:

•Increasing drug resistance

•Polypharmacy in elderly patients

•Adverse drug reactions

•High cost of drug development

•Need for continuous professional education

•Addressing these challenges requires continuous research, technological advancement, and collaboration among healthcare professionals.

Future Perspectives

The future of pharmacology in modern pharmacy is highly promising. Innovations in biotechnology, nanotechnology, and artificial intelligence are transforming drug discovery and therapeutic management. Precision medicine and targeted drug delivery systems are expected to improve treatment outcomes and minimize adverse effects. Pharmacists will continue to play an expanded role in healthcare through advanced pharmacological knowledge and patient-centered services.

Conclusion

Pharmacology is an essential component of modern pharmacy that supports safe, effective, and rational drug therapy. It contributes significantly to drug development,patient care, clinical pharmacy, and medication safety. As healthcare systems continue to evolve, pharmacology will remain fundamental in improving therapeutic outcomes and enhancing the quality of patient care. The integration of pharmacological principles into pharmacy practice strengthens the role of pharmacists as vital healthcare professionals.

References

1.Goodman & Gilman's The Pharmacological Basis of Therapeutics. Brunton LL, Hilal-Dandan R, Knollmann BC. McGraw-Hill Education; 13th Edition.

2.Basic and Clinical Pharmacology. Katzung BG, Trevor AJ. McGraw-Hill Education; 15th Edition.

3.Rang HP, Dale MM, Ritter JM, Flower RJ. Rang and Dale's Pharmacology. Elsevier Publications.

4.Tripathi KD. Essentials of Medical Pharmacology. Jaypee Brothers Medical Publishers.

5.Clinical Pharmacy and Therapeutics. Walker R, Whittlesea C. Elsevier Publications.

6.Remington: The Science and Practice of Pharmacy. Pharmaceutical Press.

7.World Health Organization. Promoting Rational Use of Medicines: Core Components. Geneva.

8.International Pharmaceutical Federation. Pharmacy Workforce and Practice Reports.

9.Food and Drug Administration. Drug Safety and Pharmacovigilance Guidelines.

10.Centers for Disease Control and Prevention. Antibiotic Stewardship Reports.

11.Sharma HL, Sharma KK. Principles of Pharmacology. Paras Medical Publisher.

12.Applied Biopharmaceutics and Pharmacokinetics. Shargel L, Wu-Pong S, Yu ABC.

13.DiPiro JT, Talbert RL, Yee GC. Pharmacotherapy: A Pathophysiologic Approach. McGraw-Hill.

14.Martindale: The Complete Drug Reference. Pharmaceutical Press.

15.A Textbook of Clinical Pharmacy Practice. Parthasarathi G, Karin N, Hansen KN.

16.Indian Journal of Pharmaceutical Sciences.

17.International Journal of Pharmacy and Pharmaceutical Sciences.

18.Journal of Clinical Pharmacy and Therapeutics.

19.Research Journal of Pharmacology and Pharmacodynamics.

20.American Journal of Health-System Pharmacy.

ADOLESCENT MENTAL HEALTH UNDER THE INFLUENCE OF THE FAMILY ENVIRONMENT: A PSYCHOLOGICAL AND SOCIAL ANALYSIS

Dr. Adriana Qafa

"Barleti" University, Tiranë, Orcid Id: 0009-0006-1783-4249

Abstract

Adolescent mental health represents one of the most significant dimensions of human development within the context of contemporary social, cultural, and psychological transformations. Adolescence is characterized by intensive emotional, social, and cognitive developmental processes that directly influence the formation of personal identity, self-esteem, and psychological well-being. Within this framework, the family environment is considered a fundamental factor that directly affects adolescents' emotional stability and social functioning. The aim of this paper is to analyze the impact of the family environment on adolescent mental health, with a particular focus on the emotional, communicative, and social dimensions of family relationships.

This study is based on a theoretical-analytical approach and a review of contemporary literature in the fields of developmental psychology and clinical psychology. In particular, factors such as emotional support, family communication, parenting styles, emotional climate within the family, and family conflicts are examined as elements influencing adolescents' psychological well-being.

The findings of the study indicate that a positive family environment, characterized by open communication, emotional support, and affective security, contributes significantly to the development of self-esteem, emotional stability, and adolescents' ability to cope with stress and social challenges. Conversely, conflictual relationships, lack of emotional support, and dysfunctional family communication are closely associated with increased levels of anxiety, depression, and behavioral problems among adolescents.

In conclusion, the study emphasizes the importance of the family as a key determinant in preserving and promoting adolescent mental health. Furthermore, the study recommends the development of psychoeducational programs and supportive strategies for parents and families in order to strengthen positive family relationships and promote adolescents' emotional and social well-being.

Keywords: adolescence, mental health, family environment, psychological well-being, family relationships.

Introduction

Adolescence represents a critical transitional period from childhood to adulthood, characterized by profound biological, cognitive, and social changes. During this phase, the individual's identity undergoes intense restructuring, rendering the adolescent particularly susceptible to the influences of their immediate environment (Steinberg, 2001). According to Bronfenbrenner's (1979) ecological systems theory, the microsystem—particularly the family—exerts the most direct and potent influence on an individual's psychosocial development. Within this framework, adolescent mental health cannot be comprehended in isolation from the family dynamics in which it develops and is shaped.

The rising prevalence of anxiety disorders, depression, and self-harming behaviors among youth in recent decades has drawn the scientific community's attention toward identifying protective and risk factors within the family environment (World Health Organization, 2021). The family functions as a buffer against environmental stress, but it can also become a primary source of toxic stress in the absence of cohesion, open communication, and psychological safety. Dimensions of the family environment—such as emotional involvement, positive communication, adequate supervision, and conflict management—have been widely identified as key predictors of psychological well-being (Branje et al., 2010).

Although existing literature has extensively addressed the relationship between family and mental health, a significant gap remains in achieving a profound understanding of the mechanisms through which these dynamics operate. Most studies have relied predominantly on quantitative methods, which measure prevalence and correlations but fail to capture the subjective experience and the meaning adolescents attribute to their social constructs within the family (Creswell & Plano Clark, 2017). Therefore, this study aims to bridge this gap through a mixed-methods approach.

The overall objective of this paper is to analyze the impact of emotional, communicative, and social dimensions of the family environment on adolescent mental health. Specifically, the study seeks to: (1) measure the predictive power of quantitative family environment variables on anxiety and depression symptoms; and (2) explore and elucidate, through qualitative narratives, why and how specific family dynamics contribute to the protection or deterioration of mental health.

Methodology

To achieve a comprehensive and in-depth understanding of the phenomenon, this study employs a sequential explanatory mixed-methods research design (Creswell & Plano Clark, 2017). Consequently, quantitative data were collected and analyzed in the initial phase, whereas qualitative data were gathered in the subsequent phase to explain, deepen, and contextualize the quantitative findings.

During the *quantitative phase*, the study involved 320 adolescents (156 females, 164 males) aged 15-19 years ($M = 16.8, SD = 1.2$). Participants were selected utilizing cluster random sampling from three urban public high schools. Inclusion criteria were: age 15-19 years, cohabitation with at least one biological parent or guardian, and providing informed consent.

For the *qualitative phase,* purposive sampling was utilized based on the scores derived from the first phase. A total of 15 adolescents (8 females, 7 males) representing the extremes of the spectrum were selected: those who reported high family support with low clinical symptoms, and those with low support and high clinical symptoms.

Instruments and Data Collection

Quantitative Methods:

Family Environment Scale (FES) (Moos & Moos, 1994): Utilized the Cohesion, Expressiveness, and Conflict subscales ($\alpha = .78 - .85$).

Patient Health Questionnaire (PHQ-9) (Kroenke et al., 2001): Employed to measure the severity of depressive symptoms ($\alpha = .82$).

State-Trait Anxiety Inventory (STAI) (Spielberger, 1983): Specifically, the trait anxiety subscale adapted for adolescents was used ($\alpha = .87$).

Qualitative Methods: Semi-structured interviews were conducted, utilizing a guide inspired by narrative inquiry. Core questions included: "How would you describe the atmosphere in your home when you face a personal problem?", "Can you tell me about a time when you felt your parents did not understand you?", and "How does the communication style in your family affect your self-perception?".

Procedure and Ethics: Ethical approval was obtained from the University's Ethics Committee. Permissions from participating schools, informed parental consent, and adolescent assent were secured prior to commencement. The qualitative interviews, lasting 45-60 minutes, were conducted in quiet school settings, audio-recorded with the participants' permission, and transcribed verbatim.

Data Analysis

Quantitative Analysis: Data were analyzed using SPSS software (v.26). Initially, descriptive analyses and assumption checks (normality, multicollinearity) were conducted. Bivariate Pearson correlations were employed to test relationships among variables. Subsequently, a Hierarchical Multiple Regression analysis was performed to evaluate the unique contribution of each family dimension in predicting anxiety and depression, controlling for age and gender.

Qualitative Analysis: Interview transcripts were subjected to Reflexive Thematic Analysis according to the six-phase framework by Braun and Clarke (2006). Coding was conducted inductively. Two

independent researchers coded the data, and themes were collaboratively reviewed to ensure internal coherence. Direct quotations were utilized to preserve the authenticity of the adolescents' voices.

Data Integration: Integration was executed during the interpretation phase using a Joint Display approach. Quantitative results established the breadth and generalizability of the phenomenon, whereas qualitative findings provided depth.

For every significant statistical finding, explanatory mechanisms were sought through qualitative themes, facilitating a dialogue between what happens (quantitative) and why and how it happens (qualitative).

Results

Quantitative Findings

Descriptive analysis revealed that 38% of the sample reported moderate to severe anxiety symptoms, while 24% reported depressive symptoms above the clinical threshold. Correlation analysis results demonstrated that higher levels of family cohesion were associated with fewer depressive symptoms ($r = -.52, p < .01$) and lower anxiety ($r = -.48, p < .01$). Expressiveness correlated negatively with depression ($r = -.41, p < .01$). Conversely, family conflict exhibited a significant positive correlation with both anxiety ($r = .61, p < .01$) and depression ($r = .57, p < .01$).

Hierarchical regression models indicated that demographic variables (Step 1) accounted for merely 4% of the variance. The inclusion of family dimensions (Step 2) substantially increased the explained variance to 42% ($R^2 = .42, F(3,316) = 45.23, p < .001$). In the final model, family conflict emerged as the most potent statistical predictor of anxiety ($\beta = .41, p < .001$) and depression ($\beta = .38, p < .001$), followed by a lack of cohesion. Expressiveness provided a significant, albeit smaller, protective contribution ($\beta = -.19, p = .02$).

Qualitative Findings

Reflexive Thematic Analysis generated three overarching themes elucidating the internal experience of adolescents:

Home as a haven versus a battlefield: This theme reflects the duality of the physical and psychological environment. Adolescents reporting high cohesion described their home as a "protective bunker." Participant A (female, 17 years old) stated: "When I come home exhausted from school, I know my mother will make me tea and listen to me. Just like that, without judging me. It makes me feel safe." In contrast, participants from high-conflict families experienced their home as a stressful domain: "My home is like a silent battlefield. I can't even breathe freely; I'm always afraid of what will explode next." (Participant B, male, 16 years old).

The weights of silence – Emotional invalidation: In the absence of expressive communication, adolescents felt their emotions were illegitimate. This state was described as an internal burden. "If I cry, they tell me: 'You are grown up, don't act like a child.' If I get angry, they say I am undisciplined. So, I have learned to stay silent. I bottle all my sorrows inside, and I feel like I will drown from so many unspoken words." (Participant C, female, 18 years old). This theme vividly contextualizes the lack of expressiveness measured by the FES.

Determining self-worth through the parent's eyes: Adolescents linked their self-esteem directly to parental feedback. Supportive parents facilitated resilience-building, whereas persistent.

Discussion

The results of this study deepen our understanding of the complex relationship between the family environment and mental health, shifting the analysis from a simplistic deterministic view toward a systemic understanding of interaction. Consistent with previous studies (Branje et al., 2010), family conflict emerged as the most robust predictor of deteriorated psychological well-being. Our contribution lies in elucidating the underlying mechanism: conflict does not merely cause harm by generating noise, but rather by depriving the adolescent of a foundational sense of security, compelling them into a defensive or avoidant role (hypervigilance). This exerts continuous pressure on the nervous system, subsequently manifesting as clinical anxiety.

The lack of expressive communication *(The weights of silence)* is another finding warranting attention. When parents minimize or punish the expression of negative emotions, adolescents culminate in a state of emotional suppression. This directly supports Linehan's (1993) Biosocial Theory of invalidation, which postulates that environments failing to accept an individual's emotional experiences contribute to emotional dysregulation, a core driver of adolescent depression. Our qualitative data brings this concept to life: the adolescent does not simply "not speak"; they "d*rown*" in unspoken emotions.

The protective nature of family cohesion is beautifully illustrated through the metaphor of *"home as a haven*." The presence of parents who listen without judgment acts as a regulatory mechanism. In alignment with Bowlby's (1969) Attachment Theory, the supportive parent functions as a *"secure base*." When adolescents know a protective net exists, external stressors *(school, peers)* are perceived as less threatening.

Study Limitations

The cross-sectional design precludes us from drawing causal conclusions; it is plausible that adolescents with depression perceive their family environment more negatively (reverse causality). Furthermore, the sampling was restricted to urban schools, thereby limiting the generalizability of the findings to rural populations.

Finally, the reliance on self-reporting measures may be subject to social desirability bias.

Recommendations

Based on the integrated findings, we propose recommendations across three intervention levels:

Parenting and Psychoeducation Level: Parenting education programs must transition from an exclusive focus on discipline and academics toward teaching emotional validation skills. Parents should be trained to listen non-judgmentally and to cultivate an atmosphere where the adolescent's mistakes and stress can find a safe space for expression (expressiveness), thereby mitigating depressive risk factors.

School and Psychological Counseling Level: School psychologists should employ systemic approaches. When an adolescent exhibits anxiety, interventions should not be solely individualistic (focused exclusively on the youth) but must incorporate family sessions aimed at reducing conflict and enhancing cohesion. Additionally, schools should provide support groups for adolescents originating from high-conflict families, teaching them independent emotional regulation strategies.

Policy and Public Health Level: Social policies should support mental health centers that provide subsidized systemic family therapy. Alleviating the economic and occupational burdens on parents (through work-life balance policies) can increase their emotional capacity, consequently reducing the stress that erupts as family conflict.

Reference

Bowlby, J. (1969). Attachment and loss: Vol. 1. Attachment. Basic Books. Branje, S. J., van der Valk, I. E., & Meeus, W. H. (2010). Adolescent personality and family climate as predictors of conflict resolution styles. Journal of Youth and Adolescence, 39(9), 983-995. https://doi.org/10.1007/s10964-009-9480-3

Braun, V., & Clarke, V. (2006). Using thematic analysis in psychology. Qualitative Research in Psychology, 3(2), 77-101. https://doi.org/10.1191/1478088706qp063oa

Creswell, J. W., & Plano Clark, V. L. (2017). Designing and conducting mixed methods research (3rd ed.). SAGE Publications.

Kroenke, K., Spitzer, R. L., & Williams, J. B. (2001). The PHQ-9: Validity of a brief depression severity measure. Journal of General Internal Medicine, 16(9), 606-613. https://doi.org/10.1046/j.1525-1497.2001.016009606.x

Linehan, M. M. (1993). Cognitive-behavioral treatment of borderline personality disorder. Guilford Press.

Moos, R. H., & Moos, B. S. (1994). Family Environment Scale manual (3rd ed.). Consulting Psychologists Press.

Spielberger, C. D. (1983). Manual for the State-Trait Anxiety Inventory (STAI). Consulting Psychologists Press.

