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Polycystic Ovary Syndrome (PCOS): A Biochemical and Physiological Perspective on a Common Gynaecological Disorder in a Local Hospital of Peshawar

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ABSTRACT

Polycystic ovary syndrome (PCOS) is a common endocrine disorder affecting reproductive and metabolic health. It is characterized by hormonal imbalances, insulin resistance, dyslipidemia, and chronic inflammation, increasing long-term health risks. **Objective:** To compare biochemical, metabolic, and ultrasound markers in women with and without PCOS. **Methods:** A comparative cross-sectional study was conducted at Health Net Hospital, Peshawar, over six months. In total, 110 participants were recruited and divided equally into 2 groups, with each group considered as PCOS (n=55) and Non-PCOS (n=55). PCOS was diagnosed using the Rotterdam Criteria. Hormonal, metabolic, and inflammatory markers, including luteinizing hormone, Follicle-Stimulating Hormone, testosterone, Dehydroepiandrosterone Sulphate, Anti-Müllerian Hormone, fasting glucose, Homeostasis Model Assessment of Insulin Resistance (HOMA-IR), lipid profile, C-reactive protein, Malondialdehyde, and Total Antioxidant Capacity (TAC), were analyzed. Ultrasound findings assessed ovarian morphology, endometrial thickness, and stromal resistance index. Data were analyzed using SPSS. **Results:** PCOS patients had significantly higher BMI, insulin resistance, and androgen levels. Luteinizing hormone/Follicle-Stimulating Hormone ratio and Anti-Müllerian Hormone were elevated, while Follicle-Stimulating Hormone was lower. Metabolic markers showed increased fasting glucose, HOMA-IR, and dyslipidaemia, with higher LDL and triglycerides and lower HDL. Inflammatory and oxidative stress markers (C-reactive protein, Malondialdehyde) were significantly elevated, while TAC was reduced. Ultrasound findings showed increased endometrial thickness and ovarian stromal resistance in PCOS. **Conclusions:** It was concluded that PCOS is associated with significant hormonal, metabolic, and inflammatory disturbances. Elevated androgens, insulin resistance, and oxidative stress highlight the need for early screening and a multidisciplinary approach for Effective Management.

INTRODUCTION

Polycystic Ovary Syndrome (PCOS) affects 6% to 21% of reproductive-age women, involving hormonal, metabolic, and ovarian abnormalities [1, 2]. The Rotterdam Criteria, the most used diagnostic tool, requires two of the following: oligo/anovulation, hyperandrogenism, or polycystic ovaries [3, 4]. Beyond reproduction, PCOS poses lifelong metabolic risks, including insulin resistance and cardiovascular disease. PCOS disrupts hormonal and metabolic balance. Androgen excess causes hirsutism, acne, and alopecia due to elevated testosterone and Dehydroepiandrosterone Sulphate (DHEA-S). An altered luteinizing hormone (LH)/Follicle-Stimulating Hormone (FSH) ratio contributes to ovarian dysfunction. High Anti-Müllerian Hormone (AMH) reflects increased ovarian follicles. Insulin resistance worsens hormonal dysregulation, raising risks for type 2 diabetes and

