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THE RELATIONSHIP BETWEEN POLYCYSTIC OVARY SYNDROME AND CARDIOVASCULAR RISK FACTORS

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Abstract

Background: *Polycystic ovary syndrome (PCOS) is a common endocrine condition that affects women of reproductive age. It is characterized by a hormonal imbalance that produces a range of symptoms, including irregular ovulation and overproduction of androgens, many of which are associated with risk factors of cardiovascular disease (CVD).*

Objective: *To evaluate the relationship between polycystic ovary syndrome and cardiovascular risk factors.*

Materials and Methods: *A cross-sectional study was conducted at Khyber Teaching Hospital (KTH) in Peshawar, Pakistan, from April 2024 to March 2025. The study included 210 women of reproductive age (18-45 years) who were selected by a simple random sampling method from the gynecology and endocrinology outpatient departments. Major factors, such as blood pressure, body mass index (BMI), biochemical tests, hormonal profiles, and lifestyle influences of the patients, were evaluated. The data collected was analyzed by SPSS version 25 using descriptive statistics, chi-square tests, and logistic regression to assess the association between PCOS and CVD risk factors. The statistical significance level was set at $p < 0.05$.*

Results: *Of the 210 patients from the cross-sectional study, the following were observed: hypertension was present in 47.1% of patients, insulin resistance in 68.1% of patients, and dyslipidemia in 62.4% of patients. The logistic regression analysis determined that PCOS patients had a 2.8-fold higher risk of developing hypertension ($p < 0.01$) and a 3.5-fold higher risk of developing insulin resistance ($p < 0.001$).*

Conclusion: *The study finds a significant association between PCOS and CVD risk factors that ultimately increases the risk of developing CVD in patients with PCOS. To improve long-term outcomes and reduce CVD risk, early detection, lifestyle modification, and interventional therapies are recommended, alongside routine cardiovascular assessments. Subsequently, further research needs to be conducted on tailored interventional therapies to lower mortality and morbidity from CVD in patients with PCOS.*

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INTRODUCTION

Polycystic ovary syndrome (PCOS) is the most common endocrinopathy and leading cause of anovulatory infertility in women during their reproductive ages, with a prevalence between 6% and 13% [1]. Classical features of PCOS include hyperandrogenism, ovulatory dysfunction, and polycystic ovaries [2]. Although several genetic and environmental factors contribute to PCOS, the exact etiology remains unclear. This syndrome of hormonal imbalance is characterized by a wide range of signs and symptoms related to ovarian dysfunctions, including hirsutism, acne, androgenic alopecia, obesity, insulin resistance, infertility, and pregnancy complications [3]. Women with PCOS, especially those who develop insulin resistance, also suffer from higher rates of metabolic dysfunction and cardiovascular diseases (CVD) [4]. Due to its broad spectrum of symptoms, there is still much confusion around the diagnosis of PCOS, and approximately 70% of women with PCOS remain undiagnosed [1].

There have been numerous diagnostic criteria throughout the years, but the most widely accepted are the 2003 Rotterdam criteria. It defines PCOS based on the presence of at least two of the following three criteria: oligo- or chronic anovulation, hyperandrogenism (clinical and/or biological), and polycystic ovaries on ultrasound [5]. It is a diagnosis of exclusion, meaning other endocrine and gynecological disorders must be ruled out before a diagnosis can be made [5,6]. The overlapping of these criteria creates four different phenotypes of PCOS: Phenotype A (classic PCOS: oligo- or chronic anovulation, hyperandrogenism, and polycystic ovaries), Phenotype B (hyperandrogenic anovulation PCOS: oligo- or chronic anovulation and hyperandrogenism), Phenotype C (ovulatory PCOS: hyperandrogenism and polycystic ovaries), and Phenotype D (non-hyperandrogenic PCOS: oligo- or chronic anovulation and polycystic ovaries). The classical type of PCOS comprises Phenotypes A and B, and the non-classical type of PCOS comprises Phenotypes C and D. The genetic architecture of PCOS remains similar across all diagnostic criteria despite variations in symptoms [7]. Hyperandrogenism phenotypes are more closely associated with CVD risk. Nevertheless, there is an increased incidence of CVD risk factors among all women with PCOS [8].