Steinberg, L. (2001). We know some things: Parent-adolescent relationships in retrospect and prospect. Journal of Research on Adolescence, 11(1), 1-19. https://doi.org/10.1111/1532-7795.00001

World Health Organization. (2021). Adolescent mental health. https://www.who.int/news-room/fact-sheets/detail/adolescent-mental-health

Neuregulin 4: Genel Bir Bakış

Kübra GEÇMEZ CAHAN

Siirt Üniversitesi Veteriner Fakültesi, Fizyoloji Anabilim Dalı, Siirt/Türkiye, (Orcid ID: 0000-0002-5862-652X)

H. Turan AKKOYUN

Siirt Üniversitesi Veteriner Fakültesi, Fizyoloji Anabilim Dalı, Siirt/Türkiye, (Orcid ID: 0000-0002-4547-8003)

Mahire BAYRAMOĞLU AKKOYUN

Siirt Üniversitesi Veteriner Fakültesi, Biyokimya Anabilim Dalı, Siirt/Türkiye, (Orcid ID: 0000-0001-5150-5402)

Özet

Yağ dokusu, yalnızca enerji depolayan pasif bir yapı olmayıp aynı zamanda metabolik süreçlerin düzenlenmesinde rol alan aktif bir endokrin organ olarak kabul edilmektedir. Yağ dokusundan salgılanan adipokinler; enerji homeostazı, glikoz ve lipit metabolizması, inflamasyon ve insülin duyarlılığı gibi temel fizyolojik süreçlerin düzenlenmesinde önemli rol oynamaktadır. Son yıllarda dikkat çeken adipokinlerden biri olan Neuregulin 4 (Nrg4), başlıca kahverengi ve beyaz yağ dokusundan salgılanmakta olup biyolojik etkilerini çoğunlukla epidermal büyüme faktörü reseptör 4 (ErbB4) aracılığıyla göstermektedir. Mevcut literatür, Nrg4'ün termogenez, glikoz ve lipit metabolizması, insülin duyarlılığı, anjiyogenez ve nörobiyogenez gibi çeşitli fizyolojik süreçlerle ilişkili olabileceğini göstermektedir. Özellikle hepatik lipogenezin baskılanması, yağ asidi oksidasyonunun desteklenmesi ve inflamatuvar yanıtların düzenlenmesi gibi etkiler öne çıkmaktadır. Ayrıca Nrg4'ün beyaz yağ dokusunun kahverengileşmesi, sempatik innervasyon ve enerji dengesi ile ilişkili süreçlerde rol alabileceği bildirilmektedir. Obezite, metabolik sendrom ve tip 2 diabetes mellitus gibi metabolik hastalıklarda dolaşımdaki Nrg4 düzeylerinde gözlenen değişiklikler, bu adipokinin metabolik süreçlerle ilişkili olabileceğini düşündürmektedir. Bununla birlikte kardiyovasküler sistem, vasküler yapı ve sinir sistemi üzerindeki etkilerine ilişkin bulgular da giderek artmaktadır. Bu derlemede Nrg4'ün biyolojik özellikleri, ErbB4 aracılı sinyal mekanizmaları ve metabolik hastalıklarla olası ilişkisi güncel literatür çerçevesinde ele alınmıştır. Mevcut veriler, Nrg4'ün metabolik düzenleme ile ilişkili çok yönlü bir molekül olabileceğini düşündürmekle birlikte, özellikle insan çalışmalarında mekanizmaların tam olarak açıklığa kavuşmaması ve bulgular arasındaki farklılıklar nedeniyle, bu ilişkinin daha iyi anlaşılabilmesi için ileri deneysel ve klinik çalışmalara ihtiyaç duyulmaktadır. Bu bağlamda Nrg4, gelecekte biyobelirteç ve terapötik hedef potansiyeli açısından daha ayrıntılı araştırılabilecek bir aday olarak değerlendirilmektedir.

Anahtar Kelimeler: Neuregulin 4, adipokin, ErbB4

Neuregulin 4: A General Overview

Abstract

Adipose tissue is not merely a passive structure that stores energy but is also recognized as an active endocrine organ that plays a role in regulating metabolic processes. Adipokines secreted by adipose tissue play a significant role in regulating fundamental physiological processes such as energy homeostasis, glucose and lipid metabolism, inflammation, and insulin sensitivity. Neuregulin 4 (Nrg4), one of the adipokines that has garnered significant attention in recent years, is primarily secreted by brown and white adipose tissue and exerts its biological effects mainly through the epidermal growth factor receptor 4 (ErbB4). Current literature suggests that Nrg4 may be associated with various physiological processes, including thermogenesis, glucose and lipid metabolism, insulin sensitivity, angiogenesis, and neurobiogenesis. In particular, its effects on the suppression of hepatic lipogenesis,

the promotion of fatty acid oxidation, and the regulation of inflammatory responses stand out. Additionally, it has been reported that Nrg4 may play a role in processes related to the browning of white adipose tissue, sympathetic innervation, and energy balance. Changes observed in circulating Nrg4 levels in metabolic diseases such as obesity, metabolic syndrome, and type 2 diabetes mellitus suggest that this adipokine may be associated with metabolic processes. Furthermore, evidence regarding its effects on the cardiovascular system, vascular structure, and nervous system is steadily increasing. This review examines the biological properties of Nrg4, ErbB4-mediated signaling mechanisms, and its potential association with metabolic diseases within the framework of the current literature. While current data suggest that Nrg4 may be a multifaceted molecule associated with metabolic regulation, further experimental and clinical studies are needed to better understand this relationship, particularly due to the lack of full clarification of mechanisms in human studies and discrepancies among findings. In this context, Nrg4 is considered a candidate worthy of further investigation regarding its potential as a biomarker and therapeutic target in the future.

Keywords: Neuregulin 4, adipokine, ErbB4

i.Giriş

Yağ dokusu her ne kadar enerji depolama yeri olarak kabul edilse de metabolik olarak aktif bir endokrin organ olarak da bilinmektedir.[1] Yağ dokusu, enerji dengesi ve benzeri işlevlerde rol oynayan adipokinler olarak da bilinen biyolojik olarak aktif birtakım bileşiklerin sentezlenmesinden sorumludur.[2] Adipokinler glikoz metabolizması, yağ asidi kullanımı ve viseral yağ birikimi gibi kritik metabolik süreçleri yöneten terapötik hedeflerdir.[3] Neuregulin 4 (Nrg4) ise yeni keşfedilen, modüle edici bir adipokindir.[4] İlk olarak insan pankreas dokusunda ve kaslarında tespit edilmiştir.[5] Daha sonra DNA dizileme teknolojisi aracılığıyla epidermal büyüme faktörü reseptör (ErbB) ailesinin bir üyesi olan Nrg4'ün kahverengi yağ dokusu (brown adipose tissue, BAT) ve beyaz yağ dokusu (white adipose tissue, WAT) gibi 27 dokuda sentezlenip salgılandığı, fakat en yoğun olarak gözlendiği yerin BAT olduğu keşfedilmiştir.[4,6] BAT'ı takiben WAT; WAT'ı takiben ise karaciğer, kalp, beyin ve iskelet kası gibi diğer dokular bulunmaktadır.[7,8] Erişkinlerde BAT'ın belirgin şekilde gerilemesi sebebiyle, dolaşımdaki Nrg4'ün önemli kaynaklarından birinin WAT olduğu ifade edilmektedir.[4] Nrg4 ekspresyonunun adiposit farklılaşması esnasında belirgin biçimde arttığı ve kahverengi adipositlerde norepinefrin tarafından salgılanmasının tetiklendiği belirlenmiştir. Ek olarak Nrg4 ekspresyonunun soğukla düzenlendiği; kısa süreli soğuğa maruziyet durumunda BAT'ta artış gösterdiği, uzun süreli maruziyette ise soğuğa karşı adaptasyon geliştiğinden hem BAT hem de inguinal WAT'ta arttığı kaydedilmiştir.[8]

Nrg4'ün farklı hücre altı bölgelerinde bulunan A1, A2, B1, B2 ve B3 gibi beş izoformu bulunmaktadır. A1 ve A2 izoformunun plazma membranında yer aldığı[9], B izoformlarının ise hücre içi bölgede lokalize olduğu öngörülmektedir.[10] Farklı protein yapısı ve lokalizasyona sahip Nrg4 izoformlarının, proteinin biyolojik aktivitesini şekillendirebileceği düşünülmektedir. Özellikle A1 ve A2 izoformlarının lokalizasyonunun hücre zarı olması sebebiyle ya zara bağlı moleküller bulunabilir ya da kesilerek serbest kalabilirler. Nrg4'ün hücre dışından ayrılması ise üretildiği yerden uzak dokulara taşınmasına imkan sunar. B1, B2 ve B3 izoformlarının lokalizasyonu gereği hücre içinde çeşitli biyolojik rollerden sorumlu olduğuna işaret edebilmektedir. Ek olarak A1 proteinin insan, fare, kedi, domuz ve tavuklarda korunduğu, türler arasında bu proteinlerin yüksek benzerlik göstermesi, bazı süreçlerde kritik rollere sahip olacağını düşündürmektedir.[6] Fizyolojik koşullarda Nrg4, nörobiyogenez, glikoz ve lipit metabolizması, insülin duyarlılığı, termogenez ve anjiyogenezin düzenlenmesinde önemli rol oynadığı ifade edilmektedir.[4,6]

ii. Nrg4'ün Reseptörleri

Nrg4, biyolojik etkilerini başlıca ErbB reseptör ailesi üzerinden gerçekleştirmektedir. ErbB reseptör tirozin kinazları, ligand bağlanması gerçekleştikten sonra dimerizasyon ve otofosforilasyon süreçlerini aktive ederek, hücre içi sinyal iletimini başlatan, insan epidermal büyüme faktörü reseptörü (HER) ailesine ait bir proteindir. Nrg4 adlı molekülün içinde epidermal büyüme faktörü (EGF) benzeri bir yapı bulunmaktadır. Bu yapı ErbB reseptör tirozin kinazları ailesinin aktivasyonunda önemli role sahiptir.[5] Nrg4 proteolitik olarak kesildikten sonra hücre dışına salınan EGF-benzeri parçası, ErbB4'e bağlanarak hücre içinde aşağı akım sinyal iletim yollarını aktifleştirir.[5,9] Bahsi geçen ErbB4 hücre dışı ligand

bağlanma bölgesi, transmembran bölge ve tirozin kinaz aktivitesine sahip hücre içi ligand bağlanma bölgesi içeren bir glikoproteindir. Bilindiği kadarıyla insan ve fare dokularında belirlenmiş olan dört farklı ErbB4 izoformlarının hepsi Nrg4'ü tanıyabilmektedir.[11] Hatta ErbB4'ün CYT-1 izoformu, fosfoinozitid 3-kinaz (PI3K)'ın p85 alt birimine özgü bağlanma bölgesi içermesi sebebiyle PI3K/Protein kinaz B (PI3K/AKT) sinyal yolunun aktivasyonunda rol oynar.[12,13,14] Ek olarak ErbB4 izoformları, Shc proteini vasıtasıyla hücre dışı sinyal düzenleyici kinaz 1 ve 2 (Erk1/2) sinyal yolunu aktifleştirebilmektedir.[14,15] ErbB4'ün homodimer ve heterodimer olarak işlev görebilmesi, ErbB2 ve ErbB3 ile oluşturduğu heterodimer sinyal iletimine katkı sunmaktadır. Bu özellikleri bakımından ErbB4 izoformlarının, Nrg4'e bağlı hücresel yanıtların çeşitli olmasında etkili olabileceği düşünülmektedir.[6]

iii. Nrg4'ün Etkileri

iv.Termogenez

Nrg4'ün aşırı soğuk karşısındaki önemini inceleyen bir çalışmada BAT'ta yüksek düzeyde, WAT'ta ise daha düşük düzeyde eksprese edildiği anlaşılmıştır. Ek olarak iskelet kası, karaciğer, beyin ve kalp gibi diğer dokularda ise daha düşük düzeyde eksprese edildiği belirlenmiştir. Akut soğuk maruziyetinden sonra da BAT'taki Nrg4 ekspresyonunun arttığı belirlenmiştir. Buna karşın Nrg4 eksikliği oluşturulan hayvan modeli çalışmasında, kontrol grubu ile Nrg4'ün eksik olduğu fareler arasında rektal vücut sıcaklığı, uncoupling protein 1 (UCP1) ve deiyodinaz 2 ekspresyonları ile plazmadaki insülin, lipokalin ve leptin düzeyleri açısından benzerlik saptanmıştır. Bu doğrultuda Nrg4'ün BAT termogenezinde doğrudan yer almadığı, diğer dokular üzerinden dolaylı etkiler gösterebileceğine inanılmaktadır.[8]

Nrg4'ün merkezi sinir sisteminde nöronal dendtrit büyümesini düzenleyen bir faktör olduğu bilinmektedir.[16,17,18] Sıcak ve soğuk ortam çalışmalarında farelerin farklı yağ dokularında, Nrg4'ün olgun adipositlerden salgılanarak nöronal uzantı gelişimini desteklediği belirlenmiştir.[7] Ek olarak Nrg4 baskılandığında, kahverengi adipositlerde nöral büyümenin sınırlandığı belirlenmiştir. Bu nedenle Nrg4 adiposit-sinir hücresi iletişimi yoluyla BAT innervasyonunu artırabileceği öne sürülmüştür.[19]

Nrg4'ün ayrıca WAT'ın kahverengileşme süreci, adiposit sayısı ve preadiposit farklılaşmasına da etkilerinin olabileceği ifade edilmektedir. Özellikle kahverengi adipositlerde adrenerjik uyarılara duyarlılık oluşturarak termogenezi artıran kemik morfogenetik protein 8b'nin (BMP8b),[20] Nrg4 ekspresyonunu artırarak sempatik akson dallanması ve büyümesini desteklediği bilinmektedir. Ayrıca yağ dokusunun sempatik innervasyonunu artırdığı da belirtilmiştir. Adipositlerde anjiyogenik faktörleri artırarak vasküler yapılanmayı uyardığı bilinmekte, tüm bu bulgular göz önüne alındığında, BMP8b ve Nrg4 arasındaki etkileşimin termogenezde önemli rol oynayabileceğine işaret etmektedir.[21]