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cardiovascular disease [5]. Beyond hormonal imbalances, metabolic dysfunction is a major concern in PCOS. Insulin resistance and hyperinsulinemia occur even in normal-weight women [6]. These metabolic shifts increase dyslipidaemia risk, characterized by high cholesterol and LDL with low HDL, elevating cardiovascular disease risk. Oxidative stress and chronic low-grade inflammation, marked by elevated C-reactive protein (CRP) and Malondialdehyde (MDA), further exacerbate metabolic and reproductive complications [7, 8]. Ultrasound is a key diagnostic tool for PCOS, revealing increased ovarian volume, multiple small follicles, and altered ovarian stromal vascularity [9]. However, not all women with PCOS exhibit polycystic ovarian morphology, and some without PCOS may present similar findings. This highlights the complexity of PCOS and the need for a multidimensional approach combining biochemical, metabolic, and imaging assessments for accurate diagnosis and management [10]. Despite extensive research, gaps remain in understanding the biochemical, metabolic, and inflammatory profile of PCOS across different populations. Most studies focus on either reproductive or metabolic aspects, with few taking an integrated approach. The link between insulin resistance, inflammation, and oxidative stress in PCOS warrants further investigation to enhance comprehensive disease management. Another key research gap is the role of systemic inflammation and oxidative stress in PCOS. While CRP and MDA are linked to insulin resistance and cardiovascular risk, their exact contribution to PCOS pathophysiology remains unclear. Additionally, transvaginal ultrasound findings, particularly ovarian stromal resistance index (RI), require further correlation with biochemical markers. Most studies focus on Western populations, emphasizing the need to examine these variations in the Pakistani population, particularly in Peshawar, where genetic predisposition, diet, and lifestyle may influence PCOS presentation and progression.

PCOS is a prevalent endocrine-metabolic disorder affecting reproductive-aged women and is associated with hormonal imbalance, insulin resistance, dyslipidaemia, oxidative stress, and chronic inflammation, yet its full biochemical and physiological profile remains insufficiently characterized in local Pakistani populations. Most existing studies have focused separately on reproductive or metabolic aspects, with limited integrated evaluation of hormonal, metabolic, inflammatory, and ultrasound parameters within a single framework. This study aims to comprehensively compare PCOS and non-PCOS women by evaluating hormonal, metabolic, inflammatory, and ultrasound parameters. Addressing these gaps enhances understanding of PCOS pathophysiology, supporting improved diagnosis and management strategies.

METHODS

A comparative cross-sectional analysis was conducted at Health Net Hospital, Peshawar. The study adhered to ethical guidelines outlined in the Declaration of Helsinki. Ethical approval was granted by the Ethics Review Committee of Health Net Hospital (Ref No: 3002/HNH/HR). All participants were provided written informed consent before data collection, and confidentiality of personal and medical information was strictly maintained. The study was carried out over six months, from January 2024 to June 2024. The sample size was initially calculated using Cochran's formula, considering a 95% confidence interval, an expected PCOS prevalence of 10%, and a 5% margin of error, which suggested a requirement of 138 participants [11]. However, due to practical constraints, a final sample of 110 participants was selected. To ensure adequate statistical power, a post-hoc power analysis was conducted, confirming that the sample size retained sufficient power for detecting significant differences between the groups. Additionally, a finite population correction was applied to improve the accuracy of estimates given the restricted hospital-based population. A non-probability consecutive sampling technique was used to recruit participants meeting the eligibility criteria. Participants were divided into two groups: COS Group (n=55): Women diagnosed with PCOS based on the Rotterdam criteria, requiring at least two of the following: oligo/anovulation, hyperandrogenism (clinical/biochemical), or polycystic ovarian morphology, Non-PCOS Group (n=55): Age-matched women with regular menstrual cycles, no signs of hyperandrogenism, and normal ovarian function. Exclusion criteria included pregnancy, lactation, use of hormonal medications within the past three months, diabetes, thyroid disorders, adrenal disorders, and other metabolic or endocrine conditions that could influence study variables. Data collection included demographic and clinical characteristics, such as age, height and weight were measured to calculate BMI (kg/m2, Marital status, education level, employment status, physical activity, dietary habits, smoking status, and history of infertility were recorded through a structured questionnaire. Blood samples were collected after overnight fasting following standard phlebotomy protocol and analysed using a fully automated chemistry analyzer (Abbott Architect c4000, Abbott Diagnostics, USA) following laboratory quality control standards and manufacturer's guidelines. Hormonal and biochemical markers were analyzed using Chemiluminescent Immunoassay kits (Innovative Research) following the manufacturer's instructions and guidelines. Hormonal and biochemical markers were analysed using Chemiluminiscent Immunoassay kits (Innovative

