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Metabolic and Hormonal Profiles in Women With Hirsutism: A Comparison Between Polycystic Ovary Syndrome and Idiopathic Hirsutism

Short Title: Comparison of Idiopathic Hirsutism and PCOS

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Abstract

Background: Hirsutism is a common endocrine complaint most frequently associated with polycystic ovary syndrome (PCOS), but it may also occur in idiopathic hirsutism (IH). Because

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the two conditions differ in long-term metabolic risk and management, distinguishing them is clinically important, yet reliable, routinely available discriminators remain incompletely defined. Rather than re-describing established differences, this study aimed to determine whether routine hormonal and biochemical parameters can help discriminate PCOS from IH in women presenting with hirsutism, independent of the confounding effect of severe obesity.

Methods: In this retrospective cross-sectional study, 275 women with hirsutism (69 with IH and 206 with PCOS) were evaluated. To minimize the confounding effect of severe obesity, women with a body mass index (BMI) >40 kg/m² were excluded. Clinical, biochemical, and hormonal parameters were compared between groups, and multivariable logistic regression was performed to identify parameters independently associated with PCOS.

Results: Compared with women with IH, women with PCOS had significantly higher triglycerides, alanine aminotransferase (ALT), aspartate aminotransferase (AST), the ALT/AST ratio, thyroid-stimulating hormone (TSH), luteinizing hormone (LH), the LH to follicle-stimulating hormone (FSH) ratio, and total testosterone. In contrast, BMI, fasting insulin, homeostasis model assessment of insulin resistance (HOMA-IR), and lipid parameters other than triglycerides did not differ significantly between groups. In multivariable logistic regression, only the LH/FSH ratio (odds ratio [OR] 2.86; 95% confidence interval [CI] 1.589–5.135) and the ALT/AST ratio (OR 2.70; 95% CI 1.057–6.892) remained independently associated with PCOS, whereas total testosterone did not. A model combining these routinely available markers discriminated PCOS from IH with an area under the receiver operating characteristic (ROC) curve (AUC) of 0.728 (95% CI 0.661–0.794), exceeding that of any single marker, with good calibration (Hosmer–Lemeshow p = 0.361).

Conclusion: After minimizing the confounding effect of severe obesity, women with PCOS and IH showed comparable classic metabolic indices (fasting insulin, HOMA-IR, and lipids), but differed in hormonal profile and in two routinely available laboratory ratios — LH/FSH and ALT/AST — that were independently associated with PCOS. These inexpensive, widely available ratios may serve as a practical adjunct for distinguishing PCOS-related hirsutism from idiopathic hirsutism, pending prospective validation.

Keywords: Hirsutism, Polycystic Ovary Syndrome, Idiopathic Hirsutism, clinical differentiation, Hormonal Profiles.

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1. Introduction

Hirsutism represents a clinical condition distinguished by the abnormal manifestation of terminal hair growth resembling male-pattern distribution in females, which may lead to significant cosmetic and psychological distress [1,2]. This condition impacts approximately 5% to 15% of premenopausal women within the general population [3,4]. The underlying etiology is commonly related to increased androgen production or enhanced sensitivity of hair follicles to circulating androgens, frequently reflecting an underlying endocrine disturbance [5]. Polycystic ovary syndrome (PCOS) represents the most common etiological cause of hirsutism. Other conditions associated with hirsutism include idiopathic hirsutism (IH), Cushing syndrome, congenital adrenal hyperplasia, and androgen-secreting tumors [6].

PCOS is recognized as one of the most widespread endocrinological disorders affecting women of reproductive age, characterized by chronic anovulation, hyperandrogenism, and the presence of polycystic ovarian morphology [7,8]. In addition to reproductive manifestations, PCOS is frequently associated with obesity, insulin resistance, dyslipidemia, and increased cardiometabolic risk, supporting its recognition as a systemic metabolic-endocrine disorder rather than an isolated reproductive condition [9–12]. Hirsutism is one of the most common manifestations of PCOS and is present in a substantial proportion of affected women [1,7].

In contrast, idiopathic hirsutism is typically defined as isolated hirsutism in women with regular menstrual cycles, normal androgen levels, and no identifiable endocrine disorder. It accounts for approximately 10–15% of hirsutism cases [3,13]. Although traditionally considered a relatively benign entity, abnormalities in peripheral androgen metabolism and altered follicular sensitivity have been proposed in its pathophysiology [3,5,13,14]. Moreover, some studies suggest that metabolic alterations may not be entirely absent in women with IH, further complicating its distinction from PCOS [9,15].

Although clinical hirsutism may appear similar in both conditions, differentiating idiopathic hirsutism from PCOS is clinically important because of differences in long-term metabolic implications, follow-up strategies, and management approaches. However, biochemical and metabolic differences between these conditions remain incompletely characterized, particularly when the confounding effect of obesity is considered. Whether differences attributed to PCOS

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reflect syndrome-specific alterations or are partly driven by obesity remains insufficiently clarified.

Clinical assessment of hirsutism commonly relies on the modified Ferriman–Gallwey score (mFGS), while differential diagnosis requires integration of hormonal evaluation and exclusion of secondary causes of hyperandrogenism [1,16,17]. In this context, identifying routinely available biochemical markers that may aid in distinguishing PCOS-related hirsutism from IH may have practical clinical relevance.

Therefore, rather than re-describing the hormonal and metabolic differences between idiopathic hirsutism and PCOS already reported in the literature, the present study focused on whether a small set of inexpensive, routinely available biochemical parameters — including simple laboratory ratios — can discriminate the two conditions in everyday clinical practice, and whether such discrimination persists after minimizing the confounding effect of severe obesity.

2. Participants and Methods

2.1. Study Design and Participants

This retrospective, cross-sectional study was conducted on female patients over the age of 18 who presented to the endocrinology out-patient clinic of Recep Tayyip Erdogan University Hospital with complaints of hirsutism between 2022 and 2024. The study was approved by Recep Tayyip Erdogan University Local Ethics Committee, and the guides of the Declaration of Helsinki were strictly adhered to throughout the study. Hirsutism was defined as excessive terminal hair growth in androgen-dependent body areas in women and was assessed using the mFGS. Women with an mFGS score of ≥8 were considered to have hirsutism and were included in the study [17–19]. All modified Ferriman–Gallwey assessments were performed by a single experienced the same investigator, thereby eliminating inter-observer variability in hirsutism scoring. In the process of documenting patient information, each individual was assigned an identification number, ensuring that all participants remained anonymized.

Among 365 women presenting with hirsutism, one patient was diagnosed with adrenal oncocytoma, three with nonclassic congenital adrenal hyperplasia, and three with Cushing syndrome. Twenty-nine patients were excluded because of incomplete laboratory data. Following detailed clinical and laboratory evaluation, 81 women were diagnosed with idiopathic hirsutism

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and 248 with PCOS. In addition, to minimize the confounding effect of severe obesity on metabolic and endocrine comparisons, women with body mass index (BMI) >40 kg/m² were excluded from both groups. After applying all exclusion criteria, the final study population consisted of 69 women with idiopathic hirsutism and 206 women with PCOS, and all analyses were performed in this cohort. The flow diagram of patient selection is shown in Figure 1.