Nrg4'ün termogenez üzerindeki etkilerini inceleyen bir başka çalışmada, yağ asidi sentaz (FASN) eksikliğinin oluşturduğu termojenik sinyallerin sempatik aktivite ve Nrg4 ekspresyonunu artırdığı bildirilse de bu sürecin Nrg4'ten bağımsız ilerleyebileceği de kaydedilmiştir. Buna karşılık soğuk maruziyetine bağlı gelişen termogenezde Nrg4'ün gerekli olduğu; Nrg4 eksikliği gözlenen farelerde UCP1 ekspresyonunun azaldığı ve WAT kahverengileşme sürecinin baskılandığı ifade edilmektedir.[22] Nrg4'ün aşırı eksprese edilmesi halinde BAT termojenik genlerini artırdığı ve vücut sıcaklığını yükselttiği de bildirilmektedir.[23] Ek olarak yapılan bazı klinik çalışmalar göstermiştir ki, Nrg4 ekspresyonu UCP1 gibi termojenik genlerle pozitif ilişkili olup, Nrg4 beige adipositler için potansiyel bir belirteç olarak değerlendirilmiştir.[24]

v.Nörobiyogenez

Nöronlar vücutta bilgi iletiminin merkezi olarak görev yapmakta olup, sinapslar aracılığıyla aynı anda binlerce mesaj alabilmektedirler. Organizmada bulunan birçok doku sinirsel yapı bakımından zengin olduğu için, nörogenez sinirler aracılığıyla bilgi iletim hızı ve organizmanın işlevselliği açısından çok önemlidir.[25,26] Nrg4'ün de özellikle nöral gelişim ve fonksiyonun birçok aşamasında önemli rol oynadığı bilinmektedir.[6] MSS gelişiminde, frontal/motor korteks ile somatosensoriyel korteksin rostral bölgesinde bulunan neokortikal piramidal nöronların apikal ve bazal dendrit yapılarının, Nrg4'ten yoksun farelerde, kontrollere kıyasla belirgin derecede az gelişmiş olduğu tespit edilmiştir. Ek olarak bu farelerde dendrit uzunluğunun kısaldığı, dendritik diken sayısının azaldığı ve piramidal nöronların akson ile dendrit dallanmasının gerilediği de kaydedilmiştir. Nrg4'ün rekombinant olarak uygulanmasının ise nöronal yapıdaki bozuklukları büyük ölçüde düzelttiği ifade edilmektedir.[16] Nrg4 eksikliğinin nöronların sitozolik alanını azalttığı, motor korteksteki piramidal nöron soma boyutunda küçülmeye yol açtığı da

bildirilmiştir.[17] Ayrıca embriyonik kortikal nöronların çoğundan Nrg4 ve ErbB4 ekspresyonunun görülmesi, Nrg4'ün ErbB4 aracılığıyla sinyal yolakları üzerinden kortikal piramidal nöron gelişimini desteklediği fikri ortaya çıkmaktadır.[6] Nrg4'ün yağ dokusunda sempatik sinir innervasyonunun artırılmasında potansiyel role sahip olduğunu düşündüren soğuk maruziyeti uygulanan bir çalışmada norepinefrinin, adipositlerden Nrg4 ekspresyonu ve salınımını artırdığı ve bu durum neticesinde de nöronlara sinyal göndererek akson büyümesini desteklediği bildirilmektedir.[19] Tüm bu bilgiler ışığında Nrg4'ün nöronal büyüme ve morfolojiyi desteklemesinin otokrin/parakrin mekanizmalar aracılığıyla olabileceği fikrini düşündürmektedir.[6]

vi.Anjiyogenez

Yağ dokusu zengin vasküler ağa sahiptir ve Nrg4'ün de özellikle vasküler koruyucu etkilere sahip olabileceği düşünülmektedir.[27] İnguinal WAT'ta Nrg4 ekspresyonunun, anjiyogenezin temel düzenleyicilerinden biri olan vasküler endotelyal büyüme faktörü (VEGF) [28] düzeyleri ile pozitif ilişkili olduğunu göstermiştir. Buna bağlı olarak subkutan adipoz dokuda da anjiyogenezi artırdığı bildirilmiştir.[29] Nrg4 geninden yoksun farelerde WAT ve BAT'ta damarlaşmanın azaldığı da ifade edilen bilgiler arasındadır. Özellikle de BAT'a özgü Nrg4 eksikliğinin, damar yoğunluğunu azaltarak, obezite tablosunu kötüleştirdiği kaydedilmiştir.[30] Yapılan çalışmalarda Nrg4 aracılığıyla gerçekleşen anjiyogenez sürecinde Nrg4/ErbB4 sinyal yolunun temel rol oynadığı ifade edilmektedir. Nitekim adipoz dokuda Nrg4'ün aşırı salınımı bulunan farelerde WAT'ta damar yoğunluğunun arttığı, doku hipoksisinin azaldığı ve ErbB4 inhibitörleri kullanıldığında bu etkilerin ortadan kalktığı gözlenmiştir.[31] Elde edilen bu bulgular, Nrg4/ErbB4 sinyalinin anjiyogenez için potansiyel terapötik hedef olabileceğini düşündürmektedir.[6]

vii.Lipit Metabolizması

Nrg4'ün BAT olmak üzere, yağ dokuda yaygın olarak bulunduğu bilinmektedir.[7] Obez bireylerde dolaşımda bulunan Nrg4 seviyelerinin, adiposit farklılaşmasını teşvik eden ve lipit birikimini artıran[32,33,34] adipsin seviyeleri ile negatif ilişkili olduğu belirtilmiştir.[35] Dolayısıyla Nrg4'ün lipit metabolizmasının düzenlenmesinde önemli rol oynayarak enerji depolanması ve enerji homeostazının korunmasına katkı sağladığı bilinmektedir.[36,37,38] Karaciğerde de novo lipogenez yolunu baskılayarak Sterol Düzenleyici Element Bağlayıcı Protein 1c (SREBP-1c), yağ asidi sentazı (FASN) ve stearoil koenzim A desatüraz-1 (SCD1) gibi lipogenezle ilişkili genlerin ekspresyonunda azalmaya neden olmaktadır.[8,23] Özellikle hepatositlerde STAT5a aktivasyonunu sağlayarak, karaciğer X reseptörü (LXR) transkripsiyon aktivitesini baskılar ve SREBP-1c aracılığıyla lipogenez yolunu inhibe eder.[8] Dahası Nrg4, peroksizom proliferatör aktifleşmiş reseptör alfa (PPARα) ve karnitin palmitoiltransferaz 1A (CPT1A) ekspresyonunu artırır. Buna bağlı olarak yağ asidi β-oksidasyonu ve ketogenez süreçleri teşvik edilir.[39] Nitekim açlık durumunda Nrg4 aktivitesinin artması, β-hidroksibütirat düzeylerinin yükselmesini, yağ asidi oksidasyonunun ve ketogenezin aktive olmasını sağlar.[40] Dolayısıyla Nrg4'ün lipit metabolizmasında hem lipogenez hem de yağ asidi oksidasyonu ile metabolik homeostazın korunmasına katkı sağladığı ifade edilmektedir.[39,40]

viii.Glikoz Metabolizması

Nrg4, vücudun enerji ihtiyacını karşılayan temel süreçlerden biri olan glikoz metabolizması üzerinde glikoz alımı ve taşınımını sağlayarak etki göstermektedir.[41,42] Özellikle farelerde epididimal WAT'ta glikoz alımını artırdığı bildirilmektedir. ErbB4 eksikliği bulunan farelerde ise adipositlerde glikoz alımında artışa neden olmadığı için,[42] Nrg4/ErbB4 sinyal yolunun bu durumun düzenlenmesinde rol oynadığı düşünülmektedir.[6]

3T3-L1 adipositleri üzerinde yapılan Nrg4 uygulaması ile glikoz taşıyıcı 4 (GLUT4)'ün plazma membranına translokasyonu artmış olup, bu durum glikoz alımını da tetiklemiştir.[42] Ayrıca Nrg4 geninden yoksun olan 3T3-L1 hücrelerinde insülin aracılı glikoz alımının inhibisyona uğradığı kaydedilmiştir.[41] Özellikle Nrg4 eksikliğinin memeli rapamisin hedefi kompleksi 1 (mTORC1) aktivitesinin baskılanmasına sebep olarak otofaji aracılığıyla GLUT4 yıkımını artırabilir. Bunun neticesinde adipositlerde insülin direnci gelişebilir. Fakat Nrg4'ün glikoz metabolizması üzerindeki etkilerinin doğrulanması ve ortaya koyulması için daha fazla çalışmaya ihtiyaç duyulmaktadır.[6]

ix.İnsülin Direnci

Yapılan bazı çalışmalarda Nrg4'ün pankreasta adacık endokrin hücrelerinin farklılaşması ve gelişmesi üzerinde düzenleyici rollere sahip olabileceği gözlenmiştir. Özellikle Nrg4'ün insülin salınımını çok güçlü şekilde uyardığı bildirilmiştir. Bu durum da Nrg4'ün adacık hücre büyümesinde ve sekresyonunda etkili olabileceğini düşündürmüştür.[43] Nrg4 salınımının kan glikozu ve plazma insülin düzeyleri ile negatif ilişkiye sahip olmasından dolayı, bu adipokinin glikoz homeostazı ve insülin duyarlılığı üzerinde regüle edici etkilere sahip olabileceği düşünülmektedir. Nitekim Nrg4 transgenik fareleri üzerinde yapılan hiperinsülinemik-öglisemik klemp çalışmasında periferik glikoz kullanımının ve insülin duyarlılığının arttığı bildirilmiştir.[40]

Nrg4'ün inflamasyonu baskılayarak da insülin direncini iyileştirebildiği belirtilmektedir. Yüksek yağlı diyet ile obezite oluşturulan fareler üzerinde Nrg4 uygulamasının, adipoz doku üzerinde makrofaj infiltrasyonunu azaltarak ve insülin duyarlılığını iyileştirerek beyaz yağ dokudaki kronik inflamasyonu inhibe ettiği gözlenmiştir.[23] Nrg4 eksikliği ile adipositlerde insülin reseptörü ve GLUT4 düzeylerinde azalma, otofaji ve insülin direncinde artış gözlenmiş olup, Nrg4 uygulandığı takdirde bu değişikliklerin tam tersi duruma geldiği ifade edilmektedir.[41] Fakat insanlar üzerinde yapılan çalışmalarda insülin duyarlılığı üzerinde çelişkili sonuçlar ortaya çıkmıştır. Dolayısıyla Nrg4'ün insülin direnci üzerindeki etkilerinin anlaşılabilmesi için daha ileri çalışmalara ihtiyaç duyulmaktadır.[44]

x. Obezite ve Diyabet

Yağ dokuda Nrg4 mRNA ekspresyon seviyesinin hem farelerde hem de obeziteli insanlarda azalması[8] ve farelerde epididimal beyaz yağ dokusu ve karaciğerdeki Nrg4 düzeylerinin zayıf kontrollere kıyasla daha düşük olması[23] dolayısıyla bu adipokinin obeziteye karşı koruyucu bir role sahip olabileceğini düşündürmektedir.[21]

Ayrıca obezite, adipoz dokuda kronik inflamatuvar infiltrasyon ile karakterize olduğundan, proinflamatuvar sinyallerin de azalan Nrg4 ekspresyonuna katkıda bulunabileceği düşünülmektedir. Yapılan bir in vitro çalışmada adipositlerin tümör nekroz faktörü-α (TNF-α) ve interlökin-1β (IL-1β) ile muamele edilmesiyle Nrg4 ekspresyonunun azaldığı belirlenmiştir.[8] Nrg4 ekspresyonunun aşırı artması ile adipoz dokudaki inflamasyonun azaldığı ve obezite gelişiminin önlendiği bilinmektedir. Ancak mevcut obezite ve vücut ağırlığı üzerinde belirgin etkide bulunmadığı da kaydedilen bilgiler arasındadır.[23]

Nrg4 transgenik fareler üzerinde yapılan bir çalışmada enerji harcamasının ve hücrelerin enerji üretmek için besinleri oksijen kullanarak parçalama sürecinin arttığı, leptin düzeylerinin ise azaldığı kaydedilmiştir. Bu durum Nrg4'ün enerji metabolizmasını katabolik yönde düzenleyebileceğini düşündürmektedir.[40] Ek olarak bu farelerde adipsin, adiponektin ve vasküler endotelyal büyüme faktörü-α (VEGF-α) gibi çeşitli adipokinlerin mRNA ekspresyonlarında artışlar gözlenmiştir.[45,46,47] Bu gözlemler Nrg4'ün adipokin profilinin iyileştirilmesine de katkıda bulunabileceğini düşündürmektedir. Dahası ErbB4 eksikliğinin de şiddetli inflamasyona, lipogeneze ve serum leptin seviyelerinin yükselmesiyle pozitif korelasyon göstermesi de obezitenin iyileştirilmesinde ErbB4'ün de gerekli olduğu ifade edilmektedir.[42]

Nrg4'ün adipoz dokuda anjiyogenezi artırdığı ve metabolik sağlığı olumlu etkilediği, yapılan in vivo ve in vitro çalışmalarda WAT ve BAT'ta damar oluşumunu artırdığı bilinmektedir. Nrg4 eksikliğinde ise normal diyet koşullarında bile adipoz dokuda vaskülarizasyonun azalmasına ve obezitenin gelişimine yol açtığı ifade edilmektedir.[30] Bazı klinik çalışmalarda dolaşım Nrg4 düzeylerinin metabolik sendroma sahip hastalarda, kontrollere kıyasla düşük olduğu kaydedilmiştir.[48] Ek olarak Nrg4 düzeylerinin bel çevresi ve beden kütle indeksi (BKİ) ile negatif ilişki gösterdiği bildirilmiştir.[24,29] Fiziksel aktivitenin Nrg4 düzeyleri üzerinde etkinliğinin incelendiği bir çalışmada, obez erkek hastalara 12 haftalık direnç egzersizi uygulanmış ve dolaşımdaki Nrg4 düzeylerinin anlamlı şekilde arttığı kaydedilmiştir.[49] Ayrıca yüksek yoğunluklu interval antrenman (HIIT), dairesel direnç antrenmanı (CRT) ve orta yoğunluklu sürekli egzersizin (MICT) serum Nrg4 düzeylerini artırarak metabolik parametrelerde iyileşme sağladığı ifade edilmektedir.[50]

Diyabetli hastalarda dolaşımdaki Nrg4 düzeylerinin sağlıklı bireylere göre düşük seviyelerde olduğu kaydedilmiştir.[51,52] Özellikle bu adipokinin dolaşımda düşük olması, gestasyonel diyabetes mellitus

(GDM) için bir risk faktörü olabileceği bildirilmiştir.[53] Nrg4'ün glikoz homeostazı ve glukoneogenez düzenlenmesinde rol oynayabileceği bildirilmektedir.[54] Bununla birlikte diyabetli bireylerde dolaşımdaki NRG4 düzeylerine ilişkin çalışmalar çelişkili sonuçlar göstermektedir. Bazı çalışmalarda tip 2 diabetes mellitus (T2DM) hastalarında serum Nrg4 düzeylerinin arttığı bildirilirken[55,56,57], diğer çalışmalarda düşük Nrg4 düzeylerinin diyabet gelişimi ile ilişkili olduğu ifade edilmektedir.[52,53,58] Bu farklılıkların etnik özellikler, klinik heterojenite ve ölçüm yöntemlerinden kaynaklanabileceği düşünülmektedir.[59] Dolaşımdaki ilgili adipokinin düzeylerinin T2DM'de periferik nöropatinin şiddetiyle negatif ilişki olduğu da ifade edilmektedir.[60,61] Fakat Nrg4'ün diyabeti nasıl ve ne derece etkileyebildiği ile ilgili yeterince verinin bulunmaması nedeniyle bu hastalıktaki spesifik rollerinin incelenmesi için daha fazla çalışmaya ihtiyaç duyulmaktadır.[6]

xi.Kardiyovasküler Hastalıklar

Dolaşımdaki Nrg4 düzeylerinin araştırıldığı çalışmada aterosklerozun önemli bir belirteci olan karotis intima-media kalınlığı (CIMT) ile negatif ilişkili olduğu bildirilmiştir.[62] Koroner arter hastalığına sahip kişilerde Nrg4 düzeylerinin anlamlı ölçüde düşük olduğu da kaydedilen bilgiler arasındadır.[63] Ayrıca Nrg4 düzeylerinin akut koroner sendrom riski ile negatif korelasyon gösterdiği de bildirilmektedir.[64] Nrg4 uygulaması yapılan farelerde miyokardiyal iskemi hasarının azaldığı gözlenmekle birlikte,[65] yine hayvan çalışmalarında Nrg4/ErbB4 sinyal yolunun kardiyomiyositlerin yaşamı, büyümesi, farklılaşması ve migrasyonunun düzenlenmesinde rol oynadığı da kaydedilmiştir.[66] Bu bilgiler ışığında Nrg4'ün kardiyoprotektif özelliklere sahip olduğu düşünülmektedir. Fakat kardiyovasküler sistemdeki kesin etkilerinin tam olarak aydınlatılması için daha fazla çalışmaya gerek duyulmaktadır.[4]

xii.Sonuç

Nrg4, metabolik süreçlerin düzenlenmesinde çok yönlü etkiler gösteren ve son yıllarda önemi giderek daha iyi anlaşılan yeni nesil adipokinlerden biridir. Güncel bulgular, Nrg4'ün enerji homeostazının korunması, termogenezin desteklenmesi, glikoz ve lipit metabolizmasının düzenlenmesi ile inflamasyonun baskılanması gibi birçok kritik süreçte rol oynadığını ortaya koymaktadır. Özellikle obezite, insülin direnci ve T2DM gibi metabolik hastalıklarda değişen Nrg4 düzeyleri, bu molekülün metabolik sağlık açısından önemli bir biyobelirteç olabileceğini düşündürmektedir.

Bununla birlikte Nrg4'ün yalnızca metabolik hastalıklarla sınırlı kalmayıp kardiyovasküler sistem, damar yapılanması ve sinir sistemi üzerinde de koruyucu etkiler gösterebileceğine ilişkin bulgular, bu adipokinin biyolojik önemini daha da artırmaktadır. Her ne kadar mevcut çalışmalar Nrg4'ün terapötik potansiyeline işaret etse de etki mekanizmalarının tam olarak açıklığa kavuşması ve klinik uygulamalara aktarılabilmesi için daha kapsamlı çalışmalara ihtiyaç vardır. Sonuç olarak Nrg4, gelecekte metabolik hastalıkların önlenmesi, tanılanması ve tedavisinde umut vadeden moleküler hedeflerden biri olarak değerlendirilmektedir.