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Research) following the manufacturer's instructions and guidelines. Luteinizing Hormone (LH) was measured using the Human Luteinizing Hormone Chemiluminescent Immunoassay Kit from Innovative Research (Cat#03045838). Follicle-Stimulating Hormone (FSH) was assessed with the Human Follicle-Stimulating Hormone Chemiluminescent Immunoassay Kit from Innovative Research (Cat# IRAPKT-FSH-HU). Total Testosterone was determined using the Human Total Testosterone Chemiluminescent Immunoassay Kit from Innovative Research (Cat# IRAPKT-TTESTO-HU). Free Testosterone was evaluated with the Human Free Testosterone Chemiluminescent Immunoassay Kit from Innovative Research (Cat# IRAPKT-FTESTO-HU). Dehydroepiandrosterone Sulphate (DHEA-S) was measured using the Human DHEA-S Chemiluminescent Immunoassay Kit from Innovative Research (Cat# IRAPKT-DHEAS-HU). Anti-Müllerian Hormone (AMH) was assessed with the Human AMH Chemiluminescent Immunoassay Kit from Innovative Research (Cat# IRAPKT-AMH-HU). Prolactin was determined using the Human Prolactin Chemiluminescent Immunoassay Kit from Innovative Research (Cat# IRAPKT-PRL-HU). Fasting Glucose was measured with the Glucose Assay Kit from Sigma-Aldrich (Cat# MAK181). Haemoglobin A1c (HbA1c) was assessed using the HbA1c Assay Kit from Sigma-Aldrich (Cat# MAK018). Total Cholesterol, LDL, HDL, and Triglycerides were evaluated using the Lipid Panel Assay Kit from Sigma-Aldrich (Cat# MAK045). C-Reactive Protein (CRP) was measured with the Human CRP Chemiluminescent Immunoassay Kit from Innovative Research (Cat# IRAPKT-CRP-HU). Malondialdehyde (MDA) was assessed using the MDA Assay Kit from Sigma-Aldrich (Cat# MAK085). Total Antioxidant Capacity (TAC) was determined using the TAC Assay Kit from Sigma-Aldrich (Cat# ab65329). Ultrasound parameters assessed included endometrial thickness, ovarian stromal resistance index (RI), polycystic ovarian morphology, and ovarian volume. All scans were performed by certified radiologists using a high-resolution ultrasound machine, following standardized protocols. However, individual ultrasound images were not archived for study documentation. Instead, key findings have been summarized based on standardized measurement criteria. All scans were performed by certified radiologists using a high-resolution ultrasound machine, following standardized protocols. The cut-off for an elevated ovarian stromal RI was set at ≥0.55 based on established literature [12]. Insulin resistance was assessed using HOMA-IR, calculated as (fasting insulin × fasting glucose) / 405. The oral glucose tolerance test (OGTT) was not performed in this study. To ensure validity, data collection followed standardized protocols, and biochemical analyses were conducted in a blinded manner. Reliability was maintained through duplicate testing of biochemical markers and inter-observer agreement for ultrasound evaluations, with scans reviewed independently by two radiologists. Statistical analysis was conducted using SPSS version 25. Normality of continuous variables was assessed using the Shapiro-Wilk test. For normally distributed variables, independent t-tests were used to compare means between PCOS and non-PCOS groups. These included age, LH, FSH, prolactin, fasting blood glucose, HOMA-IR, total cholesterol, LDL, HDL, triglycerides, CRP, MDA, TAC, endometrial thickness, and ovarian stromal resistance index. Non-normally distributed variables, including BMI, LH/FSH ratio, total testosterone, free testosterone, DHEA-S, AMH, and HbA1c, were analyzed using the Mann-Whitney U test. Categorical variables, marital status, education level, employment status, physical activity level, dietary habits, smoking status, parity, history of infertility, polycystic ovarian morphology, and increased ovarian volume, were analyzed using the Chi-square test. Post-hoc Bonferroni corrections were applied to employment status and education level due to their significant Chi-square results. A significance level of $p<0.05$ was considered statistically significant.