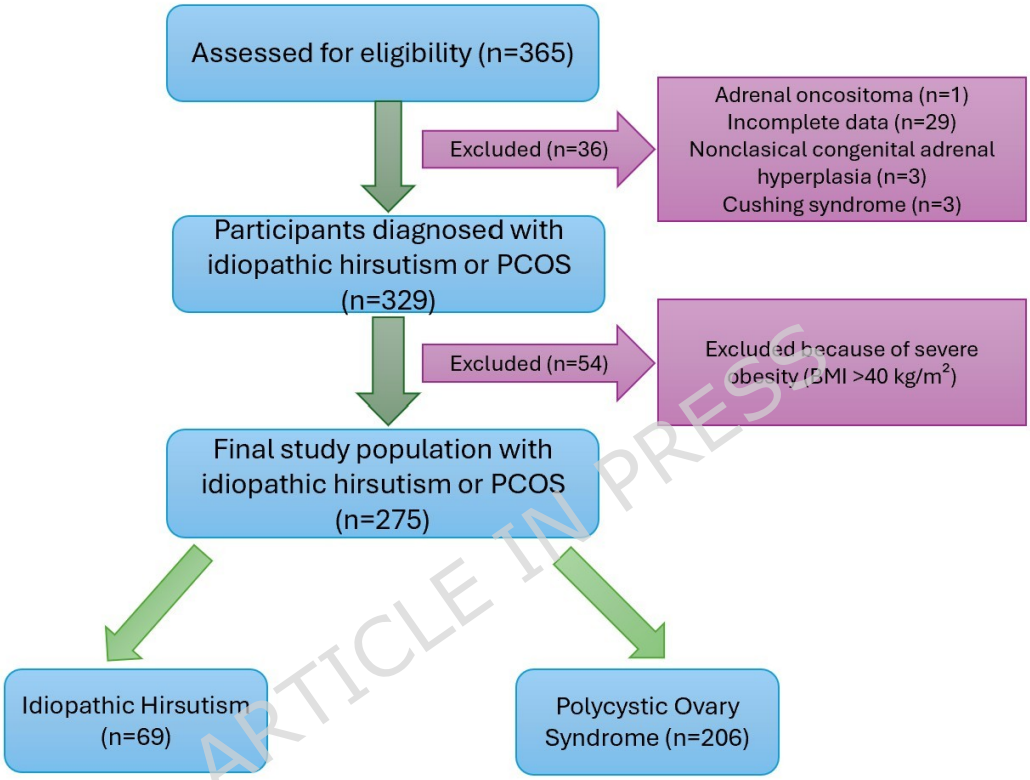


Figure 1. Flow diagram of patient selection and final analytical cohort after exclusion of women with BMI >40 kg/m².

PCOS was diagnosed according to the 2003 Rotterdam criteria. According to these criteria, the presence of at least two of the following conditions is requisite: oligo/anovulation, clinical or biochemical hyperandrogenism, and the morphological characteristics of polycystic ovaries as determined through ultrasonography [16,20,21]. Idiopathic hirsutism was defined as the presence of hirsutism in women with regular ovulatory menstrual cycles, normal serum androgen levels, and no identifiable secondary cause of hyperandrogenism or endocrine disease. The diagnosis was established after excluding other etiologies including PCOS, nonclassic congenital adrenal hyperplasia, Cushing syndrome, adrenal or ovarian tumors, thyroid dysfunction,

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hyperprolactinemia, and medication-related causes through clinical history, physical examination, laboratory investigations, and imaging studies when necessary [1].

Inclusion criteria: Female individuals aged 18 years or older, mFGS ≥8, clinical diagnosis of PCOS or idiopathic hirsutism.

Exclusion criteria: Exclusion criteria included the presence of adrenal or ovarian neoplasms, Cushing syndrome, acromegaly, hyperprolactinemia, thyroid disorders, known chronic liver or renal disease, hirsutism secondary to medications, genetic predisposition to hypertrichosis, pregnancy, lactation, and severe obesity (BMI >40 kg/m²), the latter excluded to minimize the confounding effect of extreme adiposity on metabolic and endocrine comparisons. Patients using medications that could affect androgen levels or menstrual function, including oral contraceptive pills, spironolactone, cyproterone acetate, finasteride, glucocorticoids, danazol, and anabolic steroids, were also excluded.

Exclusion of secondary causes of hirsutism was based on clinical history, physical examination, laboratory evaluation, and imaging studies when clinically indicated. Thyroid dysfunction and hyperprolactinemia were excluded using serum thyroid-stimulating hormone and prolactin levels. Nonclassic congenital adrenal hyperplasia was excluded using 17-hydroxyprogesterone levels, while Cushing syndrome was evaluated using cortisol measurements and, when necessary, a 1 mg dexamethasone suppression test. Adrenal and ovarian tumors were excluded by imaging studies in selected patients.

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2.2. Data Collection and Evaluation

During the process of data collection, the demographic characteristics of patients, including age and BMI, along with biochemical parameters such as serum total testosterone, luteinizing hormone (LH), follicle-stimulating hormone (FSH), estradiol, prolactin, DHEAS, and thyroid-stimulating hormone (TSH), as well as indicators of insulin resistance (HOMA-IR), lipid profile levels (total cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and triglycerides), and glucose concentrations were retrospectively obtained from the hospital's automated information system. Hormonal investigations were performed during the early follicular phase of the menstrual cycle, generally between days 2 and 5 of spontaneous menstruation whenever possible. In women with oligo/amenorrhea, blood sampling was

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performed either during a spontaneous bleeding episode or following progesterone-induced withdrawal bleeding.

All biochemical assessments were conducted within a single laboratory, utilizing blood samples obtained after an 8-10 hour fasting period, specifically during the morning hours. The body weight and height of all participants were measured in the morning while fasting, without shoes, employing calibrated medical scales according to standardized protocols. The BMI was derived by dividing the weight in kilograms by the square of the height in meters (m^2) [22]. All anthropometric evaluations were conducted utilizing a consistent methodology and by the the same investigator.

Measurements of arterial blood pressure were obtained using a conventional sphygmomanometer following a 10-minute period of rest in a seated position for the participants, with the right arm positioned at heart level, and were documented as the systolic blood pressure (SBP) corresponding to the first Korotkoff sound and the diastolic blood pressure (DBP) linked to the fifth Korotkoff sound. The SBP/DBP values were established by calculating the mean of two distinct measurements [23].

The insulin sensitivity of participants was determined through the utilization of the HOMA-IR methodology, employing the equation [Fasting serum glucose (mg/dL) x fasting serum insulin (μIU/mL)]/405. Subjects exhibiting a HOMA-IR score of ≥2.5 were classified as possessing insulin resistance [24,25].