Kaynakça

1. Mahat RK, Rathore V. Circulating asprosin and neuregulin-4 in metabolic dysfunction-associated steatotic liver disease (MASLD): a systematic review and meta-analysis. *Clin Epidemiol Glob Health*. 2025;33:102041. doi:10.1016/j.cegh.2025.102041
2. Francisco V, Pino J, Campos-Cabaleiro V, Ruiz-Fernández C, Mera A, Gonzalez-Gay MA, et al. Obesity, fat mass and immune system: role for leptin. *Front Physiol*. 2018;9:640. doi:10.3389/fphys.2018.00640
3. Polyzos SA, Perakakis N, Mantzoros CS. Fatty liver in lipodystrophy: a review with a focus on therapeutic perspectives of adiponectin and/or leptin replacement. *Metabolism*. 2019;96:66-82. doi:10.1016/j.metabol.2019.05.001
4. Dan X, Li K, Xu J, Yan P. The potential of neuregulin 4 as a novel biomarker and therapeutic agent for vascular complications in type 2 diabetes mellitus. *J Inflamm Res*. 2024;17:8543-8554. doi:10.2147/JIR.S492115
5. Harari D, Tzahar E, Romano J, Shelly M, Pierce JH, Andrews GC, et al. Neuregulin-4: a novel growth factor that acts through the ErbB-4 receptor tyrosine kinase. *Oncogene*. 1999;18(17):2681-2689. doi:10.1038/sj.onc.1202631
6. Chen M, Zhu J, Luo H, Mu W, Guo L. The journey towards physiology and pathology: tracing the path of neuregulin 4. *Genes Dis*. 2024;11(2):687-700. doi:10.1016/j.gendis.2023.03.021
7. Rosell M, Kaforou M, Frontini A, Okolo A, Chan YW, Nikolopoulou E, et al. Brown and white adipose tissues: intrinsic differences in gene expression and response to cold exposure in mice. *Am J Physiol Endocrinol Metab*. 2014;306(8):E945-E964. doi:10.1152/ajpendo.00473.2013
8. Wang GX, Zhao XY, Meng ZX, Kern M, Dietrich A, Chen Z, et al. The brown fat-enriched secreted factor Nrg4 preserves metabolic homeostasis through attenuation of hepatic lipogenesis. *Nat Med*. 2014;20(12):1436-1443. doi:10.1038/nm.3713
9. Hayes NVL, Newsam RJ, Baines AJ, Gullick WJ. Characterization of the cell membrane-associated products of the neuregulin 4 gene. *Oncogene*. 2008;27(5):715-720. doi:10.1038/sj.onc.1210689
10. Lyne JC, Melhem MF, Finley GG, Wen D, Liu N, Deng DH, et al. Tissue expression of neu differentiation factor/heregulin and its receptor complex in prostate cancer and its biologic effects on prostate cancer cells in vitro. *Cancer J Sci Am*. 1997;3(1):21-30.
11. Junttila TT, Sundvall M, Määttä JA, Elenius K. ErbB4 and its isoforms: selective regulation of growth factor responses by naturally occurring receptor variants. *Trends Cardiovasc Med*. 2000;10(7):304-310. doi:10.1016/s1050-1738(01)00065-2
12. Elenius K, Corfas G, Paul S, Choi CJ, Rio C, Plowman GD, et al. A novel juxtamembrane domain isoform of HER4/ErbB4: isoform-specific tissue distribution and differential processing in response to phorbol ester. *J Biol Chem*. 1997;272(42):26761-26768. doi:10.1074/jbc.272.42.26761
13. Elenius K, Choi CJ, Paul S, Santiestevan E, Nishi E, Klagsbrun M. Characterization of a naturally occurring ErbB4 isoform that does not bind or activate phosphatidylinositol 3-kinase. *Oncogene*. 1999;18(16):2607-2615. doi:10.1038/sj.onc.1202612
14. Kainulainen V, Sundvall M, Määttä JA, Santiestevan E, Klagsbrun M, Elenius K. A natural ErbB4 isoform that does not activate phosphoinositide 3-kinase mediates proliferation but not survival or chemotaxis. *J Biol Chem*. 2000;275(12):8641-8649. doi: 10.1074/jbc.275.12.8641
15. Ravichandran KS. Signaling via Shc family adapter proteins. *Oncogene*. 2001;20(44):6322-6330. doi: 10.1038/sj.onc.1204776
16. Paramo B, Wyatt S, Davies AM. An essential role for neuregulin-4 in the growth and elaboration of developing neocortical pyramidal dendrites. *Exp Neurol*. 2018;302:85-92. doi: 10.1016/j.expneurol.2018.01.002

17. Paramo B, Wyatt S, Davies AM. Neuregulin-4 is required for the growth and elaboration of striatal medium spiny neuron dendrites. *J Neuropathol Exp Neurol*. 2019;78(8):725-734. doi: 10.1093/jnen/nlz046

18. Paramo B, Bachmann SO, Baudouin SJ, Martinez-Garay I, Davies AM. Neuregulin-4 is required for maintaining soma size of pyramidal neurons in the motor cortex. *eNeuro*. 2021;8(1):ENEURO.0482-20.2021. doi: 10.1523/ENEURO.0288-20.2021

19. Christian M. Transcriptional fingerprinting of "browning" white fat identifies NRG4 as a novel adipokine. *Adipocyte*. 2015;4(1):50-54. doi: 10.4161/adip.29853

20. Whittle AJ, Carobbio S, Martins L, Slawik M, Hondares E, Vázquez MJ, et al. BMP8B increases brown adipose tissue thermogenesis through both central and peripheral actions. *Cell*. 2012;149(4):871-885. doi: 10.1016/j.cell.2012.02.066

21. Liu Y, Chen M. Neuregulin 4 as a novel adipokine in energy metabolism. *Front Physiol*. 2023;13:1106380. doi: 10.3389/fphys.2022.1106380

22. Henriques F, Bedard AH, Guilherme A, Kelly M, Chi J, Zhang P, et al. Single-cell RNA profiling reveals adipocyte-to-macrophage signaling sufficient to enhance thermogenesis. *Cell Rep*. 2020;32(5):107998. doi: 10.1016/j.celrep.2020.107998

23. Ma Y, Gao M, Liu D. Preventing high-fat diet-induced obesity and improving insulin sensitivity through neuregulin 4 gene transfer. *Sci Rep*. 2016;6:26242. doi: 10.1038/srep26242

24. Comas F, Martínez C, Sabater M, Ortega F, Latorre J, Díaz-Sáez F, et al. Neuregulin 4 is a novel marker of beige adipocyte precursor cells in human adipose tissue. *Front Physiol*. 2019;10:39. doi: 10.3389/fphys.2019.00039

25. Zhu JY, Chen M, Mu WJ, Luo HY, Guo L. The functional role of Higd1a in mitochondrial homeostasis and in multiple disease processes. *Genes Dis*. 2023;10(5):1833-1845. doi: 10.1016/j.gendis.2022.03.018

26. Chen M, Zhu JY, Mu WJ, Guo L. Cysteine dioxygenase type 1 (CDO1): its functional role in physiological and pathophysiological processes. *Genes Dis*. 2023;10(3):877-890. doi: 10.1016/j.gendis.2021.12.023

27. Liberale L, Montecucco F. Adipocytokines and cardiovascular diseases: putative role of neuregulin 4. *Eur J Clin Invest*. 2020;50(10):e13389. doi: 10.1111/eci.13306

28. Naito H, Iba T, Takakura N. Mechanisms of new blood-vessel formation and proliferative heterogeneity of endothelial cells. *Int Immunol*. 2020;32(5):295-305. doi: 10.1093/intimm/dxaa008

29. Wang R, Zhou W, Zhu X, Zhou N, Yang F, Sun B, Li X. Differences in neuregulin 4 expression in children: effects of fat depots and obese status. *Endocr Res*. 2020;45(3):190-201. doi: 10.1080/07435800.2020.1721528

30. Nugroho DB, Ikeda K, Barinda AJ, Wardhana DA, Yagi K, Miyata K, et al. Neuregulin-4 is an angiogenic factor that is critically involved in the maintenance of adipose tissue vasculature. *Biochem Biophys Res Commun*. 2018;503(1):378-384. doi: 10.1016/j.bbrc.2018.06.043

31. Nugroho DB, Ikeda K, Kajimoto K, Hirata KI, Emoto N. Activation of neuregulin-4 in adipocytes improves metabolic health by enhancing adipose tissue angiogenesis. *Biochem Biophys Res Commun*. 2018;504(2):427-433. doi: 10.1016/j.bbrc.2018.08.197

32. Song NJ, Kim S, Jang BH, Chang SH, Yun UJ, Park KM, et al. Small molecule-induced complement factor D (adipsin) promotes lipid accumulation and adipocyte differentiation. *PLoS One*. 2016;11(9):e0162228. doi: 10.1371/journal.pone.0162228

33. Guo LY, Guo YY, Li BY, Peng WQ, Tang QQ. Histone demethylase KDM5A is transactivated by the transcription factor C/EBPβ and promotes preadipocyte differentiation by inhibiting Wnt/β-catenin signaling. *J Biol Chem*. 2019;294(24):9642-9654. doi: 10.1074/jbc.RA119.008419

34. Liu Y, Peng WQ, Guo YY, Liu Y, Tang QQ, Guo L. Krüppel-like factor 10 (KLF10) is transactivated by the transcription factor C/EBPβ and involved in early 3T3-L1 preadipocyte differentiation. *J Biol Chem*. 2018;293(36):14012-14021. doi: 10.1074/jbc.RA118.004401

35. Guo D, Liu J, Zhang P, Yang X, Liu D, Lin J, et al. Adiposity measurements and metabolic syndrome are linked through circulating neuregulin 4 and adipsin levels in obese adults. *Front Physiol*. 2021;12:667330. doi: 10.3389/fphys.2021.667330

36. Li BY, Guo YY, Xiao G, Guo L, Tang QQ. SERPINA3C ameliorates adipose tissue inflammation through the cathepsin G/integrin/AKT pathway. *Mol Metab*. 2022;61:101500. doi: 10.1016/j.molmet.2022.101500

37. Guo YY, Li BY, Xiao G, Liu Y, Guo L, Tang QQ. Cdo1 promotes PPARγ-mediated adipose tissue lipolysis in male mice. *Nat Metab*. 2022;4(10):1352-1368. doi: 10.1038/s42255-022-00644-3

38. Peng WQ, Xiao G, Li BY, Guo YY, Guo L, Tang QQ. L-theanine activates the browning of white adipose tissue through the AMPK/α-ketoglutarate/Prdm16 axis and ameliorates diet-induced obesity in mice. *Diabetes*. 2021;70(7):1458-1472. doi: 10.2337/db20-1210

39. Zhu B, Mei W, Jiao T, Yang S, Xu X, Yu H, et al. Neuregulin 4 alleviates hepatic steatosis via activating AMPK/mTOR-mediated autophagy in aged mice fed a high-fat diet. *Eur J Pharmacol*. 2020;884:173350. doi: 10.1016/j.ejphar.2020.173350

40. Chen Z, Wang GX, Ma SL, Jung DY, Ha H, Altamimi T, et al. Nrg4 promotes fuel oxidation and a healthy adipokine profile to ameliorate diet-induced metabolic disorders. *Mol Metab*. 2017;6(8):863-872. doi: 10.1016/j.molmet.2017.03.016

41. Díaz-Sáez F, Blanco-Sinfreu C, Archilla-Ortega A, Sebastian D, Romero M, Hernández-Alvarez MI, et al. Neuregulin 4 downregulation induces insulin resistance in 3T3-L1 adipocytes through inflammation and autophagic degradation of GLUT4 vesicles. *Int J Mol Sci*. 2021;22(23):12960. doi: 10.3390/ijms222312960

42. Zeng F, Wang Y, Kloepfer LA, Wang S, Harris RC. ErbB4 deletion predisposes to development of metabolic syndrome in mice. *Am J Physiol Endocrinol Metab*. 2018;315(4):E583-E593. doi: 10.1152/ajpendo.00166.2018

43. South JC, Blackburn E, Brown IR, Gullick WJ. The neuregulin system of ligands and their receptors in rat islets of Langerhans. *Endocrinology*. 2013;154(7):2385-2392. doi: 10.1210/en.2012-2133

44. Martínez C, Latorre J, Ortega F, Arnoriaga-Rodríguez M, Lluch A, Oliveras-Cañellas N, et al. Serum neuregulin 4 is negatively correlated with insulin sensitivity in humans and impairs mitochondrial respiration in HepG2 cells. *Front Physiol*. 2022;13:950791. doi: 10.3389/fphys.2022.950791

45. Achari AE, Jain SK. Adiponectin, a therapeutic target for obesity, diabetes, and endothelial dysfunction. *Int J Mol Sci*. 2017;18(6):1321. doi: 10.3390/ijms18061321

46. Milek M, Moulla Y, Kern M, Stroh C, Dietrich A, Schön MR, et al. Adipsin serum concentrations and adipose tissue expression in people with obesity and type 2 diabetes. *Int J Mol Sci*. 2022;23(4):2222. doi: 10.3390/ijms23042222

47. Zhou Y, Zhu X, Wang H, Duan C, Cui H, Shi J, et al. The role of VEGF family in lipid metabolism. *Curr Pharm Biotechnol*. 2023;24(2):253-265. doi: 10.2174/1389201023666220506105026

48. Cai C, Lin M, Xu Y, Li X, Yang S, Zhang H. Association of circulating neuregulin 4 with metabolic syndrome in obese adults: a cross-sectional study. *BMC Med*. 2016;14:165. doi: 10.1186/s12916-016-0703-6

49. Alizadeh M, Shahrbanian S, Hackney AC. Comparison of the effects of 12 weeks of three types of resistance training (traditional, circular and interval) on the levels of neuregulin 4, adiponectin and leptin in non-athletic men with obesity. *Arch Med Deporte*. 2021;38(6):389-396. doi: 10.18176/archmeddeporte.00066

50. Saeidi A, Shishvan SR, Soltani M, Tarazi F, Doyle-Baker PK, Shahrbanian S, et al. Differential effects of exercise programs on neuregulin 4, body composition and cardiometabolic risk factors in men with obesity. *Front Physiol*. 2022;12:797574. doi: 10.3389/fphys.2021.797574

51. Wang Y, Huang S, Yu P. Association between circulating neuregulin 4 levels and diabetes mellitus: a meta-analysis of observational studies. *PLoS One*. 2019;14(12):e0225705. doi: 10.1371/journal.pone.0225705

52. Zhang L, Fu Y, Zhou N, Cheng X, Chen C. Circulating neuregulin 4 concentrations in patients with newly diagnosed type 2 diabetes: a cross-sectional study. *Endocrine*. 2017;57(3):535-538. doi: 10.1007/s12020-017-1324-3

53. Zhang L, Lu B, Wang W, Miao S, Zhou S, Cheng X, et al. Alteration of serum neuregulin 4 and neuregulin 1 in gestational diabetes mellitus. *Ther Adv Endocrinol Metab*. 2021;12:20420188211049614. doi:10.1177/20420188211049614.