RESULTS

The study population showed significant differences between women with PCOS and those without. Women with PCOS were younger and had a higher BMI, reinforcing the link between PCOS and obesity. Employment status also varied, with fewer employed women and more students in the PCOS group. Other demographic factors did not show significant differences (Table 1).

Table 1: Demographic and Clinical Characteristics of the Study Population

Variables	Category	PCOS Group (Mean ± SD) / Frequency (%)	Non-PCOS Group (Mean ± SD) / Frequency (%)	p-Value
Age (years)	-	25.43 ± 2.75	27.97 ± 2.65	<0.001** (t-test)
BMI (kg/m^2)	-	30.08 ± 4.04	24.55 ± 2.94	<0.001 (Mann-Whitney U=410.000, Z= -6.591)
Marital Status	Married	37 (67.3%)	31 (56.4%)	0.239 (Chi-square)
	Single	18 (32.7%)	24 (43.6%)	

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Education Level	Higher	21 (38.2%)	14 (25.5%)	0.201 (Chi-square, No significant post-hoc results)
	No Education	1 (1.8%)	4 (7.3%)	
	Primary	12 (21.8%)	9 (16.4%)	
	Secondary	21 (38.2%)	28 (50.9%)	
Employment Status	Employed	14 (25.5%)	30 (54.5%)	0.004 (PCOS < Non-PCOS)
	Unemployed	22 (40.0%)	17 (30.9%)	Not significant
	Student	19 (34.5%)	8 (14.5%)	PCOS >Non-PCOS
Physical Activity	Sedentary	35 (63.6%)	27 (49.1%)	0.054 (Chi-square)
	Moderate	16 (29.1%)	15 (27.3%)	
	Active	4 (7.3%)	13 (23.6%)	
Dietary Habits	Healthy	14 (25.5%)	12 (21.8%)	0.654 (Chi-square)
	Unhealthy	41 (74.5%)	43 (78.2%)	
Smoking Status	Smoker	9 (16.4%)	6 (10.9%)	0.405 (Chi-square)
	Non-Smoker	46 (83.6%)	49 (89.1%)	
Parity	0	24 (43.6%)	19 (34.5%)	0.418 (Chi-square, No Significant post-hoc Results)
	1-2	26 (47.3%)	27 (49.1%)	
	3+	5 (9.1%)	9 (16.4%)	
History of Infertility	Yes	18 (32.7%)	17 (30.9%)	0.838 (Chi-square)
	No	37 (67.3%)	38 (69.1%)	

Hormonal analysis revealed higher luteinizing hormone (LH) and lower follicle-stimulating hormone (FSH) in PCOS, leading to an increased LH/FSH ratio. Elevated total and free testosterone, dehydroepiandrosterone sulphate (DHEA-S), and anti-Müllerian hormone (AMH) indicated androgen excess and greater ovarian reserve. Prolactin was slightly higher in the PCOS group, but the difference was minor. These findings align with typical hormonal imbalances in PCOS (Table 2).

