JHWCR JOURNAL OF HEALTH, WELLNESS AND COMMUNITY RESEARCH 3007-0570

https://doi.org/10.61919/rajekv62

Original Article

Metabolic Profile Abnormalities in Polycystic Ovary Syndrome: A Clinical Pathology Approach

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"Cite this Article" Received: 28 February 2026; **Accepted**: 23 April 2026; **Published**: 12 May 2026

Author Contributions: Concept: ZUNM; Design: SUN; Data Collection: JAZ; Analysis: IRG and AK; Drafting: NM. **Ethical Approval** was obtained from the Respective Institution. **Informed Consent**: Written informed consent was obtained from all participants; **Conflict of Interest**: The authors declare no conflict of interest. **Funding**: No external funding; **Data Availability**: Available from the corresponding author on reasonable request; **Acknowledgments**: N/A.

ABSTRACT

Background: Polycystic ovary syndrome is a common endocrine-metabolic disorder in reproductive-aged women and is associated with insulin resistance, dyslipidemia, impaired glucose regulation, and hepatic biochemical abnormalities that may increase long-term cardiometabolic risk. Objective: This study aimed to compare fasting glucose, insulin resistance markers, lipid profile, and liver enzymes between women with polycystic ovary syndrome and age- and BMI-matched healthy controls attending tertiary-care hospitals in Sindh, Pakistan. Methods: This case-control study included 150 women aged 18–40 years, comprising 75 women diagnosed with polycystic ovary syndrome using Rotterdam criteria and 75 healthy controls matched for age and body mass index. Clinical assessment, anthropometric measurements, and fasting biochemical testing were performed. Fasting glucose, fasting insulin, HOMA-IR, total cholesterol, triglycerides, HDL-C, LDL-C, alanine aminotransferase, and aspartate aminotransferase were compared between groups using appropriate statistical tests, and correlations between HOMA-IR and metabolic parameters were assessed. Results: Women with polycystic ovary syndrome had higher fasting glucose than controls (104.5 ± 12.3 vs 89.2 ± 8.6 mg/dL; $p < 0.001$), fasting insulin (18.7 ± 5.6 vs 9.5 ± 3.2 µIU/mL; $p < 0.001$), and HOMA-IR (4.8 ± 1.4 vs 2.1 ± 0.7; $p < 0.001$). They also showed higher triglycerides, LDL-C, total cholesterol, ALT, and AST, with lower HDL-C. HOMA-IR correlated positively with triglycerides ($r = 0.63$), LDL-C ($r = 0.42$), and ALT ($r = 0.38$), and negatively with HDL-C ($r = -0.51$). Conclusion: Women with polycystic ovary syndrome demonstrated a coordinated adverse metabolic profile involving insulin resistance, atherogenic dyslipidemia, and hepatic enzyme elevation despite comparable BMI. Routine metabolic profiling may support early risk identification and preventive management. Keywords: Polycystic ovary syndrome, insulin resistance, HOMA-IR, dyslipidemia, fasting glucose, liver enzymes, cardiometabolic risk, Sindh.

INTRODUCTION

Polycystic ovary syndrome is one of the most common endocrine disorders affecting women of reproductive age and is clinically characterized by ovulatory dysfunction, hyperandrogenism, and polycystic ovarian morphology. Although traditionally approached as a reproductive disorder, increasing evidence shows that PCOS is a systemic metabolic condition associated with insulin resistance, impaired glucose regulation, atherogenic dyslipidemia, central adiposity, and hepatic enzyme abnormalities. These metabolic disturbances increase the long-term risk of type 2 diabetes mellitus, cardiovascular disease, and possible hepatic dysfunction, making early metabolic risk identification an essential component of PCOS evaluation and management (1).

The global prevalence of PCOS varies widely according to diagnostic criteria, population characteristics, and ethnicity, with reported estimates ranging from approximately 5% to 20%. South Asian women appear to carry a particularly high burden of PCOS-related metabolic complications, likely due to differences in genetic susceptibility, adiposity patterns, diet, physical inactivity, and earlier onset of insulin resistance. In Pakistan, hospital-based studies suggest that PCOS is frequently encountered among reproductive-aged women presenting with menstrual irregularity, infertility, and symptoms of androgen excess, yet systematic metabolic assessment is not consistently integrated into routine clinical care (2,3).

Insulin resistance is central to the pathophysiology of PCOS and may occur in both obese and non-obese women. Compensatory hyperinsulinemia contributes to ovarian androgen excess by stimulating theca-cell androgen production and reducing sex hormone-binding globulin concentrations, thereby worsening clinical hyperandrogenism and reproductive dysfunction. Beyond its reproductive effects, insulin resistance also promotes abnormalities in glucose metabolism and interacts closely with lipid and hepatic pathways, supporting the need to evaluate fasting glucose, fasting insulin, and derived indices such as the homeostatic model assessment for insulin resistance in women with PCOS (4,5).