54. Zhang L, Bai M, Tang H, Zhou F, Zhu Q, Wang S, et al. Role of hepatic neuregulin 4 in the regulation of gluconeogenesis in mice. *Life Sci*. 2019;217:185-192. doi: 10.1016/j.lfs.2018.12.006

55. Kang YE, Kim JM, Choung S, Joung KH, Lee JH, Kim HJ, et al. Comparison of serum neuregulin 4 (Nrg4) levels in adults with newly diagnosed type 2 diabetes mellitus and controls without diabetes. *Diabetes Res Clin Pract*. 2016;117:1-3. doi: 10.1016/j.diabres.2016.04.007

56. Chen LL, Peng MM, Zhang JY, Hu X, Min J, Huang QL, et al. Elevated circulating neuregulin 4 level in patients with diabetes. *Diabetes Metab Res Rev*. 2017;33(4):e2870. doi: 10.1002/dmrr.2870

57. Kocak MZ, Aktas G, Erkus E, Yis OM, Duman TT, Atak BM, et al. Neuregulin-4 is associated with plasma glucose and increased risk of type 2 diabetes mellitus. *Swiss Med Wkly*. 2019;149:w20139. doi: 10.4414/smw.2019.20139

58. Kralisch S, Hoffmann A, Kratzsch J, Blüher M, Stumvoll M, Fasshauer M, et al. The brown-fat-secreted adipokine neuregulin 4 is decreased in gestational diabetes mellitus. *Diabetes Metab*. 2018;44(2):150-154. doi: 10.1016/j.diabet.2017.06.001

59. Mikhail N, Wali S, Brown AF. Ethnic disparities in diabetes. *Endocrinol Metab Clin North Am*. 2021;50(3):475-490. doi: 10.1016/j.ecl.2021.05.006

60. Yan P, Xu Y, Zhang Z, Gao C, Zhu J, Li H, Wan Q. Decreased plasma neuregulin 4 levels are associated with peripheral neuropathy in Chinese patients with newly diagnosed type 2 diabetes: a cross-sectional study. *Cytokine*. 2019;113:356-364. doi: 10.1016/j.cyto.2018.10.007

61. Yan P, Zhang Z, Miao Y, Xu Y, Zhu J, Wan Q. Changes of circulating neuregulin 4 and its relationship with 25-hydroxy vitamin D and other diabetic vascular complications in patients with diabetic peripheral neuropathy. *Diabetol Metab Syndr*. 2020;12(1):42. doi: 10.1186/s13098-020-00550-2

62. Jiang J, Lin M, Xu Y, et al. Circulating neuregulin 4 levels are inversely associated with subclinical cardiovascular disease in obese adults. *Sci Rep*. 2016;6:36710. doi: 10.1038/srep36710

63. Tian QP, Liu ML, Tang CS, Xue L, Pang YZ, Qi YF. Association of circulating neuregulin-4 with presence and severity of coronary artery disease. *Int Heart J*. 2019;60(1):45-49. doi: 10.1536/ihj.18-130

64. Rahimzadeh M, Farshidi N, Naderi N, Farshidi H, Montazerghaem H. Clinical significance of serum concentrations of neuregulin-4 in acute coronary syndrome. *Sci Rep*. 2020;10(1):5797. doi: 10.1038/s41598-020-62680-x

65. Liu SQ, Tefft BJ, Roberts DT, et al. Cardioprotective proteins upregulated in the liver in response to experimental myocardial ischemia. *Am J Physiol Heart Circ Physiol*. 2012;303(12):H1446-H1458. doi: 10.1152/ajpheart.00362.2012

66. Yang Z, Wang Y, Li T, Ren M, Li Y. Cardioprotective effect of NRG-4 gene expression on spontaneous hypertension rats and its mechanism through mediating the activation of ErbB

signaling pathway. *Cell Mol Biol (Noisy-le-grand)*. 2022;68(1):89-101. doi: 10.14715/cmb/2022.68.1.12

A Review on Feature Extraction Techniques for Medicinal Plant Identification

Reshma
Research Scholar, Computer Science and Engineering,
Punjabi University, Patiala
Kanwal Preet Singh Attwal
Associate Professor, Computer Science and Engineering,
Punjabi University, Patiala

Abstract

The process of identifying medicinal plants has crucial importance for healthcare, pharmacology, botany and traditional medicine. The proper identification of medicinal plants serves as a critical requirement to ensure correct herbal resource usage while preventing dangerous outcomes from plant misidentification. The growing fields of artificial intelligence, image processing and computer vision technology have created a research focus on automated systems for plant identification. The stage of feature extraction stands as the most crucial point in these systems because it defines the quality and efficiency of plant identification and classification processes. The review article examines all existing feature extraction methods, which researchers use to identify medicinal plants. The study investigates traditional feature extraction methods, which require manual work to extract features from plant materials through shape and texture and color and vein pattern analysis. The paper evaluates how different feature extraction models perform on leaf images and plant datasets by showing their strengths and weaknesses. The study shows how traditional machine learning methods perform when compared to deep learning methods by measuring their accuracy and processing efficiency and system durability. The review findings demonstrate that deep learning feature extraction methods have improved the identification accuracy of medicinal plant systems while traditional techniques remain effective in environments with limited resources. The paper provides researchers with complete details about current feature extraction methods

while showing which areas need research to create effective and trustworthy medicinal plant identification systems.

I. Introduction

Since ancient times, medicinal plants have been used for healing purposes. Medicinal herbs are still important in many countries where they form an integral part of their health care systems. In fact, traditional medicine like as Ayurveda, Traditional Chinese Medicine and native herbal treatments heavily depend on plant-based remedies [1]. Plants have got high concentration of biologically active compounds which have been utilized by the pharmaceutical industries for the production of herbal medicines, supplements and natural products [2].

However, it is most important to accurately identify the medicinal plants, due to the fact that there are numerous similarities between plant shapes and physical features. Misidentification may result in the use of poisonous plants, reduced effectiveness of herbal medicine or severe side effects. The traditional identification process involves examining the leaf morphology, flowers, stems and seeds of plants and seeds by experts. The identification process is time consuming and laborious such processes [3].

With the rapid development of digital imaging and machine learning, automated medicinal plant identification has become an important research area. Plant recognition using leaf images is possible using image processing techniques. The feature extraction step is regarded as one of the key steps in automated identification systems as it converts the basic image data into meaningful features for the classification stage [4].

The function of feature extraction is to extract important visual patterns from the plant image. These patterns can be the shape and texture of the leaves, distribution of colour, venation and surface characteristics. Traditional systems have manual features that are designed through image processing

algorithms. But recent advancements in deep learning have brought automatic feature extraction with neural networks [5].

The field of computer vision has been greatly enhanced by the advent of deep learning. It allows machines to learn critical features from images without having to be handcrafted. This is useful for the medicinal plant identification since the natural variation in the images, such as lighting, angle, background, partial occlusion, etc., makes manual feature extraction challenging [6]. Current deep learning techniques like Convolutional Neural Network offer effective solutions by directly extracting hierarchical features from input images.

This review is aimed to discuss the traditional and modern techniques of feature extraction which are applied in identification of medicinal plants and their evaluation of their performance, advantages and disadvantages.

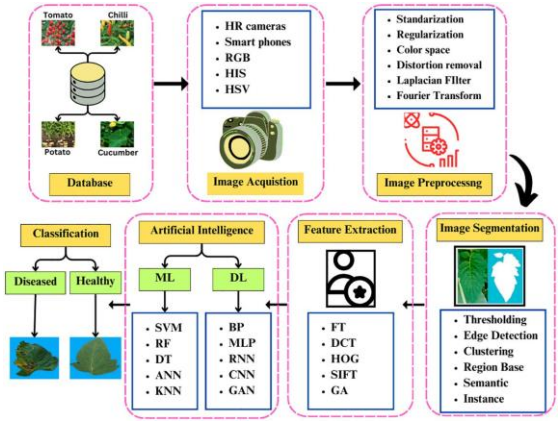


Figure 1 — Overall medicinal plant identification process

2. Literature Review

Medicinal plant identification can be done with various feature extraction techniques which can be classified into traditional hand crafted and deep learning based methods.

2.1 Traditional Feature Extraction

The traditional feature extraction approaches rely on manually defined image descriptors. Botanical knowledge is used to select plant image characteristics. There are several techniques in general, which are shape-based, texture-based, color-based and vein-based extraction.

One of the first types of methods is shape based. The outline and structure of the leaves vary among the various medicinal plants. Geometric descriptors such as area, perimeter, length, width, aspect ratio and compactness are commonly used. The descriptors are a simple numerical representation of the leaf [7]. Moreover, moment invariants are employed since they are consistent to translation, scaling and rotation. Hu moments are generally used for shape recognition.

Contour based methods (like Fourier descriptors) transform the outline of the leaf into a frequency representation [8]. These words contain general shape and edge information. They can be used to determine species that have distinctive leaf edges. Shape-based methods, however, are prone to damage, overlapped leaves and folded leaves [20].

Another important technique is texture based extraction. There are patterns on the inside of the leaf which are different between species. Texture methods work best when the leaf shapes of the species are alike [9]. Local Binary Patterns is one of the popular approaches. Processes the relationship of adjacent pixels and creates pattern of binary data for micro-texture.

There is also a considerable amount of use of Gray-Level Co-occurrence Matrix. It determines the statistics relationships between adjacent pixels. A matrix is formed from this matrix and features like

contrast, homogeneity, energy and correlation are extracted [10]. These features are the distribution of texture in space.

One more important technique is Gabor filter. Gabor filters are used to analyze the orientation and frequency components. They work well on finding veins and repetitive structures in leaves [11].

Information about plants can be given from their color features. Usually used are RGB and HSV colour spaces. Color distribution is represented by the histograms and statistical moments. But lighting, camera settings and the light environment influence the color. So, color is frequently used in conjunction with shape and texture.

The extraction of vein patterns is becoming an important issue. The veins are very characteristic for each species of plant. The extraction process consists of image enhancement, thresholding and morphological processing [12]. Vein density, branching angles and fractal dimension are computed. Vein based techniques achieve high precision, however, they rely on high-quality images.

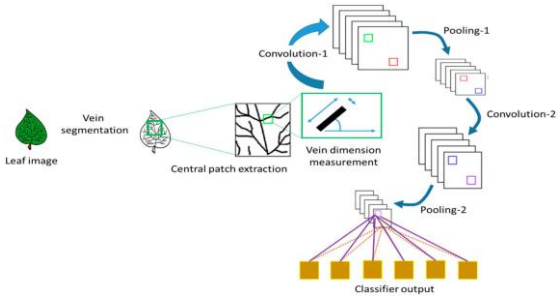


Figure 2 — Traditional feature extraction methods

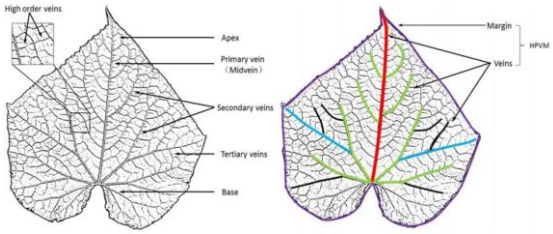


Figure 3 — Vein pattern extraction

2.2 Feature extraction using deep learning techniques

Automatic feature learning has revolutionized image analysis with the advent of deep learning. Unlike the conventional approaches, deep learning does not require manual feature design.

The most popular deep learning model for plant identification is Convolutional Neural Network. CNNs are composed of several layers which automatically learn image characteristics. Early layers detect basic edges/corners. Patterns and textures are detected in the middle layers. The final layers are used to classify complicated structures for each plant species.

A few CNN architectures are used in the field of medicinal plant identification. One of the earliest models to be used was called AlexNet.One of the first models was named AlexNet. It proved to be much better than old-fashioned solutions [13]. Denser and deeper networks like VGG16 were able to provide more accurate feature extraction later.

In ResNet-50, the residual connections enable deeper networks to be trained. ResNet is well suited for medicinal plant datasets as it is able to learn high-level discriminative features. MobileNet and EfficientNet are optimised for mobile deployment [14]. They can be used in the field where computation resources are limited.

The concept of transfer learning is now a key approach in the recognition of medicinal plants. Typically, the medicinal plant data sets are small. To train deep models from scratch, extensive data is needed [15]. Transfer learning: pre-trained models from ImageNet fine-tuned for plant identification. This enhances the performance and lowers the computational cost.

Attention mechanisms are used to further enhance feature extraction. Attention models are applied to regions of importance in the image, such as the edges of the leaves, the tips and the veins. This facilitates accuracy and interpretation [16].

Deep learning methods are found to have a higher recognition accuracy than traditional methods in studies. In fact, some machine learning techniques are also useful for detecting plant and leaves disease [21]. Typical, handcrafted methods yield a reasonable level of accuracy ranging from 70-85%, whereas deep learning can exceed 95%.

3. Discussion on Deep Learning

Today, the most promising technique for medicinal plant identification is deep learning. It owes its success to its capability of finding features within complex images which are relevant to the problem. Deep learning is adaptable to other environments unlike handcrafted systems.

CNN based systems are good in difficult scenarios like heavy leaves, cluttered background and rotated leaves. This allows them to be used practically [17].

One of the other important benefits is feature hierarchy. Low level features are lines and edges. Semantics structures are captured by high level features. This hierarchical learning enhances the classification.

Deep learning has its drawbacks, though. It demands huge amounts of data, costly computer hardware and time in training [18]. The models are often called black-box models since it is hard to explain why a certain decision is made.

However, these obstacles have not stopped deep learning from being the preferred approach for plant recognition studies because of its high accuracy and robustness.

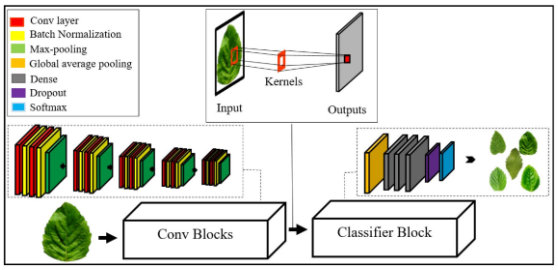


Figure 4 — Deep learning architecture

4. Future Work

A blend of AI and botany expertise is the future of medicinal plant identification.

A key area is the creation of hybrid systems based on both handcrafted features and deep features. These systems can learn and capture features specific to the domain as well as learned.

Explainable AI is another significant aspect. Regions that affected classification can be revealed using techniques like Grad-CAM [19]. This enhances users' confidence in automated systems.

Light weight models are also required. Offline mobile applications for field identification might be required by many users. This can be achieved with efficient architectures like MobileNet and quantized.

More attention needs to be directed towards establishing large scale standardised medicinal plant databases in the future. Such datasets should be for seasons, different growth stages and images taken under real conditions.

Emerging transformer models such as Vision Transformer offer promising opportunities. These models could be more effective than CNNs in future applications.

Another future direction of integration is the integration of multimodal data. Leaf images, along with flower, stem and chemical properties can increase the accuracy.

5. Conclusion

Identifying medicinal plants is one of the important applications of image processing and AI technology. Proper identification is essential for health-care safety, herbal medicine and to avoid substitutions.

The key to automated identification systems is feature extraction. Shape, texture, color and vein analysis are traditional feature extraction methods, which give useful information, but are limited in complex environment.

The advancement of deep learning techniques has greatly enhanced feature extraction capabilities. CNNs automatically learn robust features and achieve superior performance. The combination of transfer learning and lightweight architectures creates the possibility of deep learning for real applications.

While deep learning offers outstanding performance, traditional approaches are still valuable in resource constrained settings. It is expected that future systems will be a hybrid of both methods to be accurate, efficient and interpretable.

The continuous development of explainable AI, mobile computing and large datasets will further enhance medicinal plant identification systems. There is great potential in this field for healthcare, the conservation of biodiversity and herbal medicine research.

References

[1] Jaiswal, Y., Liang, Z., & Zhao, Z. (2016). Botanical drugs in Ayurveda and traditional Chinese medicine. *Journal of ethnopharmacology*, *194*, 245-259.

[2] Ahad, B., Shahri, W., Rasool, H., Reshi, Z. A., Rasool, S., & Hussain, T. (2021). Medicinal plants and herbal drugs: An overview. *Medicinal and aromatic plants: healthcare and industrial applications*, 1-40.

[3] Wang, M., Lin, H., Lin, H., Du, P., & Zhang, S. (2024). From species to varieties: How modern sequencing technologies are shaping Medicinal Plant Identification. *Genes*, *16*(1), 16.

[4] Li, X., Li, C., Rahaman, M. M., Sun, H., Li, X., Wu, J., ... & Grzegorzek, M. (2022). A comprehensive review of computer-aided whole-slide image analysis: from datasets to feature extraction, segmentation, classification and detection approaches. *Artificial Intelligence Review*, *55*(6), 4809-4878.