Table 2: Hormonal Profile of PCOS and Non-PCOS Groups

Variables	PCOS Group (Mean ± SD)	Non-PCOS Group (Mean ± SD)	p-Value
LH (mIU/mL)	11.15 ± 1.93	7.14 ± 1.44	<0.001** (t-test)
FSH (mIU/mL)	5.59 ± 1.06	6.44 ± 0.98	<0.001** (t-test)
LH/FSH Ratio	2.09 ± 0.65	1.13 ± 0.29	<0.001** (Mann-Whitney U=169.000, Z= -8.032)
Total Testosterone (ng/dL)	65.99 ± 11.48	34.57 ± 7.39	<0.001** (Mann-Whitney U=29.000, Z= -8.869)
Free Testosterone (pg/mL)	5.03 ± 1.03	2.02 ± 0.43	<0.001** (Mann-Whitney U=2.000, Z= -9.030)
DHEA-S (µg/dL)	178.25 ± 33.25	124.95 ± 18.68	<0.001** (Mann-Whitney U=242.000, Z = -7.595)
AMH (ng/mL)	7.32 ± 1.57	2.99 ± 1.05	<0.001** (Mann-Whitney U=20.000, Z= -8.922)
Prolactin (ng/mL)	14.63 ± 3.31	13.48 ± 2.36	0.038* (t-test)

Metabolic markers showed elevated fasting blood glucose, insulin resistance (HOMA-IR), and haemoglobin A1c (HbA1c) in PCOS, highlighting glucose metabolism disturbances. Lipid profile abnormalities included higher total cholesterol, low-density lipoprotein (LDL), and triglycerides, with lower high-density lipoprotein (HDL). Inflammatory and oxidative stress markers, such as C-reactive protein (CRP) and malondialdehyde (MDA), were elevated, while total antioxidant capacity (TAC) was reduced, indicating increased oxidative stress (Table 3).

Table 3: Metabolic and Oxidative Stress Profile of PCOS and Non-PCOS Groups

Variables	PCOS Group (Mean ± SD)	Non-PCOS Group (Mean ± SD)	p-Value
Fasting Blood Glucose (mg/dL)	98.96 ± 5.09	89.39 ± 5.15	<0.001** (t-test)
HOMA-IR	3.38 ± 0.65	2.10 ± 0.47	<0.001** (t-test)
HbA1c (%)	5.81 ± 0.32	5.33 ± 0.20	<0.001** (Mann-Whitney U=278.000, Z= -7.380)
Total Cholesterol (mg/dL)	206.26 ± 20.31	189.85 ± 13.68	<0.001** (t-test)
LDL (mg/dL)	129.77 ± 14.41	110.30 ± 12.02	<0.001** (t-test)
HDL (mg/dL)	42.64 ± 5.16	51.04 ± 3.82	<0.001** (t-test)
Triglycerides (mg/dL)	157.02 ± 22.77	119.46 ± 19.04	<0.001** (t-test)
CRP (mg/L)	3.55 ± 1.24	2.25 ± 0.92	<0.001** (t-test)
MDA (nmol/L)	4.58 ± 0.87	2.94 ± 0.61	<0.001** (t-test)
TAC (mmol/L)	0.92 ± 0.20	1.33 ± 0.28	<0.001** (t-test)

Gynaecological and ultrasound findings further supported PCOS diagnosis. Endometrial thickness was significantly greater, likely due to prolonged estrogen exposure. The ovarian stromal resistance index (RI) was also higher, indicating altered ovarian blood flow. However, polycystic ovarian morphology and ovarian volume did not significantly differ, reflecting variability in ultrasound features among individuals with PCOS (Table 4).

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Table 4: Gynaecological and Ultrasound Features of PCOS and Non-PCOS Groups

Variables	Category	PCOS Group (Mean ± SD) / Frequency (%)	Non-PCOS Group (Mean ± SD) / Frequency (%)	p-Value
Endometrial Thickness (mm)	-	9.66 ± 1.72	7.19 ± 1.62	<0.001**
Ovarian Stromal RI	-	0.60 ± 0.11	0.40 ± 0.07	<0.001**
Polycystic Ovarian Morphology	Yes/No	44 (80.0%) / 11 (20.0%)	43 (78.2%) / 12 (21.8%)	0.815
Increased Ovarian Volume	Yes/No	39 (70.9%) / 16 (29.1%)	43 (78.2%) / 12 (21.8%)	0.381