Dyslipidemia is another clinically important metabolic feature of PCOS. Women with PCOS commonly demonstrate elevated triglycerides, increased low-density lipoprotein cholesterol, and reduced high-density lipoprotein cholesterol, a pattern that contributes to a higher lifetime burden of cardiometabolic risk. These lipid abnormalities are often linked to insulin resistance and central adiposity, but they may also be present despite comparable body mass index, indicating that BMI alone is insufficient for risk stratification. Therefore, comprehensive lipid profiling is necessary to detect early atherogenic changes and guide preventive interventions in affected women (6,7).

Liver enzyme abnormalities, particularly elevated alanine aminotransferase and aspartate aminotransferase, have also been reported in women with PCOS and may reflect underlying hepatic metabolic stress. Although liver enzymes alone cannot establish a diagnosis of non-alcoholic fatty liver disease, their elevation in the context of insulin resistance and dyslipidemia may identify women who require further hepatic evaluation. This is particularly relevant in tertiary-care settings where patients often present with multiple overlapping reproductive and metabolic risk factors (8,9).

Despite extensive international literature on PCOS-related metabolic dysfunction, locally generated evidence from Sindh, Pakistan remains limited, particularly studies that compare women with PCOS against age- and BMI-matched controls while simultaneously assessing glucose metabolism, insulin resistance, lipid profile, and liver enzymes. This gap is important because regional differences in diet, body-fat distribution, family history of diabetes, access to care, and clinical presentation may influence the severity and pattern of metabolic abnormalities. Generating local evidence can help clinicians identify high-risk women earlier and support the development of standardized metabolic screening protocols in tertiary hospitals (10,11).

The present case-control study was therefore designed using a PICO-oriented framework: the population comprised reproductive-aged women attending tertiary hospitals in Sindh, Pakistan; the exposure was diagnosis of PCOS based on accepted clinical criteria; the comparison group consisted of age- and BMI-matched healthy women; and the outcomes included fasting glucose, fasting insulin, HOMA-IR, lipid parameters, and liver enzymes. The study aimed to determine whether women with PCOS demonstrate a higher burden of metabolic abnormalities than matched controls and to examine the relationship between insulin resistance, dyslipidemia, and liver enzyme elevation. The primary objective was to compare fasting glucose, insulin resistance markers, lipid profile, and liver enzymes between women with PCOS and healthy controls, with the hypothesis that PCOS is associated with significantly adverse metabolic profiles even when age and BMI are comparable (12).

MATERIALS AND METHODS

This case-control study was conducted in selected tertiary-care hospitals in Sindh, Pakistan, from January 2025 to December 2025 to compare metabolic profile abnormalities between women diagnosed with polycystic ovary syndrome and healthy women without PCOS. A case-control design was selected because it allowed efficient comparison of fasting glucose, insulin resistance markers, lipid parameters, and liver enzymes between affected and non-affected participants while controlling for key demographic and anthropometric characteristics through age and body mass index matching. The study population comprised women of reproductive age, and the exposure of interest was the presence of PCOS, while the main outcomes were fasting glucose, fasting insulin, HOMA-IR, total cholesterol, triglycerides, HDL-C, LDL-C, alanine aminotransferase, and aspartate aminotransferase.

Women aged 18–40 years were eligible for inclusion. The case group included women diagnosed with PCOS according to the Rotterdam diagnostic criteria, requiring the presence of at least two of the following features: oligo-ovulation or anovulation, clinical or biochemical hyperandrogenism, and polycystic ovarian morphology on ultrasonography. The control group consisted of healthy women of similar age and body mass index who had regular menstrual cycles, no clinical features suggestive of hyperandrogenism, and no known diagnosis of PCOS. Controls were matched to cases by age within ±2 years and BMI within ±1 kg/m² to reduce confounding by these variables. Women were excluded if they had known diabetes mellitus, thyroid disease, cardiovascular disease, chronic liver disease, renal disease, pregnancy, or use of medications known to affect glucose metabolism, lipid metabolism, liver enzymes, or reproductive hormones during the preceding three months, including metformin, hormonal therapy, corticosteroids, or lipid-lowering drugs.

A total of 150 participants were enrolled, including 75 women with PCOS and 75 healthy controls. The sample size was determined using prevalence estimates from regional studies, with a 95% confidence level and 80% statistical power, allowing adequate comparison of metabolic parameters between the two groups. Participants were recruited consecutively from outpatient gynecology and endocrinology clinics. Women presenting with menstrual irregularity, infertility, clinical hyperandrogenism, or other symptoms suggestive of PCOS were screened for eligibility. Healthy controls were recruited from hospital staff, relatives of patients, and community volunteers after confirmation that they met the control-group criteria. All eligible participants were informed about the study objectives, procedures, expected benefits, potential risks, confidentiality safeguards, and their right to withdraw at any time before written informed consent was obtained.

Data were collected using a structured questionnaire, clinical examination, anthropometric assessment, gynecological evaluation, ultrasonography, and biochemical testing. The questionnaire recorded age, marital status, menstrual history, infertility history, symptoms of androgen excess, family history of diabetes or cardiovascular disease, lifestyle factors, medication history, and relevant clinical comorbidities. Height was measured using a stadiometer with the participant standing barefoot, and weight was measured using a calibrated weighing scale with light clothing. Body mass index was calculated as weight in kilograms divided by height in meters squared. Waist circumference was measured midway between the lower margin of the last palpable rib and the top of the iliac crest, while hip circumference was measured at the widest portion of the buttocks; waist-to-hip ratio was calculated by dividing waist circumference by hip circumference. Blood pressure was measured using a calibrated sphygmomanometer after the participant had rested in a seated position.