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2.3. Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics version 22 (IBM Corp., Armonk, NY, USA). The normality of continuous variables was assessed using the Shapiro–Wilk and Kolmogorov–Smirnov tests, together with Q–Q plots and skewness and kurtosis values. Descriptive statistics were presented as number and percentage for categorical variables, and as mean ± standard deviation for continuous variables; for non-normally distributed variables, the median (interquartile range) was additionally considered. Categorical variables were compared using the chi-square test. For comparisons between two independent groups, the Independent-Samples t-test was used when the assumption of normality was met, and the Mann–Whitney U test was used otherwise; for the Mann–Whitney U test, the standardized test statistic (Z) is reported.

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Associations between two quantitative variables were assessed using Pearson correlation analysis when both variables were normally distributed and Spearman correlation analysis otherwise.

To identify markers that independently discriminated the two groups, a multivariable binary logistic regression model was constructed, with group (PCOS vs idiopathic hirsutism) as the dependent variable and total testosterone, the LH/FSH ratio, and the ALT/AST ratio as independent variables, entered simultaneously (Enter method). Candidate predictors were selected on the basis of the preceding univariate analyses and clinical relevance. Results were expressed as odds ratios (OR) with 95% confidence intervals (CI).

Multicollinearity among the independent variables was assessed using variance inflation factors (VIF) and tolerance values, with VIF < 5 considered acceptable; strongly inter-correlated variables were not entered together, and the individual components of the ratio variables (LH, FSH, ALT, AST) were not co-entered alongside the corresponding ratio in order to avoid structural collinearity.

Model performance was evaluated in terms of overall significance (omnibus test), explained variance (Nagelkerke R^2), calibration (Hosmer–Lemeshow goodness-of-fit test), and classification accuracy. Discrimination was assessed using receiver operating characteristic (ROC) curve analysis; the area under the curve (AUC) with 95% CI was calculated both for each individual marker and for the model's predicted probabilities, and optimal cut-off values were determined using the Youden index. Statistical significance was set at $p < 0.05$.

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3. Results

A total of 275 women, including 69 with idiopathic hirsutism and 206 diagnosed with PCOS, were included in the study. The mean age was 24.52±5.99 years in the idiopathic hirsutism group and 23.17±5.78 years in the PCOS group. The presence of diabetes, acne, alopecia, and acanthosis nigricans did not differ between the groups. A comparison of the sociodemographic and clinical characteristics of the idiopathic hirsutism and PCOS groups is presented in Table 1.

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Table 1. Sociodemographic and Clinical Characteristics of Women with Idiopathic Hirsutism and PCOS.

		IH n %	PCOS n %	chi-square/ t	Mean± SD	p
Age (year)	IH			-1.660	24.52±5.99	0.098
	PCOS				23.17±5.78	
BMI (kg/m^2)	IH			1.391	27.22±6.24	0.165
	PCOS				28.38±5.93	
Smoking status	Yes	8-(11.6)	25-(12.1)	0.000		1
	None	61-(88.4)	181-(87.9)			
Family history	Yes	35-(50.7)	117-(56.8)	0.771		0.380
	None	34-(49.3)	89-(43.2)			
DM status	None	50-(72.5)	139-(67.5)	0.807		0.535
	Prediabetes	18-(26.1)	65-(31.6)			
	Yes	1-(1.4)	2-(1.0)			
Acne	Yes	41-(59.4)	127-(62)	0.139		0.709
	None	28-(40.6)	78-(38)			
Alopecia	Yes	36-(52.2)	91-(44.2)	1.331		0.249
	None	33-(47.8)	115-(55.8)			
Acanthosis nigricans	Yes	23-(33.3)	71-(34.5)	0.01		0.980
	None	46-(66.7)	135-(65.5)			
Menstrual pattern	Regular	66-(95.7)	75-(36.4)	72.614		<0.001
	Irregular	3-(4.3)	131-(63.6)			

Data are presented as mean ± standard deviation or n (%). Comparisons were performed using Independent Samples t-test or chi-square test as appropriate. P<0.05 was considered statistically significant. Abbreviations: BMI, body mass index; DM, diabetes mellitus; IH, idiopathic hirsutism; PCOS, polycystic ovary syndrome; SD, standard deviation.

When biochemical parameters were compared between the idiopathic hirsutism and PCOS groups, triglyceride levels (p=0.008), ALT (p=0.001), AST (p=0.002), ALT/AST ratio (p=0.014), LH/FSH ratio (p<0.001), total testosterone (p<0.001), and TSH levels (p=0.032) were found to be significantly higher in the PCOS group compared to the idiopathic hirsutism group. A comparison

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of biochemical parameters between the idiopathic hirsutism and PCOS groups is presented in Table 2.

Table 2. Comparison of Biochemical Parameters Between the Idiopathic Hirsutism and PCOS Groups.

	IH n=69	PCOS n=206	t,Z	p
	Mean± SD	Mean± SD		
FPG (mg/dL)	96.04±9.13	95.32±9.89	-0.560*	0.575
Insulin (µIU/mL)	9.30±5.27	10.71±5.43	1.892	0.060
HOMA-IR	2.23±1.33	2.54±1.38	1.625	0.105
SBP (mmHg)	124.32±14.30	124.50±15.29	0.084	0.933
DBP (mmHg)	76.13±12.25	75.82±11.49	-0.191	0.849
HDL-C (mg/dL)	51.59±10.46	50.34±11.44	-0.807	0.421
Triglycerides (mg/dL)	98.30±95.44	110.50±58.58	-2.649*	**0.008**
Total cholesterol (mg/dL)	188.75±39.07	189.08±40.75	0.058	0.954
LDL-C (mg/dL)	114.59±30.95	117.01±34.27	0.518	0.605
ALT (U/L)	14.45±5.78	20.10±13.99	-3.329*	**0.001**
AST (U/L)	16.09±4.05	18.70±7.51	-3.039*	**0.002**
ALT/AST ratio	0.91±0.31	1.02±0.35	2.429	**0.014**
fT4 (ng/L)	1.14±0.19	1.13±0.16	-1.559*	0.119
TSH (mIU/L)	1.99±1.46	2.45±2.03	-2.142*	**0.032**
LH (IU/L)	4.30±1.95	5.76±3.45	-3.448*	**0.001**
FSH (IU/L)	5.21±1.75	4.46±1.19	-3.353*	**0.001**
LH/FSH ratio	0.91±0.57	1.49±2.19	-4.939*	**<0.001**
Estradiol (pg/mL)	38.97±19.71	41.61±21.82	-0.983*	0.325
Prolactin (µg/L)	19.02±11.75	19.58±13.69	-0.299*	0.765
Total testosterone (ng/mL)	0.80±0.53	1.02±0.62	-3.942*	**<0.001**
DHEAS (µg/dL)	289.55±155.73	285.64±125.34	-0.211	0.833
mFGS	12.88±3.85	13.66±3.81	1.460	0.145

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Values are presented as mean ± SD for all variables to maintain a uniform format. Variables marked with * were non-normally distributed and were compared using the Mann-Whitney U test, for which the reported statistic is a standardized Z value (degrees of freedom do not apply); the remaining variables were compared using the independent-samples t-test. P<0.05 was considered statistically significant. Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; DBP, diastolic blood pressure; DHEAS, dehydroepiandrosterone sulfate; FPG, fasting plasma glucose; FSH, follicle-stimulating hormone; fT4, free thyroxine; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment of insulin resistance; IH, idiopathic hirsutism; LDL-C, low-density lipoprotein cholesterol; LH, luteinizing hormone; mFGS, modified Ferriman–Gallwey score; PCOS, polycystic ovary syndrome; SBP, systolic blood pressure; SD, standard deviation; TSH, thyroid-stimulating hormone.