[5] Abdou, M. A. (2022). Literature review: Efficient deep neural networks techniques for medical image analysis. *Neural Computing and Applications*, *34*(8), 5791-5812.

[6] Tan, C., Tian, L., Wu, C., & Li, K. (2024). Rapid identification of medicinal plants via visual feature-based deep learning. *Plant Methods*, *20*(1), 81.

[7] Gautam, V., Kaur, G., Ghantasala, G. P., Vidyullatha, P., Allabun, S., Othman, M., & Zheleznyak, A. (2025). A lightweight deep learning method for medicinal leaf image classification using feature fusion. *Scientific Reports*, *15*(1), 34417.

[8] Mahurkar, D. P., & Patidar, H. (2023). Revealing leaf species through specific contour and region-based features extraction. *e-Prime-Advances in Electrical Engineering, Electronics and Energy*, *5*, 100228.

[9] Vayssade, J. A., Jones, G., & Paoli, J. N. (2023). Towards the characterization of crop and weeds at leaf scale: A large comparison of shape, spatial and textural features. *Smart Agricultural Technology*, *5*, 100245.

[10] Zubair, A. R., & Alo, O. A. (2024). Grey level co-occurrence matrix (GLCM) based second order statistics for image texture analysis. *arXiv preprint arXiv:2403.04038*.

[11] Khuat, T. P., Van, T., & Van, H. T. (2025). Plant Leaf Recognition using OSSGabor filter and Vision Transformer. *Journal of Universal Computer Science*, *31*(6), 623.

[12] Karthik, C. R., Adithya, P. M., Nidadavolu, N., Balasundaram, A., & Shaik, A. (2026). Fusing appearance and vein morphology using dual-branch deep networks for accurate medicinal plant identification. *Frontiers in Artificial Intelligence*, *9*, 1771431.

[13] Mundlamuri, R., Gunnam, G. R., Mysari, N. K., & Pujuri, J. (2025). The Evolution of AI: From Classical Machine Learning to Modern Large Language Models. *Ieee Access*.

[14] Wahyudi, I. P. A. T., Sudipa, I. G. I., Libraeni, L. G. B., Radhitya, M. L., & Asana, I. M. D. P. (2025). Performance Comparison of MobileNet and EfficientNet Architectures in Automatic Classification of Bacterial Colonies. *Indonesian Journal of Data and Science*, *6*(2), 333-342.

[15] Kaya, A., Keceli, A. S., Catal, C., Yalic, H. Y., Temucin, H., & Tekinerdogan, B. (2019). Analysis of transfer learning for deep neural network based plant classification models. *Computers and electronics in agriculture*, *158*, 20-29.

[16] Qian, X., Zhang, C., Chen, L., & Li, K. (2022). Deep learning-based identification of maize leaf diseases is improved by an attention mechanism: Self-attention. *Frontiers in plant science*, *13*, 864486.

[17] Beikmohammadi, A., Faez, K., & Motallebi, A. (2022). SWP-LeafNET: A novel multistage approach for plant leaf identification based on deep CNN. *Expert Systems with Applications*, *202*, 117470.

[18] Justus, D., Brennan, J., Bonner, S., & McGough, A. S. (2018, December). Predicting the computational cost of deep learning models. In *2018 IEEE international conference on big data (Big Data)* (pp. 3873-3882). IEEE.

[19] Ennab, M., & Mcheick, H. (2025). Advancing AI interpretability in medical imaging: a comparative analysis of pixel-level interpretability and Grad-CAM models. *Machine Learning and Knowledge Extraction*, *7*(1), 12.

[20] Attwal, K. P. S. (2024, April). A review on medicinal plant identification through leaf image. In *2024 Sixth International Conference on Computational Intelligence and Communication Technologies (CCICT)* (pp. 27-33). IEEE.

[21] Reshma, Singh, S., Alok, A., Sahu, P., & Alok, V. (2025, October). Plant disease detection using machine learning. In *AIP Conference Proceedings* (Vol. 3343, No. 1, p. 040020). AIP Publishing LLC.

GIANT COLONIC LIPOMA MIMICKING MALIGNANCY: A CASE REPORT

Dr. Onur Aydoğan

Kırıkkale University Faculty of Medicine, Department of Pathology, ORCID:0009-0001-3772-90-21

Dr. Şeyma Öztürk

Kırıkkale Üniversitesi Tıp Fakültesi Tıbbi Patoloji Anabilim Dalı/ Doktor Öğretim Üyesi, ORCID:0000-0002-2167-4253

ABSTRACT

Purpose: Colonic lipomas are rare benign mesenchymal tumors of the gastrointestinal tract and are usually asymptomatic. However, as their size increases, they may cause symptoms and especially large lesions can mimic malignant tumors. This may lead to difficulties in diagnosis and treatment processes. In this study, we aimed to present a case of a giant colonic lipoma that raised suspicion of malignancy during colonoscopy and was surgically resected.

Materials and Methods: A 70-year-old female patient presented with a long-standing complaint of constipation. Her medical history included diabetes mellitus, hypertension, and hypothyroidism. Colonoscopic examination revealed a giant, polypoid, pedunculated lesion at the level of the hepatic flexure. The endoscopic appearance was considered suspicious for malignancy, and the patient was referred to general surgery. A left hemicolectomy was performed. The resection material was examined macroscopically and microscopically.

Results: Macroscopic examination revealed a well-circumscribed mass lesion measuring 5×5×2 cm located near the ileocecal valve. Microscopic examination showed that the lesion was located in the submucosa and consisted of mature adipose tissue, consistent with a submucosal lipoma. No evidence of malignancy was observed. The postoperative course was uneventful, and the patient was discharged.

Conclusion: Although giant colonic lipomas are rare, they can mimic malignant lesions clinically and endoscopically. Especially in lesions larger than 4 cm, the likelihood of symptoms increases and surgical treatment may be preferred due to diagnostic uncertainty. However, accurate diagnosis can be achieved with appropriate preoperative evaluation and careful analysis of endoscopic findings. Colonic lipomas should always be considered in the differential diagnosis to avoid unnecessary extensive surgical resections.

Keywords: Colonic lipoma, giant lipoma, colonoscopy, benign tumor, differential diagnosis

THE RELATIONSHIP BETWEEN ADULTS' SENSE OF MEANING IN THEIR LIVES AND THEIR PERCEPTION OF LIFE, AND THEIR AWARENESS OF CARDIOVASCULAR DISEASE RISK

Yeşim Ceylantekin

Afyonkarahisar Health Sciences University, Faculty of Health Sciences, Department of Public Health Nursing. ORCID: 0000-0003-3410-9496

Dudu Zeynep Arı

Master's Student, Department of Public Health Nursing, Faculty of Health Sciences, Afyonkarahisar Health Sciences University. ORCID: 0009-0004-4981-6673

Tuğçe Erdal

Master's Student, Department of Public Health Nursing, Faculty of Health Sciences, Afyonkarahisar Health Sciences University. ORCID: 0009-0008-8272-6804

ABSTRACT

Objective: Finding meaning in life and shaping behaviours according to that meaning is of unparalleled importance today. The meaning attributed to life is associated with less struggle with cardiovascular disease, less depression, and stronger coping skills. This study aims to investigate the relationship between the meaning in the lives of adult individuals and their understanding of life, as well as their awareness of cardiovascular disease risk.

Materials and methods: This study is descriptive and correlational. Data were collected between 15 December 2025 and 15 April 2026. The sample comprised 341 adult individuals in public spaces. Data were gathered using a socio-demographic questionnaire, the Meaning of Life Scale, and the Cardiovascular Disease Risk Awareness Assessment Scale. In the analysis of the data, normal distribution was tested using the Kolmogorov-Smirnov test. Descriptive statistics, number, percentage, mean, ANOVA, t-test, and regression analysis were used in the analysis of the data.

Findings: The mean age of the participants was 38.93 ± 12.67 years. 55.4% of the participants were female, and 44.6% were male. The mean life meaning score for adults was 43.86 ± 0.43, and the total cardiovascular disease risk awareness score was 44.54 ± 0.47. The perceived heart attack/stroke risk in adults was 28.44 ± 0.38. A significant difference was found in cardiovascular risk awareness among adults over 40 years of age ($F=4.175$, $p=0.042$). On the other hand, a significant difference was found between those who viewed life positively and those who perceived the meaning of life ($F=27.606$, $p=0.000$). The meaning of life was a significant and positive predictor of cardiovascular disease risk awareness ($\beta = 0.262$, $t = 4.993$, $p < 0.001$). The meaning of life explained 6.9% of the variance in cardiovascular disease risk awareness (Adj. $R2 = 0.069$).

Conclusion: Cardiovascular disease risk awareness increased with age. Those who reported feeling happy had a higher sense of the meaning of life. There is a significant relationship between cardiovascular risk awareness and the meaning attributed to life.

Keywords: Adult, value of life, heart disease, public health nursing

GİRİŞ

İnsan, varoluşsal olarak tüm yaşamı boyunca aklının yönlendirilmesiyle hayatın anlamını aramıştır. Bu durum, 2. Dünya Savaşı'nda yaşanılan travmatik tecrübeler sonucunda bir olgu olarak bilimsel olarak araştırılmaya başlanmıştır (Dezutter et al., 2014). Viktor Emil Frankl, hayatta en temel motive edici gücün bireyin varoluşunun anlamını keşfetme arzusu olduğunu savunmuştur (Arlı Çil & Soltekin, 2021). Hayatın anlamı, bireyin hayatına aynı zamanda bir amaç olarak da yansımıştır. Hayatın anlamına sahip olmak ruh sağlığını güçlendirdiği ifade edilmiştir. Yetişkinlerin hayatı anlamlandırma biçimleri ise mutluluklarını doğrudan biçimlendirir. Yaşama verilen anlam doğrudan psikolojik iyi oluşu etkileyebilir.

Psikolojik iyi oluş, mevcut fiziksel sağlığın yanında, gelecekteki fiziksel sağlığı da etkilemektedir (Steger et al., 2006). Yetişkinlerin mutluluğu algılamasının farklı şekillerde olduğu öngörülmektedir. (Fredrickson ve ark., 2013). Hedonik ve ödomonik mutluluk şeklinde isimlendirilen iki türde insan davranışları değişmektedir. Hedonik mutlulukta kişisel tatmin ön plandadır. Eğlenmek, yemek yeme, konfor alanında uyku, sıcak bir yatak örnek olarak verilebilir. Ödomonik mutluluk ise kişisel tatminden ziyade toplum yararına bir şeyler yapmak ve topluma katkı sağlamak esastır. Bu fakir birini doyurmak, çocuk yetiştirmek, hatta yerden bir çöp almak bile olabilir. Aslında, toplum yararına katkı sağlamak kişiyi kişisel tatmine ulaştırabilir. Çevredekilere yardım edildiğinde ya da çevre iyileştirildiğinde kişi tatmin olmuş hisseder ve bu tatmin hedonik mutluluğa göre daha kalıcı hale gelir. Hedonik mutluluğa sahip olanlar genetik olarak strese baskılanmaya maruz kalmışlardır (McEwen & Gianaros, 2010) Stres ise hayatın anlamlandırılmasında önemli bir yere sahiptir. Hayatı doğru anlamlandırma, mutluluğu doğru yerlerde arama sağlığı da doğrudan etkilemektedir. Sağlığın geliştirilmesinin bir adımı olan beslenmede iyileşmeye, uykuya özendirmeye, stresi azaltmaya yardımcı olabilir. Kişinin mutlu olması ve hayatı anlamlandırması sağlığı geliştirme, daha sağlıklı olma çabası ve özelinde kardiyovasküler hastalık oluşumunu önlemede hayata bakışına etki edebilir (Cohen et al., 2016)

Kardiyovasküler hastalıklar (KVH) günümüzde erişkinlerde morbidite ve mortalite sebeplerinin başında gelmektedir (Dülek et al. 2018). Kalp damar hastalıkları tek başına kardiyolojik ölümlerin yarısını oluşturmakta ve Doğu Avrupa gibi bölgelerde tüm ölümlerin %60'ını oluşturarak dünya genelinde önde gelen ölüm nedeni olarak görülmektedir (Dugani ve Gaziano, 2016). Dünya Sağlık Örgütü'ne (DSÖ) göre, kardiyovasküler hastalıklar dünya genelinde her yıl yaklaşık 17,9 milyon insanın ölümüne neden olmaktadır. Kardiyovasküler hastalıkların küresel prevalansı son 20 yılda neredeyse iki katına çıkmıştır. Türkiye İstatistik Kurumu verilerine göre 2022 yılında önde gelen ölüm nedenleri incelendiğinde %35,4 ile dolaşım sistemi hastalıkları ön sırada yer almaktadır. (Türkiye İstatistik Kurumu, 2025). Koroner ve serebrovasküler hastalıkların erken tanı ve tedavisi KVH'nin mortalite ve morbiditesinin azaltılmasında önemlidir. KVH'den korunmak için hiperlipidemi, hipertansiyon ve diabetes mellitusun değerlendirilmesi, kontrolünün sağlanması, hastaların tedavilerine ve sağlık önerilerine uyum göstermeleri gerekmektedir. KVH'nin bilinen sosyal ve çevresel risk faktörlerini azaltmak için bireylerin sağlıklı yaşam tarzı davranışlarını kazanmaları gerekmektedir. Sağlıksız yaşam tarzı alışkanlıkları: hipertansiyon, aşırı kilo veya obezite, hiperglisemi, kan lipitlerinin yükselmesi gibi metabolik ve fizyolojik değişikliklere neden olarak ateroskleroz, koroner ve beyin damar hasarına yol açmaktadır (Sağlık Bakanlığı, 2015; World Health Organization, 2025). Kardiyovasküler hastalıkların büyük bir bölümü, tütün kullanımı, sağlıksız beslenme, yetersiz fiziksel aktivite ve alkol kullanımı gibi davranışsal risk faktörlerinin azaltılmasıyla engellenebilmektedir. Bu girişimlerle ilgili olarak DSÖ'nün kardiyovasküler hastalığı önleme ve kontrolüne yönelik yayımladığı kılavuzda primer korunma önlemlerinden olan kolesterol, kan basıncı, obezite ve tütün kullanımında eşzamanlı olarak toplumsal düzeyde az da olsa bir düşüş gerçekleşirse kardiyovasküler hastalıklara bağlı ölümlerin üçte ikisinin önlenebileceği bildirilmektedir (İnangil & Şendir, 2014; World Health Organization, 2025).

Hemşirelik, tıp, psikoloji, felsefe, din ve sanat gibi çeşitli disiplinler, insanın anlam arayışını hayattaki temel bir güç ve bireyin karşılaştığı en temel zorluklardan biri olarak görmektedir. Bu nedenle hayatın anlamı hem zihinsel hem de fiziksel iyilik hâli için büyük önem taşımakta, sağlık ve yaşam kalitesini etkilemektedir (Haugan ve Dezutter, 2021). Kişinin mutlu olması, hayatını anlaması ve olumlu düşünmesi onun hastalıkları önleme veya hastalıkla baş etme süreçlerini değiştirebilir. Kronik hastalık gelişen bireylerde mutluluk durumları literatürde incelenmiş (Karataş ve Özdemir 2024; Genç ve ark. 2025), ancak hayatını anlayan ve anlamlandıran bir kişinin hasta olmadan önce dünyada en fazla ölüm nedeni olarak gösterilen kardiyovasküler hastalıkları önleme yönelik risklere bakış açısını da değiştirebileceğini araştıran çalışmaya rastlanmamıştır. Araştırma ile literatürdeki bu boşluk kapatılması amaçlanmıştır. Bu çalışmanın amacı, yetişkin bireylerin hayatlarındaki anlam veya hayatı anlamlandırması ile kardiyovasküler hastalık risk farkındalığı ilişkisini belirlemektir.

Araştırma Soruları

Yetişkin bireylerin hayatlarını anlamlandırma durumu nedir?

Yetişkin bireylerin kardiyovasküler risk farkındalığı tutumu nedir?

Yetişkin bireylerin hayatlarındaki anlam ve anlamlandırma durumu ile kardiyovasküler risk farkındalığı arasında anlamlı ilişki var mıdır?

GEREÇ VE YÖNTEM

Araştırmanın türü: Tanımlayıcı ve ilişki arayıcı türde bir çalışmadır.