The pathophysiological process of PCOS commonly involves insulin resistance (IR) and hyperandrogenemia. These two features of PCOS contribute to several cardiometabolic abnormalities, including obesity, diabetes, hypertension, dyslipidemia, and metabolic syndrome [9]. IR varies among the PCOS phenotypes and is thought to play a role in the pathogenesis of PCOS [10]. IR enhances oxidative stress and promotes vascular endothelial injury, atherosclerosis, and hypertension, thereby further increasing the risk of CVD in women, such as heart attacks, coronary artery disease, and stroke [11]. IR and hyperinsulinemia increase aldosterone secretion, decrease prostacyclin synthesis, and increase vascular smooth muscle cell (VSMC) proliferation, all of which promote hypertension and vascular damage [9,11]. Changes in intrinsic risk mechanisms, including lower levels of high-density lipoprotein cholesterol (HDL-C) and higher levels of low-density lipoprotein cholesterol (LDL-C), triglycerides, C-reactive protein (CRP), and apolipoprotein B/A1 ratio, are associated with worsening cardiometabolic profiles and elevated risk for atherosclerosis and cardiovascular events [12].

PCOS is a systemic disease that affects multiple aspects of a woman's health, with long-term consequences that go beyond the reproductive system. It extends to several cardiometabolic abnormalities that contribute to increase in occurrences of CVD events [13]. Women with PCOS have a higher prevalence of CVD precursors, such as coronary artery calcium (CAC), carotid intima-media thickness (CIMT), C-reactive protein (CRP), and endothelial dysfunction [14]. Some studies have shown that PCOS women with coronary artery disease (CAD) have more extensive coronary lesion compared to patients without PCOS [15]. More than 270 million women with CVD and 9 million CVD-related deaths were reported in 2019. CVD continues to be a global burden and should not be overlooked [16]. Understanding the underlying mechanisms as well as the correlation of PCOS and CVD risk factors will not only enhance preventative strategies but lessen global health challenges.

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Materials and Methods

We conducted a cross-sectional study at Khyber Teaching Hospital (KTH) in Peshawar, Pakistan, to evaluate the relationship between polycystic ovary syndrome and cardiovascular disease risk factors. 210 women between the ages of 18 and 45 years were selected by a simple random sampling method from outpatient settings. These patients had a history of PCOS and were previously diagnosed according to Rotterdam criteria. Women who had undergone hysterectomy and those who were menopausal or pregnant were excluded from the study. The cardiovascular risk factors of these patients were collected through clinical examinations, anthropometric measures, biochemical assessments, and standardized questionnaires. Each patient was given comprehensive questionnaires to complete concerning medical histories, reproductive histories, and lifestyle choices. Statistical analysis of the data collected was done using IBM SPSS version 25 (IBM Corp.), and a p-value < 0.05 was considered statistically significant. Descriptive statistics were used to evaluate characteristics of the participants, and chi-square tests were performed to assess the correlation between PCOS and CVD risk factors.

Results

A total of 210 women participated in the study, and the average age of these women with PCOS was 30.5 ± 5.8 years. The clinical and demographic profiles of the patients are shown in Table 1. Weight abnormalities were common among the women; the majority (72.3%) of participants had a BMI of 25 kg/m² or more, and 58.6% were centrally obese with an elevated waist-to-hip ratio (WHR > 0.85). Approximately 35.7% of the study group led a sedentary lifestyle, and 42.8% had a family history of cardiovascular diseases (CVD), as shown in Table 1.

Table 1. Clinical and Demographic Features of PCOS Patients (n = 210)

Characteristic	Mean ± SD or n (%)
Age (years)	30.5 ± 5.8
BMI ≥ 25 kg/m²	152 (72.3%)
Central Obesity (WHR > 0.85)	123 (58.6%)
Family History of CVD	90 (42.8%)
Sedentary Lifestyle	75 (35.7%)

Abbreviations: PCOS, polycystic ovary syndrome; SD, standard deviation; BMI, Body Mass Index; WHR, waist-hip ratio; CVD, cardiovascular disease.

The following characteristics were observed in patients with polycystic ovary syndrome: Hypertension was seen in 47.1% of patients, with 26.2% having stage 1 hypertension and 20.9% having stage 2 hypertension, as shown in Table 2. Furthermore, 62.4% had dyslipidemia, 36.2% and 14.3% of patients had pre-diabetes and diabetes, respectively, 68.1% had insulin resistance, and 38.7% had high homocysteine as shown in Table 2.