In the idiopathic hirsutism group, age showed a moderate positive correlation with total cholesterol (p<0.001, r=0.418) and LDL-C (p<0.001, r=0.420), while it showed a significant moderate negative correlation with prolactin (p=0.045, r=-0.242) and mFGS (p=0.008, r=-0.319). In the PCOS group, the LH/FSH ratio showed a negative correlation with age (p=0.011, r=-0.177), whereas the ALT/AST ratio showed a moderate positive correlation with BMI (p<0.001, r=0.371). The relationships between age, BMI, and biochemical parameters in patients with idiopathic hirsutism and PCOS are presented in Table 3.

Table 3. Relationships Between Age, BMI, and Biochemical Parameters in Patients with Idiopathic Hirsutism and PCOS.

Variable		IH		PCOS	
		Age	BMI	Age	BMI
FPG (mg/dL)	r	0.235	0.203	0.073	0.078
	p	0.052	0.094	0.299	0.262
Insulin (µIU/mL)	r	-0.193	0.479	-0.089	0.474
	p	0.111	**<0.001**	0.204	**<0.001**
HOMA-IR	r	-0.159	0.499	-0.086	0.462
	p	0.193	**<0.001**	0.219	**<0.001**
SBP (mmHg)	r	0.006	0.157	0.123	0.140
	p	0.964	0.198	0.078	**0.045**
DBP (mmHg)	r	0.092	0.115	0.109	0.160
	p	0.454	0.345	0.119	**0.021**
HDL-C (mg/dL)	r	0.049	-0.197	-0.063	-0.412
	p	0.691	0.104	0.368	**<0.001**
Triglycerides (mg/dL)	r	0.193	0.351	0.156	0.473
	p	0.112	**0.003**	**0.025**	**<0.001**
Total cholesterol (mg/dL)	r	0.418	0.150	0.129	0.230
	p	**<0.001**	0.219	0.065	**0.001**

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LDL-C (mg/dL)	r	0.420	0.276	0.108	0.270
	p	**<0.001**	**0.022**	0.121	**<0.001**
ALT/AST ratio	r	-0.039	0.259	0.079	0.371
	p	0.748	**0.032**	0.258	**<0.001**
fT4 (ng/L)	r	0.041	-0.201	-0.043	-0.038
	p	0.740	0.098	0.538	0.583
TSH (mIU/L)	r	-0.114	0.050	0.008	0.131
	p	0.353	0.682	0.913	0.061
LH/FSH	r	-0.065	-0.125	-0.177	-0.053
	p	0.598	0.304	**0.011**	0.449
Estradiol (pg/mL)	r	-0.003	-0.219	0.094	-0.062
	p	0.983	0.071	0.178	0.378
Prolactin	r	-0.242	-0.257	-0.135	-0.103
(µg/L)	p	**0.045**	**0.033**	0.053	0.140
Total Testosterone (ng/mL)	r	-0.093	-0.139	-0.092	0.015
	p	0.447	0.255	0.188	0.829
DHEAS (µg/dL)	r	-0.106	-0.065	-0.095	0.013
	p	0.385	0.596	0.175	0.855
mFGS	r	-0.319	-0.065	-0.002	-0.053
	p	**0.008**	0.596	0.980	0.445

Correlation coefficients are presented as Pearson's or Spearman's rho coefficients, as appropriate. Significant correlations are shown in bold. P<0.05 was considered statistically significant. Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; DBP, diastolic blood pressure; DHEAS, dehydroepiandrosterone sulfate; FPG, fasting plasma glucose; FSH, follicle-stimulating hormone; fT4, free thyroxine; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment of insulin resistance; IH, idiopathic hirsutism; LDL-C, low-density lipoprotein cholesterol; LH, luteinizing hormone; mFGS, modified Ferriman–Gallwey score; PCOS, polycystic ovary syndrome; SBP, systolic blood pressure; TSH, thyroid-stimulating hormone.

Among women with idiopathic hirsutism and PCOS, predictive risk factors for PCOS were evaluated using logistic regression analysis (Enter model) based on potential risk factors identified in previous analyses. In the model, PCOS diagnosis was used as the dependent variable, while total testosterone level, LH/FSH ratio, and ALT/AST ratio were included as independent variables. In this analysis, the LH/FSH ratio (OR: 2.86, 95% CI [1.589–5.135]) and ALT/AST ratio (OR: 2.70, 95% CI [1.057–6.892]) were identified as predictive risk factors for PCOS diagnosis (Table 4).

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Table 4. Predictive Risk Factors for PCOS Identified by Logistic Regression (Enter Model).

Risk factors		B	SE	P value	OR (Exp(B))	OR (95% CI)	
						95% CI Lower	95% CI Upper
Step 1[a]	Total testosterone	0.684	0.365	0.061	1.98	0.970	4.049
	LH/FSH ratio	1.050	0.299	**<0.001**	2.86	1.589	5.135
	ALT/AST ratio	0.993	0.478	**0.038**	2.70	1.057	6.892
	Constant	-1.613	0.601	0.007			

Multivariable logistic regression analysis was performed using the Enter method with PCOS diagnosis as the dependent variable. P<0.05 was considered statistically significant. Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; CI, confidence interval; LH, luteinizing hormone; FSH, follicle-stimulating hormone; OR, odds ratio; PCOS, polycystic ovary syndrome; SE, standard error.

Receiver operating characteristic (ROC) analysis was performed to assess the ability of each marker to distinguish PCOS from idiopathic hirsutism (Table 5, Figure 2). The LH/FSH ratio showed the highest individual discriminatory performance (AUC 0.699, 95% CI 0.629–0.768, p < 0.001), followed by total testosterone (AUC 0.658, 95% CI 0.581–0.736, p < 0.001) and the ALT/AST ratio (AUC 0.601, 95% CI 0.524–0.678, p = 0.012). The corresponding optimal cut-off values (Youden index) were 1.03 for the LH/FSH ratio (sensitivity 60.7%, specificity 62.5%), 0.82 for total testosterone (sensitivity 53.9%, specificity 65.2%), and 0.95 for the ALT/AST ratio (sensitivity 54.9%, specificity 62.3%). For all three markers, higher values were associated with an increased likelihood of belonging to the PCOS group.