Clinical hyperandrogenism was assessed by documenting hirsutism and acne. Hirsutism was evaluated using the Ferriman-Gallwey scoring system, while ultrasonography was performed to assess ovarian morphology. PCOS diagnosis was established after integrating menstrual history, clinical or biochemical evidence of androgen excess, and ovarian morphology according to the Rotterdam framework. To reduce

measurement variability, clinical and laboratory procedures were performed according to standardized protocols, and biochemical testing was conducted in accredited hospital laboratories.

Venous blood samples were obtained after an overnight fast of 8–12 hours. Samples were collected between 8:00 AM and 10:00 AM to minimize diurnal variation. Fasting plasma glucose was measured using the enzymatic glucose oxidase method, and fasting insulin was measured using immunoassay. Insulin resistance was estimated using the homeostatic model assessment for insulin resistance, calculated as fasting insulin in μIU/mL multiplied by fasting glucose in mg/dL and divided by 405. Lipid profile testing included total cholesterol, triglycerides, high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol, measured using standard enzymatic colorimetric methods. Liver enzyme assessment included alanine aminotransferase and aspartate aminotransferase, measured using automated biochemical analyzers. Internal quality-control procedures were followed during laboratory testing, including routine calibration of equipment, use of control samples, and duplicate checking of laboratory records.

The primary exposure variable was PCOS status, categorized as PCOS or control. The primary metabolic outcomes were fasting glucose, fasting insulin, HOMA-IR, triglycerides, HDL-C, LDL-C, total cholesterol, ALT, and AST. Secondary clinical variables included age, BMI, waist-to-hip ratio, blood pressure, and family history of diabetes. Operationally, insulin resistance was assessed using HOMA-IR as a continuous measure, dyslipidemia was evaluated through lipid profile parameters, and hepatic biochemical involvement was assessed through ALT and AST concentrations. Age and BMI matching was used at the design stage to reduce confounding, while detailed clinical and family-history data were collected to allow assessment of additional metabolic risk factors.

Data were entered into Microsoft Excel using unique participant identification codes to preserve confidentiality. Data accuracy was maintained through double-checking of questionnaire entries, anthropometric values, and laboratory results by two independent researchers. Records were reviewed for completeness before analysis. Missing or implausible values were checked against source records before final analysis. Participants with incomplete core metabolic outcome data were excluded from the relevant analysis, while available complete data were retained for descriptive and comparative analysis. Continuous variables were summarized as mean ± standard deviation, and categorical variables were summarized as frequencies and percentages.

Statistical analysis was performed using SPSS version 26.0. The distribution of continuous variables was assessed before group comparisons. Independent-samples t-tests were used to compare normally distributed continuous variables between women with PCOS and controls, while non-normally distributed variables were assessed using appropriate non-parametric methods when required. Chi-square tests were used to compare categorical variables between groups. Pearson correlation analysis was used to evaluate associations between HOMA-IR and lipid or liver enzyme parameters, including triglycerides, LDL-C, HDL-C, ALT, and AST. A p-value of less than 0.05 was considered statistically significant. Where clinically appropriate, group differences were interpreted alongside the magnitude and direction of observed differences to support metabolic interpretation rather than relying only on statistical significance.

Bias and confounding were addressed through design and procedural safeguards. Age and BMI matching was used to reduce confounding by demographic and body-size differences. Standardized clinical assessment procedures were applied to both groups to reduce measurement bias. Blood sampling was performed after a uniform fasting interval and within a defined morning time window to reduce biological variability. Exclusion of participants with diabetes mellitus, thyroid disease, cardiovascular disease, liver disease, renal disease, pregnancy, or recent use of metabolism-altering medications reduced the likelihood that measured metabolic abnormalities were attributable to pre-existing systemic disease or drug effects. Laboratory analyses were conducted using standardized methods and quality-control procedures to support reliability and reproducibility.

The study was conducted in accordance with ethical principles for human-subject research. Ethical approval was obtained from the institutional review boards of the participating hospitals before data collection. Written informed consent was obtained from all participants. Participation was voluntary, and participants retained the right to withdraw without any effect on their clinical care. Confidentiality was maintained by using coded identifiers rather than personal information in the study dataset, and access to study records was restricted to authorized research personnel. All collected data were used only for research purposes, and findings were reported in aggregate form to prevent identification of individual participants.