Araştırmanın yapılacağı yer ve zaman: Araştırma kamuya açık alanlarda (kafeler, hastane bahçesinde bekleyenler, parklar ve bahçeler) 15.12.2025-15.04.2026 tarihleri arasında gerçekleştirilmiştir.

Araştırmanın evreni ve örneklemi: Araştırmanın evreni Türkiye'de bulunan 18 yaş üstü yetişkinler oluşturmuştur. Çalışmada örneklem büyüklüğü nicel veriler için (N > 10.000) önerilen $n = s^2.z\alpha^2/d^2$ formülü kullanılmıştır (Özdamar, 2001). Standart sapma = 1; 0,05 anlamlılık düzeyinde z0,05 = 1,96 ve etki büyüklüğü 0,1 olarak alındığında örneklem büyüklüğü 383 olarak hesaplanmıştır. Hatalı ve eksik veriler araştırmadan çıkarıldığında, çalışmanın örneklem sayısı 341'dir.

Araştırmaya Dahil Edilme Kriterleri

Araştırmaya katılmaya gönüllü olması, Türkçe biliyor olması,18 yaş ve üstü olması ve herhangi bir kardiyolojik problemi olmamasıdır.

Araştırmadan Dışlanma Kriterleri

18 yaşından küçük olanlar, araştırmaya katılmak istemeyenler ve kardiyolojik bir hastalığı olanlar araştırmaya alınmadı.

Veri Toplama Araçları:

Verilerin toplanmasında, sosyo-demografik tanıtıcı form, Yaşamın Anlamı Ölçeği, Kardiyovasküler Hastalık Risk Farkındalığı Değerlendirme Ölçeği kullanılmıştır.

Tanıtıcı Bilgi Formu: Bu formda yaş, eğitim durumu, gelir durumu, sigara kullanım durumu gibi 12 adet soru bulunmaktadır.

Yaşamın Anlamı Ölçeği: Bu ölçek, bireylerin genel anlamda yaşamın anlamını anlayıp anlamadıklarını değerlendirmek amacıyla geliştirilmiştir. Ölçeğin özgün formu "The Meaning in Life Questionnaire (MLQ)" olan Steger, Frazier, Oishi ve Kaler tarafından 2006 yılında geliştirilmiştir. Türkçe geçerlik güvenirliği Demirdağ ve Kalafat tarafından 2015 yılında yapılmıştır (Demirdağ ve Kalafat, 2015). Ölçeğin özgün formunda yaşamı anlamaya yönelik 10 ifade yer almaktadır. Ölçekte yer alan yaşamın anlamı ile ilgili her ifadenin geliştirilme sürecinde "Kesinlikle Yanlış" ile "Kesinlikle Doğru" olmak üzere 7'li Likert tiptedir. Ölçek maddelerinin 9'u pozitif maddelerden (1, 2, 3, 4, 5, 6, 7, 8 ve 10. maddeler), 1'i negatif maddeden (9. madde) oluşmuştur. Ölçek var olan anlam (1., 4., 5., 6. ve 9. maddeler) ve bulunmaya çalışılan anlam (2., 3., 7., 8. ve 10. maddeler) olmak üzere iki alt boyuttan oluşmaktadır. Ölçekten alınabilecek en düşük puan 10, en fazla puan 70'tir. Ölçeğin Cronbach alfa değeri var olan anlam alt ölçeği için 0.81, bulunmaya çalışılan anlam alt ölçeği için 0.85 bulunmuştur. Çalışmada Cronbach alfa değeri 0.714 bulunmuştur.

Kardiyovasküler Hastalık Risk Farkındalığı Değerlendirme Ölçeği: Kardiyovasküler Hastalık Risk Farkındalığı Değerlendirme Ölçeği (KHRFDÖ), ilk olarak Avrupa Kardiyoloji Derneği tarafından 65 madde olarak geliştirilmiş olup, bireylerin önümüzdeki on yıl içinde kardiyovasküler hastalık (KVH) ve inmeye bağlı mortalite riskini düşük, orta, yüksek ve çok yüksek düzeylerde belirtmektedir. Türkçe geçerlilik ve güvenirliği Vural Doğru ve ark. tarafından (2021) yapılmıştır. Ölçekte toplam 14 madde bulunmaktadır. Ölçek 3 alt boyuttan oluşmaktadır: algılanan kalp krizi/inme riski (7 madde), algılanan faydalar ve değişime yönelik niyetler (5 madde) ve sağlıklı beslenme niyetleri (2 madde). Ölçek 4'lü Likert tipinde olup, 1 (kesinlikle katılmıyorum)- 4 (kesinlikle katılıyorum) arasında puanlandırılmaktadır. Ölçekte ve alt boyutlarında puanın yükselmesi kardiyovasküler hastalıklara yönelik farkındalık düzeyinin yükseldiğini göstermektedir. Ölçeğin Cronbach alfa değeri $\alpha = 0.809$'dur. Çalışmada ise bu değer 0.805 olarak bulunmuştur.

Araştırmanın Bağımlı Değişkenleri

Araştırmanın bağımlı değişkenleri kategorik değişkenler için yetişkin bireylerin hayatlarını anlamlandırma durumu ve yetişkin bireylerin kardiyovasküler risk farkındalığı tutumudur. Regresyon analizi için bağımlı değişken kardiyovasküler hastalık risk farkındalığıdır.

Araştırmanın Bağımsız Değişkenleri

Araştırmanın bağımsız değişkenleri yaş, eğitim durumu, gelir durumu, sigara kullanım durumu gibi demografik değişkenlerdir. Regresyon analizi için bağımsız değişken yaşamın anlamıdır.

Verilerin Toplanması: Veriler Afyonkarahisar merkezde yaşayan, çalışmaya katılmaya gönüllü olan 18 yaş üstü bireylerden yüz yüze görüşme yöntemiyle ve Google Anket formu yöntemiyle çevrimiçi şekilde toplanmıştır. Anketlerin doldurulması için süre yaklaşık 20-25 dakikadır.

Verilerin Analizi ve Değerlendirilmesi

Toplanan veriler IBM SPSS Statistics Version 22 programında analiz edilmiştir. Tanımlayıcı istatistikler için frekans, yüzde, ortalama ve standart sapma kullanılmıştır. Ölçeklerin güvenilirliği Cronbach alfa katsayısı ile değerlendirilmiştir. Normal dağılım Kolmogorov-Smirnov testi ile test edilmiş ve verilerin normal dağıldığı tespit edilmiştir ($p<0.05$). Bu nedenle, gruplar arası farklar Mann-Whitney U ve Kruskal-Wallis testleriyle; değişkenler arası ilişkiler ise Pearson korelasyon analizi ile değerlendirilmiştir. Bağımlı ve bağımsız gruplarda t testi ve ANOVA testi kullanıldı. Bağımlı değişken ile bağımsız değişken arasındaki ilişkiyi belirlemek için regresyon analizi uygulandı. Anlamlılık düzeyi $p < 0.05$ olarak kabul edilmiştir.

Araştırmanın Etik Yönü

Araştırma için ölçek sahiplerinden izin alınmıştır. Yetişkin bireylerden anket formunu doldurmaya gönüllü olduklarına dair onam alınmıştır. Katılımcılara istediği zaman araştırmadan ayrılabileceği bilgisi de verilmiştir. Araştırma için Afyonkarahisar Sağlık Bilimleri Üniversitesi Müdahale Olmayan Bilimsel Araştırmalar Etik Kurulu'ndan (Tarih:09.01.2026, toplantı no:2026/1) kurum izni alınmıştır.

BULGULAR

Katılımcıların tanımlayıcı özellikleri Tablo 1'de verilmiştir.

Tablo 1. Katılımcıların tanımlayıcı özellikleri (n=341)

		n	%
Yaş Mean±SD 38.93±12.67 (min.-max.: 18-65)			
Cinsiyet	Kadın	189	55.4
	Erkek	152	44.6
Gelir durumu	Gelir gidere eşit	189	55.4
	Gelir giderden az	77	22.6
	Gelir giderden fazla	75	22.0
Eğitim durumu	İlköğretim	32	9.4
	Lise	74	21.7
	Üniversite ve üzeri	235	68.9
Aile tipi	Çekirdek	312	91.5

	Geniş	29	8.5
Çalışma durumu	Evet Hayır	248 93	72.7 27.3
Ailede kalp hastalığı	Var Yok	101 240	29.6 70.4
Kronik hastalık	Var Yok	121 220	35.5 64.5
Sigara kullanma	Evet Hayır	121 220	35.5 64.5
Hayatın anlamı	Olumlu ifade (mutluluk, heyecan, iyilik) Olumsuz ifade (zor, anlamsız, mutsuzluk)	184 157	53.9 46.1
Kişilik özelliği	Hayatı önemsemeyen Hayatı gerektiği kadar önemseyen Hayatı çok önemseyen	25 248 68	7.3 72.7 19.9
Kişilik özelliğiyle nasıl bir insan	Mutlu Mutsuz Değişken	127 21 193	37.2 6.2 56.6

Katılımcıların yaş ortalaması 38.93±12.67, %55.4'ü kadın, %55.4'ünün geliri giderine eşit, %68.9'u üniversite mezunu, %91.5'i çekirdek aileye sahip, %72.7'si çalışıyor, %70.4'ünün ailesinde kalp hastalığı bulunmamakta, %64.5'inin kronik hastalığı yok, %64.5'i sigara kullanmıyor, %53.9'u hayatın anlamı sizin için nedir? sorusuna mutluluk, heyecan ve iyilik gibi olumlu yanıtlar vermiştir; %72,7'si hayatı gerektiği kadar önemsememekte, %56,6'sı kişilik özelliği itibarıyla değişken bir yapıya sahip olduğunu bildirdi (Tablo 1).

Tablo 2. Katılımcıların sosyodemografik özelliklerine göre yaşamın anlamı ve kardiyovasküler hastalık risk farkındalığı (n=341)

Değişkenler		**Yaşamın Anlamı**				**Kardiyovasküler Hastalık Risk Farkındalığı**			
		Ort.	**SD**	**t/F**	**p**	**Ort.**	**SD**	**t/F**	**p**
Cinsiyet	**Kadın** **Erkek**	44.01 43.68	8.26 7.59	0.141	0.707	44.61 44.46	9.03 8.37	0.024	0.878
Yaş	**<40** **≥40**	44.15 43.50	7.69 8.28	0.572	0.450	43.68 45.61	9.58 7.44	4.175	**0.042**

Gelir durumu	**Gelir gider eşit**	44.70	7.57	2.590	0.077	44.26	9.14	0.614	0.542
	Gelir az	42.42	9.23			45.51	7.92		
	Gelir fazla	43.21	7.31			44.25	8.48		
Eğitim Durumu	**İlköğretim**	42.81	9.06	0.339	0.713	46.46	7.69	0.967	0.381
	Lise	43.77	8.50			44.77	8.59		
	Üniversite ve üzeri	44.03				44.21	8.90		
Aile tipi	**Çekirdek**	43.90	7.88	0.102	0.750	44.60	8.63	0.158	0.691
	Geniş	43.41	8.85			43.93	9.82		
Çalışma durumu	**Evet**	43.57	8.14	1.194	0.275	44.83	8.45	1.005	0.317
	Hayır	44.63	7.44			43.77	9.43		
Ailede kalp hastalığı	**Var**	43.21	7.86	0.948	0.331	44.98	9.20	0.350	0.554
	Yok	44.13	8.00			44.36	8.53		
Kronik hastalık	**Var**	43.89	7.71	0.002	0.962	45.01	8.14	0.538	0.464
	Yok	43.85	8.11			44.29	9.04		
Sigara kullanma	**Var**	43.62	8.02	0.116	0.684	44.89	8.66	0.261	0.590
	Yok	43.99	7.94			44.35	8.78		
Hayatın anlamı	**Olumsuz**	41.50	8.00	27.606	**0.000**	44.18	8.51	0.504	0.478
	Olumlu	45.88	7.37			44.85	8.92		
Kişilik özelliği	**Hayatı önemsemeyen**	42.48	10.12	0.730	0.483	44.04	7.03	0.141	0.868
	Hayatı gerektiği kadar önemseyen	43.78	7.52			44.47	9.02		
	Hayatı çok önemseyen	44.66	8.64			45.00	8.28		
Kişilik özelliğiyle nasıl bir insan	**Mutlu**	45.14	8.35	7.978	**0.000**	44.53	9.36	0.071	0.932
	Mutsuz	37.85	8.42			45.23	4.13		
	Değişken	43.67	7.34			44.48	8.69		

t: Bağımsız gruplar için t testi, F: Tek yönlü ANOVA

Kardiyovasküler risk değerlendirme kılavuzlarında 40 yaşın klinik risk başlangıç eşiği olarak kabul edilmesi nedeniyle yaş değişkeni bu değerde ele alınmıştır. 40 yaşın üstündeki bireylerde kardiyovasküler risk farkındalığı anlamlı düzeyde farklılık göstermiştir (F=4.175, p=0.042). Diğer yandan, hayatın anlamını olumlu değerlendirenlerde yaşamın anlamı anlamlı fark oluşturmuştur (F=27.606, p=0.000). Kişilik özelliği olarak mutlu hissedenlerde yaşamın anlamı arasında anlamlı fark vardır (F=7.978, p=0.000) (Tablo 2).

Tablo 3. Katılımcıların yaşam anlamları ve kardiyovasküler hastalık risk farkındalıkları

Değişkenler	**Mean**	**SD**	**Min.-max.**
Yaşamın Anlamı	43.86	0.43	9-63
Var olan anlam	26.82	0.29	5-35
Bulunmaya çalışılan anlam	21.17	0.41	5-35
Kardiyovasküler Hastalık Risk Farkındalığı	44.54	0.47	5-64
Algılanan kalp krizi/inme riski	28.44	0.38	0-43
Algılanan faydalar ve değişime yönelik niyetler	5.74	0.08	0-8
Sağlıklı beslenme niyetleri	4.45	0.10	0-8

Yaşamın anlamı ortalama değeri 43.86±0.43'tür. Var olan anlam düzeyi 26.82±0.29, bulunmaya çalışılan anlam 21.17±0.41 olarak bulunmuştur. Bireylerin kardiyovasküler hastalık risk farkındalığı toplam puanları 44.54±0.47'dir. Algılanan kalp krizi/inme riski ise 28.44 ± 0.38'dir. Algılanan faydalar ve değişime yönelik niyetlerin puan ortalaması 5.74±0.08, sağlıklı beslenme niyetlerinin puan ortalaması ise 4.45±0.10'dur (Tablo 3).

Tablo 4. Katılımcıların yaşam anlamı ile kardiyovasküler hastalık risk farkındalığı düzeyleri arasındaki ilişki

		Kardiyovasküler Hastalık Risk Farkındalığı
Yaşamın anlamı	**r**	0.262**
	p	0.000
	n	341

r: Pearson korelasyon katsayısı

Yaşamın anlamı ile kardiyovasküler hastalık risk farkındalığı arasında zayıf, pozitif ve anlamlı bir ilişki bulunmuştur (r=0.262, p=0.000) (Tablo 4).

Tablo 5. Yaşamın anlamının kardiyovasküler hastalık risk farkındalığına etkisi

Model	**B**	**β**	**t**	**p**	**Zero-order**	**Tolerance**	**VIF**
Constant	33.231		15.315	0.000			
KHRFÖ	0.239	0.262	4.993	0.000	0.262	1.000	1.000
F=24.935, Adj. R^2= 0.069, Durbin-Watson= 1.907							

KHRFÖ: Kardiyovasküler hastalık risk farkındalığı ölçeği

Yaşamın anlamı kardiyovasküler hastalık risk farkındalığı üzerinde yordayıcı bir etkiye sahiptir ve kurulan regresyon modeli anlamlıdır ($F = 24.935$, $p < 0.001$). Model, kardiyovasküler hastalık risk farkındalığındaki varyansın %6.9'unu açıklamaktadır (Adj. $R^2 = 0.069$). Kardiyovasküler hastalık risk farkındalığında yaşamın anlamı anlamlı ve pozitif bir yordayıcıdır ($\beta = 0.262$, $t = 4.993$, $p < 0.001$) (Tablo 5).