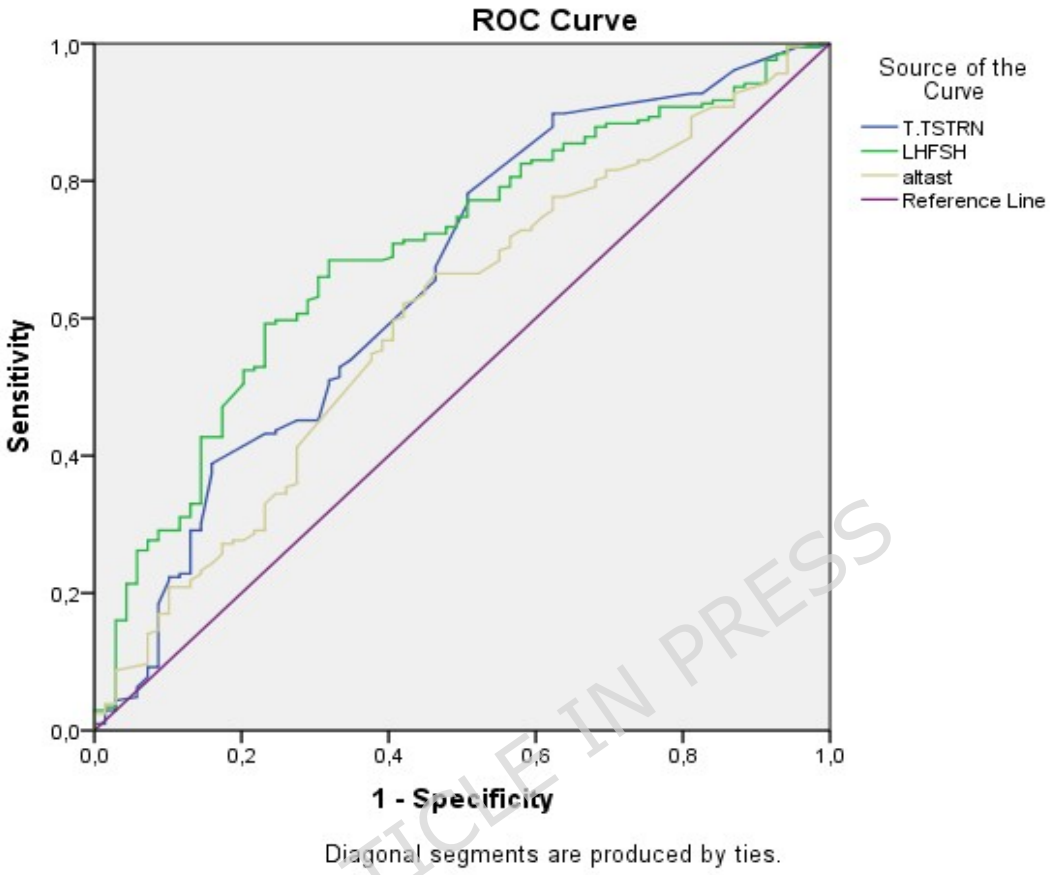
Table 5. Univariate diagnostic performance (receiver operating characteristic analysis) of total testosterone, the LH/FSH ratio, and the ALT/AST ratio in distinguishing women with polycystic ovary syndrome from those with idiopathic hirsutism.

Marker	AUC	SE	p value	95% CI	Sensitivity (%)	Specificity (%)
Total testosterone	0.658	0.040	<0.001	0.581–0.736	53.9	65.2
LH/FSH ratio	0.699	0.035	<0.001	0.629–0.768	60.7	62.5
ALT/AST ratio	0.601	0.039	0.012	0.524–0.678	54.9	62.3

Optimal cut-off values (Youden index): total testosterone 0.82; LH/FSH ratio 1.03; ALT/AST ratio 0.95. Higher values of each marker were associated with an increased likelihood of belonging to the PCOS group. AUC, area under the curve; SE, standard error; CI, confidence interval; LH, luteinizing hormone; FSH, follicle-stimulating hormone; ALT,

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alanine aminotransferase; AST, aspartate aminotransferase; PCOS, polycystic ovary syndrome. $p < 0.05$ was considered statistically significant (null hypothesis: true area = 0.5).



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Figure 2. Receiver operating characteristic (ROC) curves of individual markers (total testosterone, LH/FSH ratio, and ALT/AST ratio) for discriminating polycystic ovary syndrome from idiopathic hirsutism. Areas under the curve: total testosterone 0.658, LH/FSH ratio 0.699, ALT/AST ratio 0.601. The diagonal reference line denotes an AUC of 0.5 (no discrimination). AUC, area under the curve; LH, luteinizing hormone; FSH, follicle-stimulating hormone; ALT, alanine aminotransferase; AST, aspartate aminotransferase.

The multivariable logistic regression model was statistically significant (omnibus $\chi^2 = 31.64$, df = 3, $p < 0.001$) and showed good calibration (Hosmer–Lemeshow $\chi^2 = 8.78$, df = 8, $p = 0.361$), with a Nagelkerke R^2 of 0.161. Discrimination based on the model's predicted probabilities yielded an area under the ROC curve of 0.728 (95% CI: 0.661–0.794, $p < 0.001$), which was higher than that of any individual marker (total testosterone, 0.658; LH/FSH ratio, 0.699; ALT/AST ratio, 0.601; Table 5). At a 0.5 probability threshold the model classified 75.3% of cases correctly, with high sensitivity for PCOS (97.6%) but low specificity for idiopathic hirsutism (8.7%), reflecting

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the relative group sizes; accordingly, the AUC was regarded as the primary index of discriminatory performance (Table 6, Figure 3).

Table 6. Performance of the multivariable binary logistic regression model discriminating polycystic ovary syndrome from idiopathic hirsutism.

Performance measure	Value
Omnibus test of model coefficients	$\chi^2 = 31.64$, df = 3, $p < 0.001$
Nagelkerke R^2	0.161
Cox & Snell R^2	0.109
Hosmer–Lemeshow test	$\chi^2 = 8.78$, df = 8, $p = 0.361$
Area under the ROC curve (AUC)	0.728 (95% CI 0.661–0.794), $p < 0.001$
Overall correct classification	75.3%
Sensitivity (PCOS)	97.6%
Specificity (idiopathic hirsutism)	8.7%

Predictors entered simultaneously (Enter method): total testosterone, LH/FSH ratio, and ALT/AST ratio; dependent variable: diagnosis (PCOS = 1, idiopathic hirsutism = 0). The AUC was derived from the model-predicted probabilities. At the 0.5 probability threshold the model showed high sensitivity for PCOS but low specificity for idiopathic hirsutism, reflecting the relative group sizes (206 PCOS vs 69 idiopathic hirsutism); the AUC was therefore regarded as the primary index of discriminatory performance. AUC, area under the curve; ROC, receiver operating characteristic; CI, confidence interval; df, degrees of freedom; LH, luteinizing hormone; FSH, follicle-stimulating hormone; ALT, alanine aminotransferase; AST, aspartate aminotransferase; PCOS, polycystic ovary syndrome.