RESULTS

A total of 150 women were included in the analysis, with 75 women diagnosed with polycystic ovary syndrome and 75 healthy controls. The two groups were comparable in age and body mass index, supporting the intended age- and BMI-matched design. The mean age was 27.6 ± 4.3 years in the PCOS group and 28.0 ± 4.7 years in the control group, with no statistically significant difference between groups ($p = 0.54$). Similarly, BMI was comparable between women with PCOS and controls, at 26.1 ± 3.8 kg/m² and 25.8 ± 3.6 kg/m², respectively ($p = 0.62$). Despite comparable BMI, women with PCOS demonstrated significantly higher waist-to-hip ratio, higher blood pressure, and a greater frequency of family history of diabetes, indicating a less favorable cardiometabolic risk profile at baseline. The waist-to-hip ratio was 0.85 ± 0.05 in the PCOS group compared with 0.79 ± 0.04 in controls ($p < 0.01$), while family history of diabetes was present in 40 women with PCOS (53.3%) compared with 18 controls (24.0%; $p < 0.01$).

Table 1. Baseline Demographic and Clinical Characteristics of Participants

Variable	PCOS Group (n = 75)	Control Group (n = 75)	Mean Difference / Difference in Proportion	p-value
Age, years	27.6 ± 4.3	28.0 ± 4.7	-0.4 years	0.54
BMI, kg/m²	26.1 ± 3.8	25.8 ± 3.6	+0.3 kg/m²	0.62
Waist-to-hip ratio	0.85 ± 0.05	0.79 ± 0.04	+0.06	<0.01
Blood pressure, mmHg	122/78 ± 10/8	118/76 ± 9/7	+4/+2 mmHg	0.03
Family history of diabetes, n (%)	40 (53.3%)	18 (24.0%)	+29.3 percentage points	<0.01

Women with PCOS showed significantly higher fasting glucose, fasting insulin, and HOMA-IR values than controls. Mean fasting glucose was 104.5 ± 12.3 mg/dL in the PCOS group compared with 89.2 ± 8.6 mg/dL in controls, representing an absolute mean difference of 15.3 mg/dL ($p < 0.001$). Fasting insulin was nearly twice as high among women with PCOS, with a mean value of 18.7 ± 5.6 µIU/mL compared with 9.5 ± 3.2 µIU/mL in controls, corresponding to a mean difference of 9.2 µIU/mL ($p < 0.001$). This difference was reflected in HOMA-IR, which was markedly elevated in the PCOS group at 4.8 ± 1.4 compared with 2.1 ± 0.7 in controls, producing a mean difference of 2.7 units ($p < 0.001$). These findings indicate substantially greater insulin resistance among women with PCOS despite similar BMI between groups.

Table 2. Comparison of Glucose Metabolism and Insulin Resistance Markers

Variable	PCOS Group (n = 75)	Control Group (n = 75)	Mean Difference	p-value
Fasting glucose, mg/dL	104.5 ± 12.3	89.2 ± 8.6	+15.3 mg/dL	<0.001
Fasting insulin, µIU/mL	18.7 ± 5.6	9.5 ± 3.2	+9.2 µIU/mL	<0.001
HOMA-IR	4.8 ± 1.4	2.1 ± 0.7	+2.7	<0.001

Lipid profile analysis demonstrated a consistent atherogenic pattern among women with PCOS. Total cholesterol was higher in the PCOS group than in controls, with mean values of 202.4 ± 31.2 mg/dL and 175.8 ± 28.7 mg/dL, respectively, yielding a mean difference of 26.6 mg/dL ($p < 0.001$). Triglycerides were substantially elevated among women with PCOS, measuring 178.3 ± 45.2 mg/dL compared with 122.5 ± 34.8 mg/dL in controls, with a mean difference of 55.8 mg/dL ($p < 0.001$). LDL-C was also higher in the PCOS group by 24.2 mg/dL, while HDL-C was lower by 12.5 mg/dL. The combination of higher triglycerides, higher LDL-C, higher total cholesterol, and lower HDL-C demonstrates a clinically unfavorable lipid pattern in women with PCOS.

Table 3. Comparison of Lipid Profile Between PCOS and Control Groups

Lipid Parameter	PCOS Group (n = 75)	Control Group (n = 75)	Mean Difference	p-value
Total cholesterol, mg/dL	202.4 ± 31.2	175.8 ± 28.7	+26.6 mg/dL	<0.001
Triglycerides, mg/dL	178.3 ± 45.2	122.5 ± 34.8	+55.8 mg/dL	<0.001
HDL-C, mg/dL	42.1 ± 8.3	54.6 ± 9.1	-12.5 mg/dL	<0.001
LDL-C, mg/dL	132.6 ± 28.1	108.4 ± 24.7	+24.2 mg/dL	<0.001

Liver enzyme levels were also higher among women with PCOS. Mean alanine aminotransferase was 36.8 ± 12.5 U/L in the PCOS group compared with 22.4 ± 8.1 U/L in controls, showing an absolute difference of 14.4 U/L ($p < 0.001$). Aspartate aminotransferase was also elevated, with mean values of 32.1 ± 10.3 U/L in women with PCOS and 25.5 ± 7.2 U/L in controls, corresponding to a mean difference of 6.6 U/L ($p < 0.01$). The magnitude of ALT elevation was greater than that of AST, suggesting that ALT contributed more strongly to the observed difference in hepatic biochemical markers between groups.

