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ORIGINAL ARTICLE

Metabolic and Cardiovascular Risks in Women with Polycystic Ovary Syndrome: Focus on Type 2 Diabetes, MASLD, and Cardiovascular Disease

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ABSTRACT

Background: Polycystic ovary syndrome (PCOS) is a common endocrine disorder in women of reproductive age, associated not only with reproductive dysfunction but also with a significantly increased risk of metabolic complications.

Objective: This study aims to assess the prevalence and risk predictors of these comorbidities among women with PCOS, with emphasis on phenotypic variation.

Methods: This cross-sectional observational study was conducted at Shalamar institute of health sciences Lahore during march 2022 to march 2023. A total of 455 women with PCOS, aged between 18 and 45 years, were enrolled using consecutive sampling technique. All participants underwent a thorough clinical evaluation that included documentation of medical history, physical examination, and anthropometric measurements. Body mass index (BMI) was calculated from measured height and weight.

Results: Among 455 participants, the prevalence of T2DM was 22.4%, impaired glucose tolerance was 14.9%, MASLD was present in 31.4%, and 18.9% showed elevated CIMT. The classic PCOS phenotype (hyperandrogenism and anovulation) showed significantly higher rates of all metabolic complications. Independent predictors of T2DM included BMI ≥30 kg/m² (OR 2.31, p<0.001), HOMA-IR ≥2.5 (OR 1.84, p=0.015), and low HDL-C (OR 1.47, p=0.042). MASLD was independently associated with elevated ALT and obesity. Cardiovascular risk was strongly linked to central obesity, high LDL-C, and elevated hs-CRP.

Conclusions: It is concluded that women with PCOS, particularly those with the classic phenotype, are at high risk for T2DM, MASLD, and early CVD. These findings support the need for early metabolic screening, phenotype-based risk stratification, and multidisciplinary management to mitigate long-term complications.

Keywords: POCS, Type 2 Diabetes Mellitus, Cardiovascular Disease, MASLD

INTRODUCTION

Polycystic ovary syndrome (PCOS) is one of the most prevalent endocrine disorders in women of reproductive age, with an estimated global prevalence of 6 to 15 percent, depending on the diagnostic criteria used. PCOS prevails known for its fertility problems that affect ovulation and menstrual schedules but specialists now see it as a body-wide metabolic condition causing future health complications[1]. Women who have PCOS face a notably increased possibility of developing type 2 diabetes mellitus (T2DM), metabolic dysfunction-associated steatotic liver disease (MASLD) previously known as non-alcoholic fatty liver disease (NAFLD) together with cardiovascular disease (CVD)[2]. The combination of these comorbidities severely reduces patients' life quality and directly leads to increased long-term death risks and serious health complications[3]. PCOS as a metabolic disorder depends mostly on insulin resistance because this condition functions as a fundamental pathological process in most cases. People with PCOS may separately develop insulin resistance from obesity while their elevated insulin levels increase ovarian androgen production[4]. The result becomes a destructive circle that affects patients both hormonally and metabolically. Research indicates that insulin resistance exists in more than 70 percent of PCOS patients leading to increased susceptibility of glucose tolerance failure and eventual T2DM development. Early metabolic screening becomes necessary for PCOS patients since the age at which they experience these risks occurs sooner than their female counterparts[5]. The development of hepatic steatosis stands as another important health issue that affects women diagnosed with PCOS. Researchers have recently classified MASLD as the liver manifestation of metabolic syndrome while describing it as a redefined metabolic liver disease[6]. The risk for MASLD among women with PCOS exceeds two to three times normal when they match for age and body mass index. Females with PCOS experience the development of hepatic fat accumulation through the combination of PCOS-specific hormone and inflammatory pathways that include elevated androgen levels and dysfunctional adipokines along with mitochondrial abnormalities[7]. MASLD significantly raises the possibility of liver fibrosis and cirrhosis development and functions as an independent risk factor for cardiovascular disease. The condition that causes the most global deaths is cardiovascular disease while women with PCOS experience this condition at higher rates[8]. Experts who study epidemics have shown PCOS affects women by raising their risks of hypertension and both dyslipidemia and endothelial dysfunction along with thicker carotid intima-media which shows possible early-stage atherosclerosis[9]. Cardiovascular risks existing at elevated levels among women with PCOS are consistently revealed through various surrogate measures despite limited data about specific cardiovascular events because most cohorts include young participants[10]. The elevated risk of heart disease develops from the combination of central body fat distribution together with abnormal LDL and low HDL cholesterol levels and systemic inflammation. PCOS presents with complex characteristics because it combines multiple systemic conditions that lead to cardiovascular pathology alongside metabolic syndrome. Practicing clinicians usually underestimate these risks because they primarily concentrate on reproductive symptoms in their evaluations[11]. Most women with PCOS receive no diagnosis at all or get diagnosed after their metabolic issues become established. Healthcare providers need to implement an integrated PCOS treatment model that unites hormonal control with metabolic healthcare[12].