DISCUSSION

This research sheds light on the biochemical, physiological, and metabolic changes related to polycystic ovary syndrome (PCOS). Our results also corroborate the hormonal and metabolic imbalances described in the existing literature on PCOS, which play a crucial role in its pathophysiology. Women with PCOS showed elevated levels of luteinizing hormone (LH) and a remarkably increased LH/FSH ratio compared to those without PCOS. These findings were supported by other research that found an increased LH/FSH ratio as a defining feature of PCOS and a factor of ovarian pathology [13-15]. The increased levels of total and free testosterone, as well as DHEA-S, support the indication of hyperandrogenism, which was a prominent feature of PCOS. These results aligned with earlier studies, which suggested that elevated androgen levels are associated with the clinical features of hirsutism, acne, and alopecia [16-18]. Women with PCOS face a higher risk of insulin resistance and cardiovascular disease. Elevated fasting blood glucose and HOMA-IR levels confirm prevalent insulin resistance, which contributes to hyperandrogenism and ovarian dysfunction [19, 20]. Dyslipidaemia, marked by high cholesterol, LDL, and triglycerides, with low HDL, further exacerbates metabolic risks in PCOS. Markers of inflammation and oxidative stress suggest systemic inflammation in PCOS. Increased CRP and MDA levels indicate heightened inflammatory and oxidative stress, common in metabolic dysfunction. Reduced total antioxidant capacity (TAC) suggests impaired oxidative defence. These findings align with studies linking chronic inflammation and oxidative stress to insulin resistance and cardiovascular risk in PCOS [21-23]. Ultrasound findings support the diagnosis of PCOS, revealing ovarian abnormalities. Increased endometrial thickness results from excess estrogenic secretion due to anovulation. Elevated ovarian stromal RI suggests androgen hypersecretion and follicular arrest. However, polycystic ovarian morphology and ovarian volume did not differ significantly between groups, indicating that while common in PCOS, these features are not definitive diagnostic markers. The study findings align with existing literature, reinforcing the distinct hormonal, metabolic, and inflammatory disruptions in PCOS [24-26]. Early metabolic screening in women with PCOS is essential to prevent long-term complications such as Type 2 Diabetes and cardiovascular diseases. This study supports existing literature by validating the hormonal, metabolic, and inflammatory disruptions characteristic of PCOS [24-26]. Early metabolic screening is crucial in preventing long-term complications such as Type 2 Diabetes and cardiovascular diseases. However, further research should be conducted to focus on targeted interventions addressing both metabolic and reproductive aspects of PCOS to enhance patient outcomes.

This study was limited by its single-center, hospital-based cross-sectional design, relatively small sample size, and use of non-probability sampling, which may reduce generalizability and causal interpretation. The absence of longitudinal follow-up and lack of archived ultrasound imaging further restricted assessment of disease progression and imaging validation. Future studies should involve larger multicenter cohorts, prospective designs, and more diverse populations while incorporating long-term metabolic and reproductive outcomes to strengthen understanding and guide personalized interventions for PCOS management.

CONCLUSIONS

It was concluded that this study highlights the hormonal, metabolic and inflammatory abnormalities of PCOS. An elevated LH/FSH ratio, hyperandrogenism, and insulin resistance denote the endocrine disorder. The metabolic complications of dyslipidaemia, along with increased oxidative stress, are risk factors for cardiovascular diseases. Ultrasound findings confirm ovarian dysfunction; though polycystic morphology alone may not be a definitive diagnostic marker. Such complex findings illustrate the importance of early metabolic assessment and comprehensive intervention for the sustainability of women.

Authors' Contribution

Conceptualization: SA
Methodology: SA, SN, SJS, ET
Formal analysis: SN, SJS, MR, SS
Writing and Drafting: ET, MR, SSw
Review and Editing: ET, MR, SS, SA, SN, SJS, ET

All authors approved the final manuscript and take responsibility for the integrity of the work

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Conflicts of Interest

The authors declare no conflict of interest.

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