Table 4. Comparison of Liver Enzyme Levels Between PCOS and Control Groups

Liver Enzyme	PCOS Group (n = 75)	Control Group (n = 75)	Mean Difference	p-value
ALT, U/L	36.8 ± 12.5	22.4 ± 8.1	+14.4 U/L	<0.001
AST, U/L	32.1 ± 10.3	25.5 ± 7.2	+6.6 U/L	<0.01

Correlation analysis showed that insulin resistance was closely associated with lipid abnormalities and liver enzyme elevation among women with PCOS. HOMA-IR demonstrated a strong positive correlation with triglycerides ($r = 0.63$, $p < 0.001$), indicating that higher insulin resistance was associated with higher triglyceride levels. A moderate positive correlation was observed between HOMA-IR and LDL-C ($r = 0.42$, $p < 0.01$), while HOMA-IR was negatively correlated with HDL-C ($r = -0.51$, $p < 0.01$), showing that increasing insulin resistance was associated with lower protective cholesterol levels. ALT also showed a positive correlation with HOMA-IR ($r = 0.38$, $p < 0.01$), supporting a relationship between insulin resistance and hepatic enzyme elevation.

Table 5. Correlation of HOMA-IR With Lipid and Liver Enzyme Parameters

Correlated Variables	Correlation Coefficient (r)	Direction and Strength of Association	p-value
HOMA-IR and triglycerides	0.63	Strong positive association	<0.001
HOMA-IR and LDL-C	0.42	Moderate positive association	<0.01
HOMA-IR and HDL-C	-0.51	Moderate negative association	<0.01
HOMA-IR and ALT	0.38	Moderate positive association	<0.01

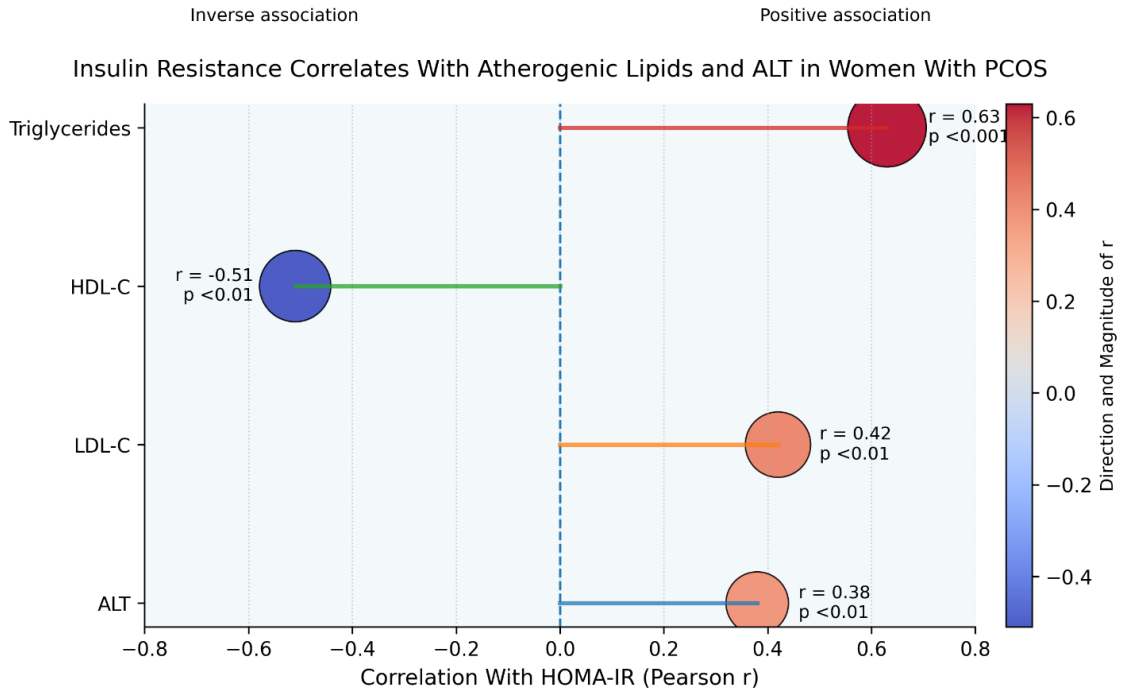

Figure 1. Insulin Resistance Correlates With Atherogenic Lipids and ALT in Women With PCOS

HOMA-IR showed the strongest positive association with triglycerides ($r = 0.63$, $p < 0.001$), indicating that increasing insulin resistance was closely aligned with higher triglyceride burden. HDL-C

demonstrated a moderate inverse association with HOMA-IR ($r = -0.51$, $p < 0.01$), showing that greater insulin resistance corresponded with lower protective cholesterol levels. LDL-C was moderately and positively associated with HOMA-IR ($r = 0.42$, $p < 0.01$), while ALT also showed a positive association ($r = 0.38$, $p < 0.01$), linking insulin resistance with both atherogenic lipid disturbance and hepatic enzyme elevation. Together, these patterns indicate that insulin resistance in women with PCOS is accompanied by a coordinated adverse metabolic profile involving hypertriglyceridemia, reduced HDL-C, increased LDL-C, and higher ALT activity.