Objective: This study aims to assess the prevalence and risk predictors of these comorbidities among women with PCOS, with emphasis on phenotypic variation.

METHODOLOGY

This cross-sectional observational study was conducted at Shalamar institute of health sciences Lahore during March 2022 to March 2023. A total of 455 women with PCOS, aged between 18

and 45 years, were enrolled using consecutive sampling technique.

Inclusion Criteria

- Female participants aged 18–45 years
- Diagnosis of PCOS based on the Rotterdam Criteria (2003), requiring at least two of the following:

1. Oligo- or anovulation
2. Clinical and/or biochemical signs of hyperandrogenism
3. Polycystic ovarian morphology on ultrasound

- Willingness to participate and provide informed consent

Exclusion Criteria

- Diagnosed with other endocrine disorders that may mimic PCOS (e.g., congenital adrenal hyperplasia, Cushing's syndrome, androgen-secreting tumors)
- Known hepatic diseases such as viral hepatitis, autoimmune hepatitis, or alcoholic liver disease
- Alcohol intake exceeding 20 g/day
- Known cardiovascular disease, diabetes mellitus, or liver cirrhosis under active treatment
- Current pregnancy or lactation
- Use of hormonal medications (e.g., oral contraceptives, anti-androgens, insulin sensitizers) within the past 3 months

Data Collection: All participants underwent a thorough clinical evaluation that included documentation of medical history, physical examination, and anthropometric measurements. Body mass index (BMI) was calculated from measured height and weight. Waist and hip circumferences were recorded, and the waist-to-hip ratio (WHR) was calculated. Blood pressure was measured using an automated sphygmomanometer after five minutes of rest, and the average of two readings was recorded. Venous blood samples were collected after an overnight fast of at least 10 hours. Laboratory investigations included fasting plasma glucose, a 2-hour oral glucose tolerance test (OGTT), glycated hemoglobin (HbA1c), fasting insulin, and lipid profile (total cholesterol, HDL-C, LDL-C, triglycerides). Liver function tests including alanine aminotransferase (ALT), aspartate aminotransferase (AST), and gamma-glutamyl transferase (GGT) were also performed. Hormonal assessments included total serum testosterone and sex hormone-binding globulin (SHBG). High-sensitivity C-reactive protein (hs-CRP) was measured as a marker of systemic inflammation. Insulin resistance was assessed using the homeostasis model assessment for insulin resistance (HOMA-IR), calculated using the formula: HOMA-IR = (fasting insulin [μU/mL] × fasting glucose [mg/dL])/405.

Diagnostic Criteria: Type 2 diabetes mellitus was diagnosed according to the American Diabetes Association (ADA) 2023 criteria, which include fasting plasma glucose ≥126 mg/dL, 2-hour OGTT ≥200 mg/dL, or HbA1c ≥6.5%. The diagnosis of MASLD was based on ultrasonographic evidence of hepatic steatosis, in the absence of secondary causes such as significant alcohol intake or viral hepatitis. In patients with elevated ALT or fatty liver index >60, further assessment of liver stiffness and fibrosis was performed using transient elastography (FibroScan®). Cardiovascular risk assessment included measurement of carotid intima-media thickness (CIMT) via B-mode ultrasound, resting electrocardiogram (ECG), and echocardiography when clinically indicated.

Statistical Analysis: Data were analyzed using SPSS v26. Continuous variables were reported as mean ± standard deviation, and categorical variables as frequencies and percentages. Group comparisons between PCOS patients with and without T2DM, MASLD, or elevated cardiovascular risk were performed using the independent t-test. A p-value < 0.05 was considered statistically significant.

RESULTS

Data were collected from 455 patients, with a mean age of 28.7 ± 6.1 years and an average BMI of 28.3 ± 5.6 kg/m². A majority were either overweight or obese (63.1%), and 58.9% had central obesity as defined by waist-to-hip ratio >0.85. Clinical or biochemical hyperandrogenism was observed in 67.5% of participants, while menstrual irregularities were reported in 81.3%, and polycystic ovarian morphology was identified in 72.6% on ultrasound.