TARTIŞMA

Bu çalışmada, yetişkin bireylerin hayatlarındaki anlam ve hayatı anlamlandırması ile kardiyovasküler hastalık risk farkındalığı arasındaki ilişkiyi belirlemek amaçlanmıştır.

Bir çalışmada kadınların kardiyovasküler hastalık risk skorları erkeklerden daha düşük bulunmuştur (Şimşek ve Bakırhan 2026). Yapılan başka bir araştırmada her iki cinsiyete sahip genç yetişkinlerin benzer yaşam anlamına sahip olduğu, erkek ve kadın arasında anlam farklılığı olmadığı ifade edilmiştir (Yüksel, 2012). Çalışmada da benzer sonuçla cinsiyet ile yaşamın anlamı arasında anlamlı bir farklılık oluşmamıştır. Bu sonuç yaşamın anlamlandırılmasında cinsiyetin rolünün olmadığını göstermektedir.

Erkekler kadınlara göre daha erken yaşta kardiyovasküler hastalığa yakalanırlar. Bunun sebebi, menopoz dönemine kadar östrojen hormonunun kadınları kardiyovasküler açıdan korumasıdır. Kardiyovasküler risk farkındalığı ile ilgili literatür tarandığında bazı sonuçlar bulunmuştur. Kadınlar kardiyovasküler hastalıkların erkeklerde daha yaygın olduğunu düşündüğünden risk algıları düşük olarak bulunmuştur (Bozdemir Özel vd., 2021). DSÖ verilerine göre kardiyovasküler hastalık sebebiyle ölüm oranları kadınlarda daha fazladır (World Health Organization [WHO], 2024). Çalışmada kardiyovasküler hastalık risk değerlendirmesi ile cinsiyet arasında anlamlı bir ilişki bulunmamıştır. Özellikle kırk yaşından sonraki yaş grubunda risk farkındalığının artış göstermesi, sağlıklı yaşama yakın davranışlar sergilendiğini ve bunun da cinsiyete göre değişmediğini akla getirebilir. Diğer yandan, algılanan risk faktörlerinin mevcut risklerin artmasıyla yükseldiğini de düşündürebilir.

Yetişkin bireylerin yaklaşık yarısı hayatını olumlu olarak mutlu, neşeli, heyecan verici ve iyi olarak tanımlarken, diğer yarısı da zor, anlamsız, mutsuzluk dolu olarak tanımlamıştır. Çalışmada yaşamını mutlu olarak değerlendirilenlerde yaşamın anlamı yüksektir. Bu da kişinin kendini tanıma ve kendine değer verme aşamalarında başarılı olduğunu gösterebilir. Mutlu insanların yaşamlarını daha anlamlı buluyor olması, yaşam ile mutluluğun pozitif birbirini etkilediğini düşündürmektedir. Literatürde de yaşamın anlamını olumlu algılayan bireylerde psikolojik iyi oluşluk düzeyinin de yüksek olduğunu ve öznel iyi oluşluğun da aynı oranda arttığını gösteren çalışmalar mevcuttur (Martela & Steger 2016; Li et al., 2024; He et al., 2023).

Başka bir çalışmada evli bireylerin manevi iyi oluş düzeyleri arttıkça yaşamın anlamının da arttığını göstermektedir (Çalışkan ve Dilmaç, 2022). Yetişkinlerde yapılan araştırmada yaşamın anlamı 47.35±8.614 olarak ifade edilmiştir (Can ve Avşin, 2023). Covid-19 döneminde yapılan bir çalışmada ise yaşamın anlamı 44.68±10.13 olarak ifade edilmiştir (Ogan et al., 2022). Çalışmada da benzer şekilde yaşamın anlamı 43.86±0.43 olarak orta- yüksek düzeyde bulundu. Yaşamın alt boyutlarından var olan anlam, bulunmaya çalışılan anlamdan daha yüksektir. Bu durum, mevcut durumda bireylerin mutlu olma durumları ile ilişkilendirildiğinde, bireylerin kendilerini tanıma davranışlarının ve var olan duruma yönelik yaşama atfettikleri anlam düzeylerine hakimiyetlerinin yüksek olduğunu göstermektedir. Araştırmada var olan anlam puanı, bulunmaya çalışılan anlamdan yüksektir. Bu da var olan yaşamın arayıştan ziyade mevcut olanı anlamlandırma eğilimi içinde olduğunu göstermektedir. Bu durum psikolojik iyi oluşluk açısından değerli görülebilir.

Kırk yaş üstü bireylerde yapılan çalışmada kardiyovasküler hastalıklar risk faktörleri toplam puanı 19,92±4,40 olarak ifade edilmiştir (Karatay et al., 2021). Başka bir çalışmada, ailelerinde kalp hastalığı olan bireylerin olmayanlara göre kalp krizi ve inme bilgi düzeyinin daha yüksek olduğu belirlenmiştir (Han Aydilek et al., 2026). Çalışmada ise ailede kalp krizi geçirenlerle kardiyovasküler hastalık riski farkındalığı arasında anlamlı bir fark bulunmamıştır.

Yapılan bir araştırmada daha önce kalp krizi geçirenlerde, bilişsel hastalık temsillerinin daha düşük olduğu, kalp krizinin tekrarlanmasının bireyin fiziksel sağlığının yanında ruh sağlığının da bozulmasına neden olduğu ifade edilmiştir (Bulantekin Düzalan, 2024). Başka bir çalışmada da önemli bir fiziksel

hastalık deneyimleme durumunun umut ve yaşamda anlamı etkilemediği sonucuna ulaşılmıştır (Kaya ve Akoğlu, 2024). Çalışmada da kronik hastalığa sahip olmak ya da ailede kalp hastalığı olması ile kardiyovasküler hastalık risk farkındalığı arasında anlamlı fark bulunmamıştır.

Yapılan araştırmalar, algılanan stres düzeyi ile kardiyovasküler hastalık risk faktörleri arasında ilişki olduğunu ifade etmektedir. Öyle ki bu psikolojik stresin sigara, fiziksel hareketsizlik ve düzensiz yeme davranışlarına eşdeğer bir risk faktörü oluşturduğu da vurgulanmaktadır (Carola et al., 2024). Araştırmada hem anlam düzeyinin hem de sağlık davranış niyetlerinin görece yüksek olması, yaşama anlam yükleyen yetişkinlerin sağlıklarını korumaya daha fazla motive olabileceklerini akla getirebilir. Diğer yandan, algılanan faydalar ve değişime yönelik niyetler alt boyutunun orta değerin üstünde olması, davranış değişimine açık bir yetişkin grubu olduğunu da göstermektedir.

Çalışmada yetişkinlerin algıladıkları kalp krizi/inme riski yüksektir. Burada birçok faktörden bahsedilebilir. Toplumda kardiyovasküler hastalıkların yaygınlığı ve görünürlüğü, medyada sık yer alması ve çevrede bu hastalıkları geçiren kişilerin bulunması gibi faktörler bireylerin risk algısını artırmış olabilir.

SONUÇ VE ÖNERİLER

Araştırma bulgularına göre, yaşa bağlı kardiyovasküler hastalık farkındalığı risk değerlendirme puanı yükselmiştir. Hayatın anlamını olumlu ve kişilik özelliği olarak kendini mutlu olarak değerlendirenlerde yaşamı anlamlandırma daha yüksek bulunmuştur. Kardiyovasküler hastalık risk farkındalığında yaşamın anlamı anlamlı ve pozitif bir yordayıcı olarak bulunmuştur.

Bu konuda toplumun ruh sağlığını korumak için insanların hayatlarına anlam ve yön vermek adına psikolojik destek hizmeti verilmelidir. Hayatı anlamlandıramayan bireylerde ise kendini tanıma, kendini geliştirme ve stres yönetimi konularında eğitimler verilmelidir. Düzenli beslenme ve fiziksel aktivite yapma gibi önerilerin uygulamaya geçilmesi için özen gösterilmelidir. Bireylerin sadece biyolojik olarak değil, psikososyal olarak da değerlendirilmesi üzerinde durulmalıdır. Düşük yaşam anlamı anlamına sahip bireylerde yalnızlık veya sosyal izolasyon gibi durumların olabileceği düşünülerek, bireylerin yaşam anlamı önemsenmelidir. Bu konuda sosyal sorumluluk projeleri, yetişkinlere yönelik hobilerin uygulamaya geçirilmesi, aktif yaşam programlarının oluşturulması sağlanmalıdır. Farklı kültürlerde ve farklı değişkenler de eklenerek deneysel çalışmaların yapılması da önerilir.

KAYNAKLAR

American Heart Association. (2023). Heart disease and stroke statistics—2023 update: A report from the American Heart Association. *Circulation, 147*(8), e93–e621. https://doi.org/10.1161/CIR.0000000000001123

Arlı Çil, D., & Soltekin, M. F. (2021). Kişilerin yaşamı anlamlandırma biçimleri ve mutluluğa bakış açıları arasındaki ilişki. *Dokuz Eylül Üniversitesi Sosyal Bilimler Enstitüsü Dergisi, 23*(3), 1053–1069. https://doi.org/10.16953/deusosbil.858137

Bower, J. E., Kemeny, M. E., Taylor, S. E., & Fahey, J. L. (1998). Cognitive processing, discovery of meaning, CD4 decline, and AIDS-related mortality among bereaved HIV-seropositive men. *Journal of Consulting and Clinical Psychology, 66*(6), 979–986.

Bulantekin Düzalan, Ö. (2024). Evaluation of life attitude in patients with acute coronary syndrome. *Turkish Journal of Cardiovascular Nursing, 15*(36), 17–24. https://doi.org/10.5543/khd.2024.75002

Can, Ş., & Avçin, E. (2023). Yaşamın anlamı ve spiritüel iyi oluş ile ölüme karşı tutum arasındaki ilişki: Tanımlayıcı bir çalışma. *Türkiye Klinikleri Hemşirelik Bilimleri Dergisi, 15*(2), 366–375.

Carola, V., Vincenzo, C., Vincenzo, G., Morale, C., Cecchi, V., & Nicolais, G. (2024). Psychological risk factors and cardiovascular disease. *Frontiers in Psychology, 15*, 1419731. https://doi.org/10.3389/fpsyg.2024.1419731

Cohen, R., Bavishi, C., & Rozanski, A. (2016). Purpose in life and its relationship to all-cause mortality and cardiovascular events: A meta-analysis. *Psychosomatic Medicine, 78*(2), 122–133. https://doi.org/10.1097/PSY.0000000000000274

Çalışkan, Ş., & Dilmaç, B. (2022). Evli bireylerde manevi iyi oluş, ailede yılmazlık ve yaşamın anlamı arasındaki yordayıcı ilişkiler. *MANAS Sosyal Araştırmalar Dergisi, 11*(1).

Demirdag, S., & Kalafat, S. (2015). Meaning in Life Questionnaire (MLQ): Turkish adaptation, validity and reliability. *İnönü Üniversitesi Eğitim Fakültesi Dergisi, 16*(2), 83–95. https://doi.org/10.17679/iuefd.16250801

Dezutter, J., et al. (2014). Meaning in life in emerging adulthood: A person-oriented approach. *Journal of Personality, 82*(1), 57–68. https://doi.org/10.1111/jopy.12033

Dugani, S., & Gaziano, T. A. (2016). 25 by 25: Achieving global reduction in cardiovascular mortality. *Current Cardiology Reports, 18*(1), 10. https://doi.org/10.1007/s11886-015-0679-4

Dülek, H., Tuzcular Vural, Z., & Gönenç, I. (2018). Kardiyovasküler hastalıklarda risk faktörleri. *Journal of Turkish Family Physician, 9*(2). https://doi.org/10.15511/tjtfp.18.00253

Fredrickson, B. L., et al. (2013). A functional genomic perspective on human well-being. *PNAS, 110*(33), 13684–13689.

Genç, C., Kıraç, R., & Eroğlu, E. (2025). Kronik hastalık öz yönetimi ile mutluluk düzeyi ilişkisi. *Gümüşhane Üniversitesi Sağlık Bilimleri Dergisi, 14*(1), 266–275.

Han Aydilek, O., Arslantaş, D., Ünsal, A., Salış, E., Yücel, E., & Altındağ, M. A. (2026). Kardiyovasküler hastalık risk farkındalığı ve fiziksel aktivite. *Adnan Menderes Üniversitesi Sağlık Bilimleri Fakültesi Dergisi, 10*(1), 55–68.

Haugan, G., & Dezutter, J. (Eds.). (n.d.). *Meaning-in-life: A vital salutogenic resource for health*. Springer.

He, X., Wang, X., Steger, M., Ji, L. J., Jing, K., Liu, M., & Ye, B. J. (2023). Meaning in life and psychological distress: A meta-analysis. *Journal of Research in Personality, 104*, 104381. https://doi.org/10.1016/j.jrp.2023.104381

İnangil, D., & Şendir, M. (2014). Coronary artery disease patients' health behaviors. *Acıbadem Üniversitesi Sağlık Bilimleri Dergisi, 5*(2), 96–101.

Karataş, G., & Özdemir, Ç. (2024). Tip 2 diyabet hastalarında mutluluk düzeyleri. *Türkiye Diyabet ve Obezite Dergisi, 8*(2), 180–190.

Karatay, G., Yeşiltepe, A., & Aktaş, H. (2021). Kardiyovasküler hastalık risk faktörleri bilgi düzeyleri. *Acta Medica Nicomedia, 4*(2), 50–55.

Kaya, B., & Akoğlu, B. (2024). Travma sonrası büyüme ve yaşamda anlam. *Humanistic Perspective, 6*(1), 33–58.

Li, T., et al. (2024). Academic satisfaction and meaning in life. *Education Sciences, 14*(4), 436. https://doi.org/10.3390/educsci14040436

Martela, F., & Steger, M. (2015). The three meanings of meaning in life. *Journal of Positive Psychology, 11*(5), 1–15. https://doi.org/10.1080/17439760.2015.1137623

McEwen, B. S., & Gianaros, P. J. (2010). Stress and adaptation. *Annals of the New York Academy of Sciences, 1186*(1), 190–222.

Ogan, S., Öz Soysal, F. S., & Uz Baş, A. (2022). Meaning of life during COVID-19. *Batı Anadolu Eğitim Bilimleri Dergisi, 13*(1), 1–26.

Pearson, T. A., et al. (2013). AHA guide for cardiovascular health. *Circulation, 127*, 1730–1753.

Rozanski, A., Blumenthal, J. A., & Kaplan, J. (1999). Psychological factors and cardiovascular disease. *Circulation, 99*(16), 2192–2217.

Ryan, R. M., & Deci, E. L. (2001). Happiness and human potentials. *Annual Review of Psychology, 52*, 141–166.

Sağlık Bakanlığı. (2015). Türkiye kalp ve damar hastalıkları önleme ve kontrol programı (2015–2020).

Şimşek, M., & Bakırhan, H. (2026). Kardiyovasküler risk ve beslenme alışkanlıkları. *Food and Health, 12*(1), 15–30. https://doi.org/10.3153/FH26002

TÜİK. (2022). Ölüm ve ölüm nedeni istatistikleri 2022. https://data.tuik.gov.tr

Vural Doğru, B., Utli, H., & Karaman, E. (2021). Kardiyovasküler hastalık risk farkındalığı ölçeği. *Turkish Journal of Cardiovascular Nursing, 12*(27), 18–25.

World Health Organization. (2025). *Cardiovascular diseases*. https://www.who.int/health-topics/cardiovascular-diseases. Erişim tarihi: 14.04.2026.

Yüksel, R. (2012). Genç yetişkinlerde yaşamın anlamı. *Sakarya University Journal of Education, 2*(2), 79–91. https://doi.org/10.19126/suje.15640

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Kep Adresi:siu@hs01.kep.tr

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EMERGENCY SURGICAL REPAIR OF A LARGE APICAL MUSCULAR VENTRICULAR SEPTAL DEFECT IN AN ELDERLY PATIENT WITH REDUCED EJECTION FRACTION: A CASE REPORT

Prof. Dr. H. Turan AKKOYUN
Head of Conference