Overall, women with PCOS demonstrated a distinct metabolic abnormality pattern compared with healthy controls. Although both groups were similar in age and BMI, the PCOS group had higher central adiposity, greater family history of diabetes, higher fasting glucose, higher fasting insulin, markedly elevated HOMA-IR, increased total cholesterol, triglycerides and LDL-C, lower HDL-C, and higher ALT and AST levels. The strongest group difference was observed for insulin resistance, with HOMA-IR more than twice as high in women with PCOS compared with controls. The correlation findings further showed that insulin resistance was not an isolated abnormality but was linked with a broader adverse metabolic pattern involving hypertriglyceridemia, reduced HDL-C, increased LDL-C, and higher ALT levels.

DISCUSSION

The present study demonstrates that women with polycystic ovary syndrome had a substantially adverse metabolic profile compared with age- and BMI-matched controls, with significantly higher fasting glucose, fasting insulin, HOMA-IR, total cholesterol, triglycerides, LDL-C, ALT, and AST, alongside lower HDL-C. These findings reinforce the concept that PCOS is not limited to reproductive dysfunction but represents a broader endocrine-metabolic disorder in which impaired insulin signaling, altered lipid metabolism, central adiposity, and hepatic biochemical changes may coexist even when overall BMI is comparable between affected and unaffected women. The comparable age and BMI between groups strengthen the interpretation that the observed differences are related to PCOS-associated metabolic dysfunction rather than simple differences in body size, although the higher waist-to-hip ratio among women with PCOS indicates that central adiposity remains an important contributor to cardiometabolic risk (13).

Insulin resistance emerged as the dominant metabolic abnormality in the PCOS group. Women with PCOS had markedly higher fasting insulin and HOMA-IR values than controls, indicating compensatory hyperinsulinemia and reduced insulin sensitivity. This finding is biologically consistent with the established role of insulin resistance in PCOS pathophysiology, where hyperinsulinemia contributes to ovarian androgen excess, reduces sex hormone-binding globulin levels, and amplifies both reproductive and metabolic manifestations of the syndrome. The magnitude of the HOMA-IR difference observed in this study suggests that insulin resistance is clinically meaningful in this population and should be evaluated early rather than reserved only for women with obesity or overt glucose intolerance (14).

The higher fasting glucose level among women with PCOS further supports the presence of early glycemic dysregulation. Although mean fasting glucose values did not by themselves establish overt diabetes, the difference between groups indicates a shift toward impaired glucose metabolism in women with PCOS. This has important clinical implications because reproductive-aged women with PCOS may remain asymptomatic while already developing metabolic abnormalities that increase future risk of type 2 diabetes mellitus. The higher frequency of family history of diabetes in the PCOS group may have further intensified this risk profile, suggesting that genetic predisposition and PCOS-related insulin resistance may interact to increase vulnerability to dysglycemia in this setting (15).

The lipid findings showed a typical atherogenic pattern, with higher total cholesterol, triglycerides, and LDL-C, and lower HDL-C among women with PCOS. This pattern is clinically important because it reflects a lipid environment associated with increased long-term cardiovascular risk. The largest lipid

difference was observed for triglycerides, which were more than 55 mg/dL higher in women with PCOS than in controls. This is consistent with the metabolic effects of insulin resistance on hepatic lipid handling, including increased very-low-density lipoprotein production, impaired triglyceride clearance, and reduced HDL-C concentrations. The lower HDL-C level observed in women with PCOS is particularly relevant because HDL-C has a protective role in reverse cholesterol transport, and reduced HDL-C may compound the cardiovascular implications of elevated triglycerides and LDL-C (16).

The correlation analysis further clarifies the interrelationship between insulin resistance and lipid disturbance. HOMA-IR showed a strong positive correlation with triglycerides and a moderate positive correlation with LDL-C, while demonstrating a moderate inverse correlation with HDL-C. These associations suggest that insulin resistance is not an isolated biochemical abnormality but part of a broader metabolic network in PCOS. The strong association between HOMA-IR and triglycerides indicates that triglyceride elevation may be a particularly sensitive marker of insulin resistance-related metabolic disruption in this population. Similarly, the inverse association between HOMA-IR and HDL-C supports the presence of an insulin resistance-linked atherogenic lipid phenotype (17).

Women with PCOS also demonstrated higher ALT and AST levels than controls, with the difference more pronounced for ALT. This finding suggests hepatic biochemical involvement in the PCOS group, likely reflecting the interaction between insulin resistance, central adiposity, and altered hepatic metabolism. ALT showed a positive correlation with HOMA-IR, supporting the interpretation that increasing insulin resistance was associated with higher hepatic enzyme activity. However, liver enzyme elevation should be interpreted as a biochemical signal rather than a definitive diagnosis of fatty liver disease, because liver imaging, fibrosis assessment, and hepatic fat quantification were not included. Even so, the observed ALT and AST elevations are clinically relevant because they identify a subgroup of women with PCOS who may require closer metabolic and hepatic evaluation (18).