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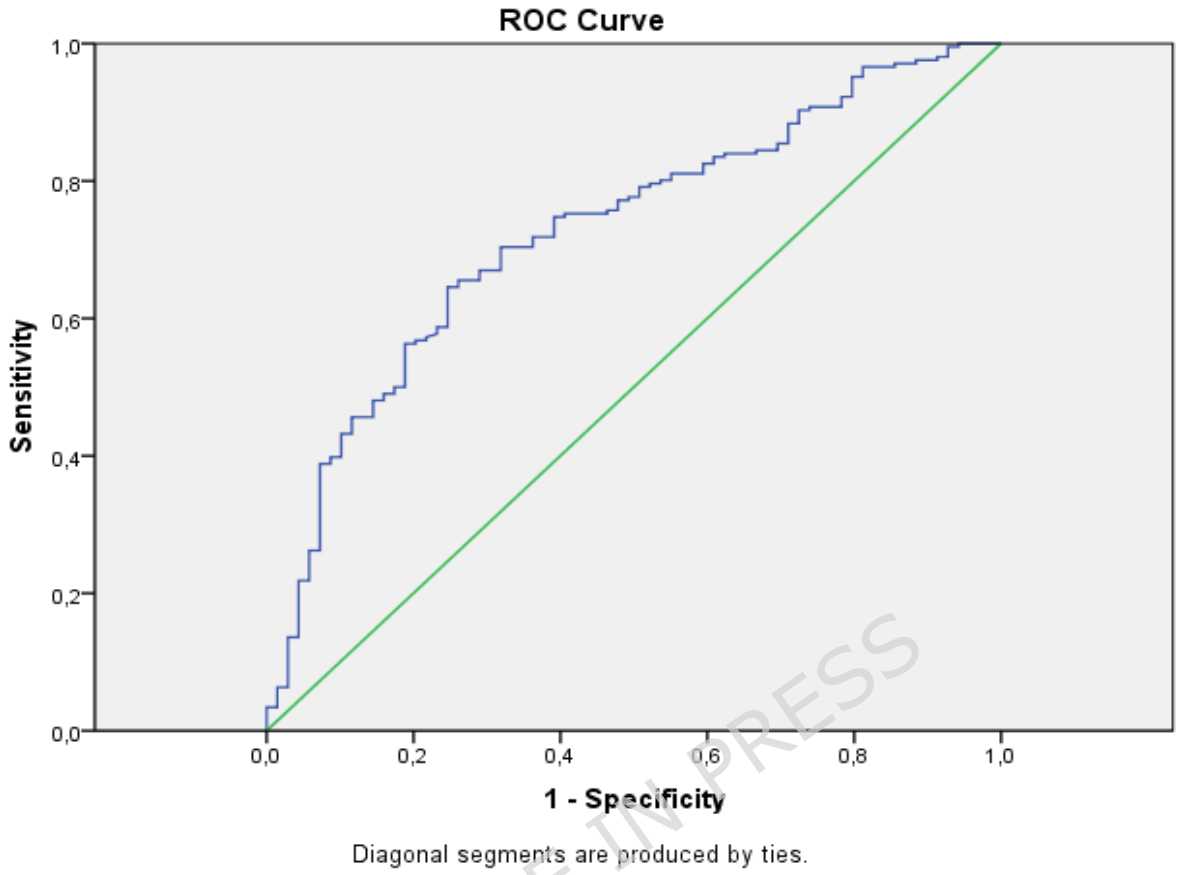


Figure 3. Receiver operating characteristic (ROC) curve of the multivariable logistic regression model (predicted probabilities) for discriminating polycystic ovary syndrome from idiopathic hirsutism. The model combined total testosterone, the LH/FSH ratio, and the ALT/AST ratio. Area under the curve = 0.728 (95% CI 0.661–0.794, $p < 0.001$), exceeding that of any individual marker (Figure 1, Table 5). The diagonal reference line denotes an AUC of 0.5 (no discrimination). AUC, area under the curve; CI, confidence interval; LH, luteinizing hormone; FSH, follicle-stimulating hormone; ALT, alanine aminotransferase; AST, aspartate aminotransferase.

4. Discussion

The present study investigated clinical, biochemical, and anthropometric differences between women with idiopathic hirsutism and PCOS using routinely available parameters applicable in daily clinical practice. In contrast to many studies in which metabolic differences may be strongly influenced by obesity, women with severe obesity (BMI >40 kg/m²) were excluded in order to reduce the confounding effect of extreme adiposity and improve comparability between groups. Within this restricted cohort, several endocrine and metabolic differences persisted between groups, suggesting that some features associated with PCOS-related hirsutism may not be solely attributable to obesity.

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In the present study, women with PCOS exhibited significantly higher triglyceride levels, liver enzymes including AST and ALT, ALT/AST ratio, LH, LH/FSH ratio, and total testosterone levels compared with women with idiopathic hirsutism, whereas BMI and several obesity-related parameters were comparable between groups. These findings support the concept that, even when severe obesity is minimized as a confounder, PCOS retains a distinct endocrine and subtle metabolic signature. The persistence of higher androgen-related parameters and altered gonadotropin dynamics in the PCOS group is consistent with the well-recognized pathophysiological characteristics of the syndrome [7,20,21,26].

An important observation in our study was that indices traditionally linked to insulin resistance, such as fasting insulin and HOMA-IR, were numerically higher but no longer significantly different between groups after restricting severe obesity. This finding deserves particular attention. It may suggest that part of the insulin resistance burden observed in previous comparisons between PCOS and idiopathic hirsutism may be mediated, at least in part, by obesity itself rather than being entirely intrinsic to PCOS. This observation does not contradict the well-established role of insulin resistance in PCOS [12,15,20,27–30], but rather emphasizes the close interrelationship between adiposity and metabolic dysfunction in these patients. It also highlights the importance of considering obesity as a major modifier when metabolic features of PCOS are interpreted.

By contrast, hormonal differences remained more robust. Higher LH levels, lower FSH, and a significantly elevated LH/FSH ratio in women with PCOS are in line with the neuroendocrine alterations commonly described in this disorder [26]. In our logistic regression analysis, the LH/FSH ratio emerged as an independent predictor of PCOS, supporting its potential utility as an adjunctive marker in the differential evaluation of women presenting with hirsutism. It should be emphasized that we do not propose the LH/FSH ratio as a diagnostic criterion for PCOS; current international evidence-based guidelines do not recommend it for this purpose, given its limited sensitivity [31]. Rather, in a population in which the diagnosis had already been established by the 2003 Rotterdam criteria, the LH/FSH ratio is evaluated here as a routinely available, adjunctive marker that may aid the biochemical differentiation of PCOS-related hirsutism from idiopathic hirsutism. Similarly, higher total testosterone levels in the PCOS group are consistent with previous reports emphasizing biochemical hyperandrogenism as a central component of the syndrome [7,32].