Table 2. Cardiovascular Risk Factor Prevalence in PCOS Patients

Risk Factor	n (%)
Insulin Resistance (HOMA-IR > 2.5)	143 (68.1%)
Pre-diabetes (Fasting glucose 100–125 mg/dL)	76 (36.2%)
Diabetes (Fasting glucose ≥ 126 mg/dL)	30 (14.3%)
Dyslipidemia (High TG, LDL, Low HDL)	131 (62.4%)
Hypertension Stage 1 Stage 2	99 (47.1%) 55 (26.2%) 44 (20.9%)
Elevated CRP (>3 mg/L)	95 (45.2%)
High Homocysteine Levels	81 (38.7%)
Elevated Testosterone (>0.7 ng/mL)	146 (69.5%)

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Abbreviations: PCOS, polycystic ovary syndrome; HOMA-IR, Homeostatic Model Assessment of Insulin Resistance; TG, triglycerides; LDL, low-density lipoprotein; HDL, high-density lipoprotein; CRP, C-reactive protein.

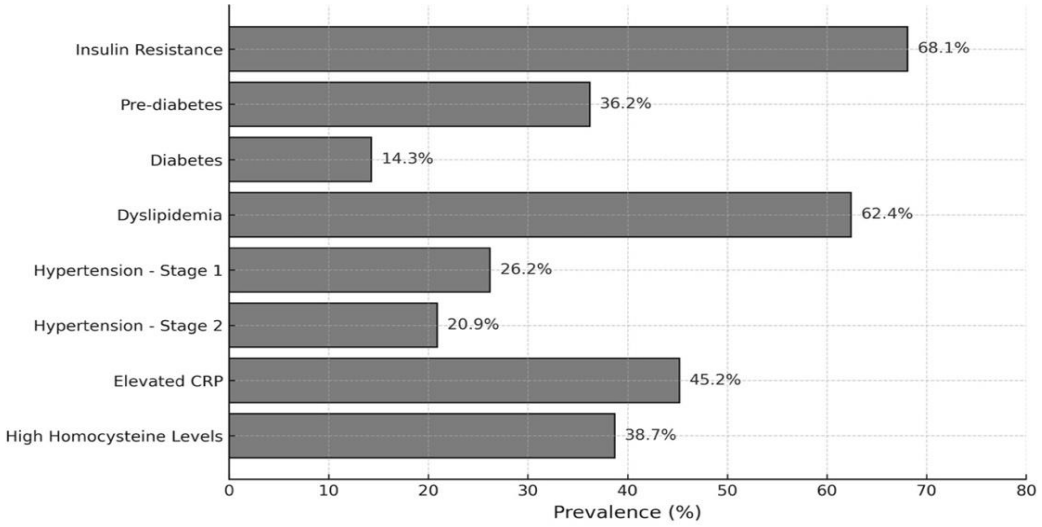

Figure 1. Cardiovascular Risk Factor Prevalence in PCOS Patients.

The study found a total of 62.4% of the patients had dyslipidemia and 68.1% of patients having insulin resistance. Additionally, inflammatory markers increased with CRP levels >3 mg/L in 45.2% of patients, as shown in Table 3.

Table 3. Associations Between PCOS and Cardiovascular Risk Factors

Variable	PCOS Patients (n=210)	p-value
Hypertension	99 (47.1%)	0.002
Dyslipidemia	131 (62.4%)	0.001
Insulin Resistance	143 (68.1%)	<0.001
Elevated CRP	95 (45.2%)	0.007

Abbreviations: PCOS, polycystic ovary syndrome; CRP, C-reactive protein.

The effect of lifestyle variables on cardiovascular risk is shown in Table 4. Sedentary women were twice as likely to have hypertension and insulin resistance (p = 0.003). Obese patients with PCOS were 4.1 times more likely to develop dyslipidemia than normal-weight patients (p < 0.001).

Table 4. Effects of Lifestyle Factors on PCOS Patients' Cardiovascular Risk

Factors	Odds Ratio (95% CI)	p-value
Sedentary Lifestyle & Hypertension	2.1 (1.3–3.5)	0.003
Obesity & Dyslipidemia	4.1 (2.5–6.7)	<0.001
Smoking & Low HDL-C	1.9 (1.1–3.2)	0.014

Abbreviations: PCOS, polycystic ovary syndrome; HDL, high-density lipoprotein.