The finding that waist-to-hip ratio was significantly higher in women with PCOS despite similar BMI highlights the importance of body-fat distribution in PCOS-related metabolic risk. BMI alone may underestimate risk because it does not distinguish between peripheral and central adiposity. Central fat accumulation is metabolically active and closely associated with insulin resistance, dyslipidemia, inflammation, and hepatic lipid deposition. Therefore, waist-to-hip ratio and other measures of central obesity should be considered alongside BMI when evaluating women with PCOS. This is especially relevant in South Asian populations, where cardiometabolic risk may occur at lower BMI thresholds and where central adiposity may be disproportionately important (19).

The clinical significance of these findings lies in the integrated pattern of abnormalities rather than in any single marker. Women with PCOS had evidence of impaired glucose metabolism, insulin resistance, atherogenic dyslipidemia, central adiposity, and liver enzyme elevation. Together, these abnormalities indicate a clustering of cardiometabolic risk factors that may precede overt diabetes, cardiovascular disease, or clinically apparent liver disease. The results support a pathology-based approach to PCOS care in which reproductive evaluation is accompanied by routine metabolic assessment, including fasting glucose, fasting insulin or HOMA-IR where available, lipid profile, liver enzymes, blood pressure, and central adiposity measurements (20).

These findings are also important for tertiary-care practice in Sindh, Pakistan. Women presenting to gynecology or endocrinology clinics with menstrual irregularity, infertility, or hyperandrogenic symptoms may already have substantial metabolic risk. If clinical care focuses only on menstrual regulation or fertility treatment, opportunities for early detection and prevention of long-term complications may be missed. A structured metabolic screening protocol at diagnosis and during follow-up could help identify high-risk women and guide timely lifestyle counseling, dietary modification, weight management, glucose monitoring, and individualized pharmacologic management when clinically indicated (21).

The study has several strengths, including its case-control design, inclusion of age- and BMI-matched controls, and assessment of multiple metabolic domains within the same participant population. The use of fasting biochemical measurements and standardized clinical assessment improves internal consistency. Matching by age and BMI helped reduce two major confounding influences and allowed clearer comparison of metabolic abnormalities between groups. The inclusion of liver enzymes in addition to glucose and lipid markers also provides a broader view of metabolic dysfunction in PCOS.

Several limitations should be acknowledged. The study was conducted in selected tertiary-care hospitals, so the findings may not fully represent women with PCOS in community settings or primary-care populations. The case-control design allows identification of associations but does not establish temporal or causal relationships. Although age and BMI were matched, residual confounding may remain due to differences in waist-to-hip ratio, family history of diabetes, diet, physical activity, socioeconomic factors, and unmeasured hormonal variables. In addition, liver enzyme elevation was assessed biochemically without imaging confirmation of hepatic steatosis, and therefore hepatic findings should be interpreted cautiously. The study also did not report androgen concentrations, inflammatory markers, or detailed PCOS phenotype stratification, which could have provided additional insight into metabolic heterogeneity.

Future research should build on these findings by using longitudinal designs to determine whether baseline insulin resistance, dyslipidemia, and liver enzyme elevation predict later diabetes, cardiovascular outcomes, or hepatic disease in women with PCOS. Larger multicenter studies across different regions of Pakistan would improve generalizability and allow comparison of urban, semi-urban, and rural populations. Future analyses should also incorporate adjusted regression models, PCOS phenotype classification, dietary and physical activity assessment, and hepatic imaging where feasible. Such work would help clarify whether specific PCOS phenotypes or metabolic profiles require more intensive screening and intervention.

In summary, the findings show that women with PCOS in this tertiary-care population had a clearly unfavorable metabolic profile compared with matched controls. Insulin resistance appeared central to this pattern and was associated with higher triglycerides, higher LDL-C, lower HDL-C, and elevated ALT. These results support the need to approach PCOS as a reproductive and metabolic disorder requiring early, integrated assessment. Routine metabolic profiling in women with PCOS may help identify high-risk individuals before the development of overt diabetes, cardiovascular disease, or clinically significant hepatic dysfunction.

CONCLUSION

This study demonstrates that women with polycystic ovary syndrome attending tertiary-care hospitals in Sindh, Pakistan, exhibit significantly greater metabolic abnormalities than age- and BMI-matched healthy controls, including higher fasting glucose, fasting insulin, HOMA-IR, total cholesterol, triglycerides, LDL-C, ALT, and AST, together with lower HDL-C. The findings indicate that insulin resistance is a central metabolic disturbance in PCOS and is closely associated with atherogenic dyslipidemia and hepatic enzyme elevation, suggesting a coordinated pattern of cardiometabolic risk rather than isolated biochemical changes. Although BMI was comparable between groups, the higher waist-to-hip ratio and greater family history of diabetes among women with PCOS highlight the importance of assessing central adiposity and inherited metabolic risk in addition to standard anthropometric measures. These results support the integration of routine metabolic profiling into PCOS care, including assessment of glucose regulation, insulin resistance, lipid profile, liver enzymes, blood pressure, and central obesity markers, to identify high-risk women early and guide timely lifestyle, preventive, and individualized clinical interventions aimed at reducing future diabetes, cardiovascular, and hepatic complications.