Table 1: Baseline Characteristics of Study Participants (N = 455)

Variable	Mean ± SD / %
Age (years)	28.7 ± 6.1
Body Mass Index (BMI, kg/m²)	28.3 ± 5.6
Overweight or Obese (BMI ≥ 25)	63.1%
Central Obesity (WHR > 0.85)	58.9%
Hyperandrogenism (Clinical/Biochemical)	67.5%
Menstrual Irregularity	81.3%
Polycystic Ovarian Morphology	72.6%

22.4% were diagnosed with type 2 diabetes mellitus, and 14.9% had impaired glucose tolerance, while insulin resistance (HOMA-IR ≥2.5) was present in 64.6% of the cohort. MASLD was detected via ultrasound in 31.4% of participants, and 25.9% of those showed signs of hepatic fibrosis on FibroScan®. Indicators of cardiovascular risk included elevated CIMT in 18.9%, an ASCVD risk score >5% in 16%, and elevated hs-CRP in 22.9%.

Table 2: Prevalence of Metabolic Comorbidities in PCOS Patients

Condition	n (%)
Type 2 Diabetes Mellitus	102 (22.4%)
Impaired Glucose Tolerance	68 (14.9%)
Insulin Resistance (HOMA-IR ≥ 2.5)	294 (64.6%)
MASLD (Steatosis by Ultrasound)	143 (31.4%)
MASLD with Fibrosis (via FibroScan®)	37 (25.9% of MASLD)
Elevated CIMT (≥ 0.7 mm)	86 (18.9%)
ASCVD 10-Year Risk Score >5%	73 (16.0%)
hs-CRP >3 mg/L	104 (22.9%)
ECG Abnormalities	52 (11.4%)

Obesity (BMI ≥30 kg/m²), insulin resistance (HOMA-IR ≥2.5), and low HDL-C independently increased the odds of type 2 diabetes, with the highest risk seen in obese participants (OR: 2.31, p<0.001). Elevated ALT was significantly associated with MASLD (OR: 1.91, p=0.011). For cardiovascular risk, LDL-C >130 mg/dL, hs-CRP >3 mg/L, and central obesity (WHR >0.85) were strong predictors, with central obesity showing the highest odds (OR: 2.43, p<0.001).

Table 3: Multivariate Logistic Regression for Predictors of T2DM, MASLD, and Cardiovascular Risk

Predictor	Associated Condition	Odds Ratio (95% CI)	p-value
BMI ≥30 kg/m²	T2DM	2.31 (1.52–3.52)	<0.001
HOMA-IR ≥2.5	T2DM	1.84 (1.12–3.03)	0.015
Low HDL-C (<50 mg/dL)	T2DM	1.47 (1.01–2.19)	0.042
Elevated ALT	MASLD	1.91 (1.15–3.16)	0.011
LDL-C >130 mg/dL	CVD Risk	1.76 (1.10–2.82)	0.018
hs-CRP >3 mg/L	CVD Risk	2.08 (1.31–3.31)	<0.001
Central Obesity (WHR >0.85)	CVD Risk	2.43 (1.56–3.80)	<0.001

Women with the classic phenotype (hyperandrogenism and anovulation) showed the highest rates of type 2 diabetes (28.1%), MASLD (38.6%), and elevated cardiovascular risk (22.4%). In contrast, those with ovulatory PCOS subtypes had notably lower rates of all three conditions.

BMI was positively correlated with HOMA-IR (r = 0.62), ALT (r = 0.45), CIMT (r = 0.33), and hs-CRP (r = 0.54), while negatively correlated with HDL-C (r = –0.48). Similarly, HOMA-IR showed strong negative correlation with HDL-C (r = –0.51) and positive correlations with ALT (r = 0.39) and hs-CRP (r = 0.41).

Table 4: Distribution of Metabolic Comorbidities Across PCOS Phenotypes

PCOS Phenotype	T2DM (%)	MASLD (%)	CVD Risk >5% (%)
Classic (HA + Anovulation)	28.1%	38.6%	22.4%
Ovulatory + Hyperandrogenism	19.7%	26.5%	14.2%
Ovulatory + Polycystic Ovaries	10.2%	17.4%	9.3%
Normoandrogenic (Anovulation + PCO)	12.6%	22.1%	11.6%
p-value	<0.01	<0.01	0.02

Table 5: Correlation Matrix of Metabolic Parameters

Parameter	BMI	HOMA-IR	HDL-C	ALT	CIMT	hs-CRP
BMI	1.00	0.62**	-0.48**	0.45**	0.33**	0.54**
HOMA-IR		1.00	-0.51**	0.39**	0.27**	0.41**
HDL-C			1.00	-0.33**	-0.29**	-0.36**
ALT				1.00	0.35**	0.28**
CIMT					1.00	0.32**
hs-CRP						1.00