Discussion

The findings of this cross-sectional study demonstrated evidence of an increased cardiometabolic risk profile in women with PCOS, suggesting an increased risk for major CVD events. Common CVDs found in patients with PCOS include heart attacks, coronary artery disease, and stroke [17]. Women of reproductive age, 18-45 years, who were diagnosed with PCOS showed a higher prevalence of CVD risk factors such as insulin

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resistance, dyslipidemia, diabetes, hypertension, and chronic inflammation. Our study highlighted the pathophysiological contributions of these risks to CVD, as well as the overlapping mechanisms that are associated with PCOS and CVD.

Results of our study showed insulin resistance was present in 68.1% of PCOS patients. Insulin resistance and corresponding hyperinsulinemia play a central role in the pathogenesis leading to glucose intolerance, obesity, hypertension, and hypertriglyceridemia, all factors that further increase CVD risk [11]. The study also found that 62.4% of patients presented with dyslipidemia. Abnormalities in lipids are from the combined actions of hyperinsulinemia and hyperandrogenism, which contribute to a poor atherosclerotic profile. The atherosclerotic profile can also be worsened by obesity, as shown in the data analysis [9,18]. 47.1% of patients with PCOS had hypertension, causing further vascular endothelial damage. The prevalence of hypertension in PCOS patients is likely attributed to activation of the renin-angiotensin system and vascular smooth muscle cell (VSMC) proliferation, in addition to other metabolic disturbances [19]. Through a logistic regression analysis, we found that women with PCOS had a 2.8-fold increased risk of developing hypertension and a 3.5-fold increased risk of developing insulin resistance.

The study also found that 45.2% of PCOS patients showed elevated inflammatory markers, particularly C-reactive protein (CRP). Long-term hyperinsulinemia and obesity associated with PCOS can cause persistent low-grade systemic inflammation that is thought to be the primary cause of inflammatory markers. In response to the chronic state of inflammation, proinflammatory markers are always on the rise in PCOS patients, as they play a key role in endothelial dysfunction and atheromatous plaque formation [20,21]. Serum levels of highly sensitive C-reactive protein (hsCRP) are higher in women with PCOS and are recognized as independent predictors of CVD events [21].

Given the correlation between PCOS and increased risk of CVD, women who are diagnosed with PCOS are recommended to screen for CVD risk factors; this includes getting their lipid profile and having their blood pressure measured annually [22]. Patients should also implement lifestyle modifications, such as a healthy diet, increased physical activity, and weight management, that specifically decrease CVD risks [23]. However, additional approaches, such as exploring the use of glucagon-like peptide-1 (GLP-1) agonists and sodium-glucose co-transporter-2 (SGLT2) inhibitors, have been proven to be effective in reducing weight and CDV risks [24]. The results of our study are in line with evidence from previous research that showed an increased risk of CVD risk factors in women with PCOS. The pathogenesis of PCOS gives rise to CVD risk factors, potentially increasing the risk of CVD in women with PCOS. Whether these are independent risk factors of CVD needs to be further studied.

Conclusion

The study concludes there is a strong association between polycystic ovarian syndrome and increased risk factors of cardiovascular disease. There is a lack of consensus on whether the increased prevalence of CVD risk factors translates to increased cardiac events in women with PCOS. However, it is important to note that CVD risk factors associated with PCOS do increase the risk of CVD in these patients. Given these findings, early screening and management are essential to mitigate CVD risks and prevent long-term consequences of PCOS. Importance should be placed on lifestyle interventions such as weight management, nutrition, and physical activity. Additionally, pharmaceutical therapy for cardiometabolic abnormalities, such as dyslipidemia, insulin resistance, and hypertension, can help reduce CVD risk in high-risk patients. While PCOS is the most common endocrine disorder in women, CVD remains the leading cause of death among women. 70% of PCOS cases remain undiagnosed, underscoring the significance of early interventions in reducing morbidity and mortality rates from PCOS and related CVD. Raising awareness of the cardiovascular risks associated with PCOS is necessary from a public health perspective. To improve long-term results, polycystic ovary syndrome care should incorporate routine cardiovascular assessments and tailored interventions to enhance the general outcome and well-being of women with PCOS.

Frontier in Medical & Health Research

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