REFERENCES

1. World Health Organization. Polycystic ovary syndrome (PCOS) [Internet]. Geneva: World Health Organization; 2026 Jan 22 [cited 2026 Apr 22]. Available from: https://www.who.int/news-room/fact-sheets/detail/polycystic-ovary-syndrome

2. Sana A, Khadija S, Shazadi R, Zafar W, Rasool K, Fazal A. Prevalence of metabolic syndrome in polycystic ovarian syndrome. Pak Biomed J. 2022;5(2):7-9. doi:10.54393/pbmj.v5i2.163

3. Hamza S, Shawar D, Gul S, Haaris A. Impact of polycystic ovary syndrome (PCOS) on female fertility and metabolic health. Pak J Med Health Sci. 2023;17(11):390. doi:10.53350/pjmhs20231711390

4. Ashraf R, Bibi R, Saleem F, Khalid Y, Akhtar N, Khan S. Association of insulin resistance, lipid profile, hormonal imbalance, and metabolic parameters in women with PCOS receiving metformin therapy. Pak J Med Health Sci. 2023;17(6):604. doi:10.53350/pjmhs2023176604

5. Luqman MS, Zeba A, Tanveer N, Kareem S. Prevalence of PCOS and its association with metabolic syndrome in reproductive-aged women. Dev Med Life Sci J. 2024;2(5):131. doi:10.69750/dmls.02.05.0131

6. Parker J, Briden L, Gersh F. Recognizing the role of insulin resistance in polycystic ovary syndrome: a paradigm shift to an insulin-centric model. J Clin Med. 2025;14(12):4021. doi:10.3390/jcm14124021

7. Singh S, Pal N, Shubham S, Sarma DK, Verma V, Marotta F, et al. Polycystic ovary syndrome: etiology, current management, and future therapeutics. Clin Chem. 2023;69(7):695-710.

8. Zhao H, Zhang J, Cheng X, Nie X, He B. Insulin resistance in polycystic ovary syndrome across various tissues: an updated review of pathogenesis, evaluation, and treatment. J Ovarian Res. 2023;16(1):9. doi:10.1186/s13048-022-01091-0

9. Taha WA, Al-Mahdawi FA, Al-Ani HM. The effect of polycystic ovary syndrome on physiological indicators including glucose and liver enzymes. Curr Issues Pharm Med Sci. 2024.

10. Stevchevska A, Milenkovic T. Effect of insulin sensitizers on glycemic and lipid profile in PCOS patients. Pril. 2025;46(3):51-62. doi:10.2478/prilozi-2025-0022

11. Kalsekar AS, Abdelrahim DN, Faris MA. Effects of calorie restriction and intermittent fasting on glucose, lipids and inflammatory markers in PCOS. Front Nutr. 2024;11:1362226. doi:10.3389/fnut.2024.1362226

12. Prosperi S, Murru FM, Del Giudice F, et al. Insulin resistance, metabolic syndrome and polycystic ovary syndrome: systematic review. Front Endocrinol. 2025;16:69716. doi:10.3389/fendo.2025.1669716

13. Moghetti P. Insulin resistance and polycystic ovary syndrome. Curr Pharm Des. 2016;22(36):5526-5534. doi:10.2174/1381612822666160425122025

14. Dunaif A. Insulin resistance and polycystic ovary syndrome: mechanism and implications for pathogenesis. Endocr Rev. 1997;18(6):774-800. doi:10.1210/edrv.18.6.0318

15. Legro RS, Castracane VD, Kauffman RP. Detecting insulin resistance in polycystic ovary syndrome: purposes and pitfalls. Obstet Gynecol Surv. 2004;59(2):141-154. doi:10.1097/01.ogx.0000112923.02230.ac

16. Wild RA, Painter PC, Coulson PB, Carruth KB, Ranney GB. Lipoprotein lipid concentrations and cardiovascular risk in women with polycystic ovary syndrome. J Clin Endocrinol Metab. 1985;61(5):946-951. doi:10.1210/jcem-61-5-946

17. Diamanti-Kandarakis E, Dunaif A. Insulin resistance and polycystic ovary syndrome revisited: an update on mechanisms and implications. Endocr Rev. 2012;33(6):981-1030. doi:10.1210/er.2011-1034

18. Haider S, Ayyaz M, Ahuja N, et al. Insulin resistance in patients with polycystic ovary syndrome. Pak J Med Health Sci. 2023;17(10):157-159. doi:10.53350/pjmhs20231710157

19. Kim MJ, Lim NK, Choi YM, Kim JJ, Hwang KR, Chae SJ, et al. Prevalence of metabolic syndrome is higher among non-obese PCOS women with hyperandrogenism and menstrual irregularity in Korea. PLoS One. 2014;9(6):e99252. doi:10.1371/journal.pone.0099252

20. Diamanti-Kandarakis E, Kouli CR, Bergiele AT, Filandra FA, Tsianateli TC, Spina GG, et al. A survey of the polycystic ovary syndrome in the Greek island of Lesbos: hormonal and metabolic profile. J Clin Endocrinol Metab. 1999;84(11):4006-4011. doi:10.1210/jcem.84.11.6148

21. Ehrmann DA. Polycystic ovary syndrome. N Engl J Med. 2005;352(12):1223-1236. doi:10.1056/NEJMra041536