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Another noteworthy finding was the persistence of higher ALT, AST, and ALT/AST ratio in the PCOS group despite comparable BMI. Although these differences were modest, they may reflect subtle metabolic or hepatic alterations accompanying PCOS beyond the effect of generalized obesity. This observation is in line with growing evidence suggesting an association between PCOS and hepatic steatosis or liver dysfunction, potentially mediated not only by adiposity and insulin resistance but also by hyperandrogenism-related mechanisms [12,33]. In our regression model, the ALT/AST ratio emerged as an independent predictor of PCOS, suggesting that routine biochemical markers may provide additional information beyond reproductive hormone profiles.

In the present study, we did not treat any single parameter as a standalone discriminator but instead examined how routinely available markers perform both individually and in combination in separating PCOS from idiopathic hirsutism. On univariate ROC analysis, the LH/FSH ratio showed the highest individual discriminatory performance, followed by total testosterone and the ALT/AST ratio. The position of the LH/FSH ratio is consistent with the neuroendocrine signature of PCOS, in which sustained rapid GnRH–LH pulsatility increases pituitary LH output relative to FSH and drives ovarian androgen production [34]. It should be emphasised, however, that current evidence-based guidelines do not endorse the LH/FSH ratio as a diagnostic criterion, given its considerable intra- and inter-individual variability and its inconsistent elevation across PCOS phenotypes [35,36]. Our use of this ratio is therefore explicitly adjunctive: it is applied to discriminate between two groups whose diagnoses have already been established by accepted criteria, not to define the diagnosis itself.

The independent contribution of the ALT/AST ratio is biologically coherent rather than incidental. PCOS and hepatic steatosis share insulin resistance as a common substrate, and aminotransferase levels — even within the normal range — track with insulin resistance and metabolic dysfunction in women with PCOS [37–39]. In this context, the ALT/AST ratio behaves as an inexpensive surrogate of the insulin-resistant, metabolically active phenotype that is more characteristic of PCOS than of idiopathic hirsutism, in which androgen excess is typically peripheral and not accompanied by the same degree of metabolic disturbance [40]. This is consistent with the notion that idiopathic hirsutism reflects increased local androgen metabolism in the pilosebaceous unit rather than the systemic hyperandrogenic–metabolic milieu of PCOS [5].

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Critically, the clinical value of these markers emerged most clearly when they were combined. The multivariable model incorporating total testosterone, the LH/FSH ratio, and the ALT/AST ratio achieved an AUC of 0.728, exceeding that of any single marker and indicating that these routinely obtainable, obesity-independent parameters carry complementary rather than redundant information. Within this model, the LH/FSH and ALT/AST ratios remained independent discriminators, whereas total testosterone lost independent significance after adjustment — suggesting that much of the discriminatory information carried by circulating androgen is already captured by these two ratios. The model was well calibrated (Hosmer–Lemeshow $p = 0.361$), although its modest Nagelkerke R^2 (0.161) and the imbalance-driven classification profile indicate that these markers are best positioned as adjunctive, low-cost aids that complement — not replace — established diagnostic criteria. Taken together, our findings suggest that in everyday practice a small panel of inexpensive laboratory values can support the distinction between these two clinically overlapping conditions, particularly where access to extended androgen work-up is limited.

The observation that total testosterone lost independent significance after multivariable adjustment, while the LH/FSH and ALT/AST ratios did not, is biologically informative rather than a statistical artefact. In univariate analysis, total testosterone clearly discriminated the two groups, consistent with hyperandrogenism being central to PCOS. Its attenuation in the adjusted model indicates that its discriminatory information is largely shared with — and captured by — the two ratios, rather than being independent of them. This is mechanistically coherent: the elevated LH/FSH ratio reflects the increased GnRH–LH pulsatility that directly stimulates ovarian theca-cell androgen production, so a substantial part of the androgen signal is upstream of, and encoded within, the gonadotropin ratio itself [26,34,41]. In parallel, the ALT/AST ratio reflects the insulin-resistant, hyperandrogenic metabolic milieu that both accompanies and amplifies ovarian androgen secretion, since hyperinsulinaemia augments theca-cell steroidogenesis and lowers sex hormone–binding globulin, thereby increasing bioavailable androgen [37,38]. Total testosterone can thus be viewed as a downstream, more variable readout of the same neuroendocrine and metabolic processes that the two ratios capture more stably. A single testosterone measurement is also subject to considerable analytical and biological variability and to assay limitations at the concentrations seen in women, which may further reduce its independent discriminatory value relative to the ratios [42].

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Clinically, this pattern is meaningful. It suggests that in the differentiation of PCOS-related from idiopathic hirsutism, the combination of a neuroendocrine marker (LH/FSH) and a hepatic–metabolic marker (ALT/AST) may convey the relevant discriminatory information more efficiently and more reproducibly than an absolute androgen level. This does not diminish the diagnostic importance of documenting hyperandrogenism; rather, it indicates that once hyperandrogenism has been established, these two inexpensive, routinely available ratios add complementary discriminatory value, whereas a single total testosterone level contributes little additional independent information. Such a pattern is particularly relevant in everyday practice and in resource-limited settings, where reliable free-androgen measurement is often unavailable.

Interestingly, hirsutism severity assessed by mFGS did not differ significantly between groups, despite clear endocrine differences. This may indicate that similar degrees of clinical hirsutism can arise in distinct biological settings and further supports the complexity of differentiating idiopathic hirsutism from PCOS based solely on clinical appearance. In this regard, integrating hormonal and metabolic parameters may improve clinical assessment beyond reliance on hirsutism severity alone.

Although thyroid function tests were within normal limits in both groups, the observed difference in TSH levels between women with PCOS and IH likely reflects underlying pathophysiological differences rather than overt thyroid disease [43,44]. PCOS is a complex endocrine-metabolic disorder characterized by insulin resistance, chronic low-grade inflammation, and neuroendocrine dysregulation [21], whereas idiopathic hirsutism is typically associated with normal ovulatory function and minimal metabolic disturbance [14,15].

One of the most plausible explanations for relatively higher TSH levels in PCOS is insulin resistance, which is a hallmark feature of the syndrome and may influence the hypothalamic–pituitary–thyroid axis, leading to subtle increases in TSH levels even within the normal range [44,45]. Supporting this, TSH levels have been shown to correlate more strongly with metabolic parameters such as insulin resistance and body mass index rather than androgen levels, suggesting that metabolic factors rather than hyperandrogenism per se may drive these differences [45]. Accordingly, TSH elevation in PCOS may represent a metabolic epiphenomenon related to insulin resistance and ectopic fat accumulation rather than primary thyroid dysfunction [44].