$p < 0.01$ for all significant correlations

DISCUSSION

The present study provides robust evidence highlighting the substantial metabolic burden experienced by women with polycystic ovary syndrome (PCOS), with a significant proportion exhibiting early markers or established forms of type 2 diabetes mellitus (T2DM), metabolic dysfunction-associated steatotic liver disease (MASLD), and elevated cardiovascular risk. This research found that 22.4% of women with PCOS had T2DM while an additional 14.9% showed signs of impaired glucose tolerance. These numbers match previously documented findings that varied between 10% and 30% depending on diagnostic criteria and ethnic background of study participants. The presence of impaired glucose tolerance represented an additional 14.9% of participants in the study but they were at risk of developing full-blown diabetes unless they received proper treatment[13]. The high number of subjects with insulin resistance measured by HOMA-IR proves that insulin dysregulation drives both the development of PCOS and its accompanying metabolic conditions. Previous research has confirmed the existence of insulin resistance in women with PCOS both at normal weight and at obesity levels but at higher degrees in obesity cases[14]. A substantial portion of the studied population (31.4%) was diagnosed with MASLD and twenty-five percent of these patients already presented with early hepatic fibrosis. Research about hepatic steatosis reveals that PCOS as an independent condition functions as a robust individual risk factor regardless of BMI because it shares pathology between insulin resistance and androgen excess and low-grade inflammatory pathways[15]. The identification of non-alcoholic steatohepatitis during its early stages in women with PCOS presents a clinical necessity because this disease progresses to cirrhosis and hepatocellular carcinoma[16]. The research identified early cardiovascular disease warning signs in many participants who had PCOS despite cardiovascular disease being the main cause of female deaths according to study findings. Elemental atherosclerosis evident through carotid intima-media thickness (CIMT) analysis existed in 18.9% of participants alongside 16% having estimated 10-year ASCVD risks reaching over 5%. PCOS patients exhibit pro-atherogenic and pro-inflammatory conditions that link to central obesity and dyslipidemia (particularly low HDL-C and high LDL-C levels) and systemic inflammation (high hs-CRP levels)[17]. The variance in metabolic risk factors depends on which phenotype of PCOS patients participate in the analysis. Individuals with the classic phenotype including hyperandrogenism combined with anovulation demonstrated the greatest prevalence of T2DM at 28.1% along with MASLD at 38.6% and cardiovascular risk at 22.4%. For the prediction of T2DM and MASLD, the following characteristics proved to be distinct independent factors: BMI at or above 30 kg/m² together with insulin resistance levels exceeding HOMA-IR ≥2.5 and low HDL-C concentrations and increased ALT enzyme levels[18]. Data obtained in this study supports the established relationship between metabolic syndrome elements for developing PCOS-related medical conditions[19]. Measures of hs-CRP and central obesity revealed their status as important risk factors for heart problems emphasizing the need to check inflammatory markers when evaluating PCOS patients. The identified clinical applications of our study results will help guide future medical practices. Treatment of PCOS requires treating it as a chronic disorder affecting multiple body systems that need specialist medical attention[20]. Individuals with PCOS benefit most from combined expert care involving endocrinologists' gynecologists and hepatologists along with cardiologists, particularly among women presenting classic traits and those with high BMI. The basic management method remains lifestyle changes although high-risk patients will benefit from using medications like insulin sensitizers plus lipid-lowering agents along with anti-inflammatory treatments. This study has some limitations. The study design prevents researchers from establishing cause-effect relationships. Hospital-based participants in the study sample might not match the composition among the wider general population demographic.

CONCLUSION

It is concluded that women living with polycystic ovary syndrome (PCOS) are at significantly increased risk of developing type 2 diabetes mellitus (T2DM), metabolic dysfunction-associated steatotic liver disease (MASLD), and early cardiovascular disease (CVD), irrespective of age or body mass index. The findings of this study highlight the systemic nature of PCOS, extending well beyond reproductive health into critical metabolic domains that can lead to long-term morbidity. The high prevalence of insulin resistance, hepatic steatosis, and subclinical atherosclerosis observed in this cohort emphasizes the importance of early and comprehensive metabolic evaluation in all women diagnosed with PCOS, particularly those exhibiting the classic phenotype. Phenotype-based risk stratification revealed that individuals with hyperandrogenism and anovulation carry the greatest burden of metabolic complications and may benefit from more intensive screening and preventive strategies.

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