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Thyroid autoimmunity may also contribute to this difference, as several studies have demonstrated a higher prevalence of thyroid autoantibodies in women with PCOS [46,47]. However, recent meta-analytic data suggest that this association may be influenced by TSH levels themselves, since the difference in anti-thyroid peroxidase antibody positivity diminishes when groups are matched for TSH, indicating that TSH may act as both a mediator and a confounding factor in this relationship [47].

In addition, altered thyroid hormone sensitivity and subtle dysregulation of the hypothalamic–pituitary–thyroid axis may play a role, as emerging evidence suggests that central resistance to thyroid hormones in PCOS may lead to compensatory increases in TSH despite normal circulating hormone levels [48]. Furthermore, interactions between the hypothalamic–pituitary–gonadal and thyroid axes may contribute to this variability, particularly in hyperandrogenic phenotypes where TSH levels have been shown to be independently associated with hyperandrogenism even in euthyroid individuals [43].

It should also be noted that findings regarding TSH levels in PCOS are not entirely consistent across studies, and this heterogeneity may be explained by differences in population characteristics, environmental factors such as iodine intake, and methodological variations including adjustment for confounding variables such as body mass index [49].

Taken together, the difference in TSH levels between PCOS and idiopathic hirsutism appears to be multifactorial, involving metabolic, autoimmune, and neuroendocrine mechanisms, as well as shared genetic and immunoendocrine pathways between the two systems [50]. The relative absence of these complex interactions in idiopathic hirsutism may explain the lower or comparable TSH levels observed in this group.

Several limitations of this study should be acknowledged. First, the retrospective and cross-sectional design precludes causal inference and does not allow assessment of temporal relationships between hormonal disturbances and metabolic alterations. Because of the retrospective design, a formal a priori sample size or power calculation was not performed, which should be considered a methodological limitation. However, the final sample represented all eligible consecutive patients meeting study criteria during the study period. Second, the study was conducted in a single center, which may limit generalizability. Third, although exclusion of women with BMI >40 kg/m² improved comparability between groups and addressed an important

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confounding concern, this restriction also reduced sample size and may have limited extrapolation of the findings to women with severe obesity, among whom PCOS is also common. In addition, because this approach represents an analytic restriction, residual confounding related to adiposity cannot be completely excluded. Fourth, although several routine biochemical markers were evaluated, more specific assessments of insulin sensitivity, visceral adiposity, or hepatic steatosis were not available. As all modified Ferriman–Gallwey scoring was performed by a single experienced examiner, inter-observer variability was avoided; nonetheless, the inherently semi-quantitative nature of the score and the absence of a second-rater reliability assessment remain minor limitations. We also acknowledge that total testosterone was measured using immunoassay rather than mass spectrometry, which may be considered a methodological limitation. Finally, the absence of longitudinal follow-up precluded evaluation of whether the observed biochemical differences translate into long-term metabolic outcomes.

Despite these limitations, the present findings suggest that even after minimizing the influence of severe obesity, women with PCOS and hirsutism exhibit persistent hormonal disturbances together with subtle metabolic differences compared with women with idiopathic hirsutism. Larger prospective studies are needed to validate whether markers such as LH/FSH ratio and ALT/AST ratio may have additional value in the clinical differentiation and risk assessment of women presenting with hirsutism. In addition, future studies should also extend beyond the parameters examined here, incorporating a broader endocrine evaluation of women presenting with hirsutism, including adrenal androgen dynamics, thyroid function, and other coexisting endocrine disorders, in order to better characterise the heterogeneity of this population.

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5. Conclusion

This study demonstrated that women with PCOS and idiopathic hirsutism differ in several hormonal and selected metabolic parameters even after minimizing the confounding effect of severe obesity. Higher LH/FSH ratio, total testosterone levels, and subtle differences in liver-related biochemical markers in women with PCOS may support clinical differentiation between these two conditions. While obesity appears to contribute substantially to some metabolic differences, persistent endocrine alterations seem to represent a more distinctive feature of PCOS-related hirsutism. Notably, after multivariable adjustment, the LH/FSH and ALT/AST ratios — but not total testosterone — remained independently associated with PCOS. Biologically, this

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indicates that once the shared hyperandrogenic–gonadotropic signal is accounted for, a neuroendocrine marker (LH/FSH) and a hepatic–metabolic marker (ALT/AST) capture the discriminatory information more stably and efficiently than an absolute, and inherently more variable, androgen level. Because both ratios derive from tests routinely performed in the initial evaluation of hirsutism, they may offer a practical, low-cost adjunct to clinical differentiation, particularly where extended free-androgen work-up is unavailable. These findings should be validated in prospective cohorts.

Author Contributions

SBS and FM contributed to the study conception and design. Material preparation and data collection were performed by FM and SMK. Statistical analysis was performed by JKS and AK. The first draft of the manuscript was written by SBS, EC and FM. All the authors have read and approved the final version of the manuscript.

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Funding Sources

None

Data Availability Statement

All data generated or analyzed during this study are included in this article. The data will be available upon reasonable request (contact persons: filizmercantepe@duzce.edu.tr, filizmercantepe@hotmail.com).

Artificial Intelligence (AI) Statement

Artificial intelligence tools were used solely for language editing and improvement of academic English. AI was not used in study design, data collection, data analysis, interpretation of results, or generation of scientific content. All scientific conclusions and interpretations are the responsibility of the authors.

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Declarations

Statement of Ethics

The study protocol was reviewed and approved by the Recep Tayyip Erdoğan University Noninvasive Clinical Research Ethics Committee (Approval Number: 2024/312, Approval Date: 26 December 2024). The study was conducted in accordance with the principles of the Declaration of Helsinki. Given the retrospective design of the study, the requirement for written informed consent was waived by the ethics committee.

Conflict of Interest Statement

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

List of Abbreviations

17-OHP — 17-Hydroxyprogesterone

ALT — Alanine Aminotransferase

AST — Aspartate Aminotransferase

AUC — Area Under the Curve

BMI — Body Mass Index

CI — Confidence Interval

DBP — Diastolic Blood Pressure

DHEAS — Dehydroepiandrosterone Sulfate

DM — Diabetes Mellitus

FPG — Fasting Plasma Glucose

FSH — Follicle-Stimulating Hormone

fT4 — Free Thyroxine

GnRH — Gonadotropin-Releasing Hormone

HDL-C — High-Density Lipoprotein Cholesterol

HOMA-IR — Homeostasis Model Assessment of Insulin Resistance

IH — Idiopathic Hirsutism

LDL-C — Low-Density Lipoprotein Cholesterol

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LH — Luteinizing Hormone

mFGS — Modified Ferriman–Gallwey Score

OR — Odds Ratio

PCOS — Polycystic Ovary Syndrome

ROC — Receiver Operating Characteristic

SBP — Systolic Blood Pressure

SE — Standard Error

TG — Triglycerides

TSH — Thyroid-Stimulating Hormone

VIF — Variance Inflation Factor

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