

Comparative study of metabolic syndrome and cardiovascular risk in women with and without polycystic ovary syndrome

 Nurgül Ulusoy¹,  Mehmet Ağar²,  Halime Çalı Öztürk³

¹Obstetrics and Gynecology Specialist, Private Gynecology and Obstetric Clinic, İstanbul, Türkiye

²Obstetrics and Gynecology Specialist, Private Clinic, Şanlıurfa, Türkiye

³Department of Obstetrics and Gynecology, Faculty of Medicine, Bezmialem University, İstanbul, Türkiye

Cite this article: Ulusoy N, Ağar M, Çalı Öztürk H. Comparative study of metabolic syndrome and cardiovascular risk in women with and without polycystic ovary syndrome. *J Controv Obstetr Gynecol Ped.* 2025;3(3):56-61.

Corresponding Author: Nurgül Ulusoy, nculusoy17@gmail.com

Received: 03/02/2025

Accepted: 20/02/2025

Published: 07/07/2025

ABSTRACT

Aims: Polycystic ovary syndrome (PCOS) is associated with an increased risk of metabolic syndrome (MetS) and cardiovascular diseases (CVD). This study aimed to evaluate the prevalence of MetS and cardiovascular risk factors in women with and without PCOS to better understand the broader implications of the syndrome.

Methods: This comparative cross-sectional study included 400 women, aged 20 to 40 years, who were recruited from an outpatient clinic. Participants were divided into two groups: group I (200 women with PCOS, diagnosed according to the Rotterdam criteria) and group II (200 age-matched controls without PCOS). The data collected included body-mass index (BMI), fasting glucose, lipid profiles, blood pressure, and inflammatory markers (CRP and IL-6). MetS was defined using the NCEP ATP III criteria. Statistical analyses were performed to compare metabolic and cardiovascular markers between groups, with a significance level set at $p < 0.05$.

Results: MetS prevalence was significantly higher in the PCOS group (60%) compared to controls (30%) ($p < 0.01$). Insulin resistance was greater in the PCOS group, with a mean HOMA-IR of 3.2 versus 1.8 in controls ($p < 0.001$), and fasting glucose levels were elevated (110 mg/dl vs. 95 mg/dl, $p < 0.001$). Lipid profiles were more atherogenic in PCOS, with higher triglycerides (150 mg/dl vs. 100 mg/dl, $p < 0.01$), higher LDL cholesterol (130 mg/dl vs. 110 mg/dl, $p < 0.01$), and lower HDL cholesterol (40 mg/dl vs. 50 mg/dl, $p < 0.05$). Blood pressure was also elevated in PCOS (systolic: 135 mmHg vs. 120 mmHg, $p < 0.05$; diastolic: 85 mmHg vs. 75 mmHg, $p < 0.05$). Inflammatory markers were significantly higher in PCOS, including CRP (4.2 mg/L vs. 2.1 mg/L) and IL-6 (6.0 pg/ml vs. 3.0 pg/ml) (both $p < 0.01$).

Conclusion: Metabolic and cardiovascular risk factors are significantly more prevalent in women with PCOS. Early intervention, including management of insulin resistance, dyslipidemia, hypertension, and inflammation, is crucial to reducing cardiovascular morbidity and long-term health risks in this population.

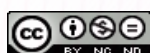
Keywords: Polycystic ovary syndrome, metabolic syndrome, cardiovascular risk, insulin resistance, dyslipidemia

INTRODUCTION

The estimation of worldwide prevalence of polycystic ovary syndrome (PCOS), the predominant endocrine condition encountered among women of reproductive age, reaches 5-10%.¹ PCOS is defined by the presence of elevated androgen levels, irregular ovulation, and the morphological appearance of polycystic ovaries. It presents as a complex and multi-faceted health challenge with aspects going beyond gynecological concerns.² Metabolic syndrome (MetS) and cardiovascular diseases (CVD) are additional long-term morbidities for which women with PCOS have been shown to be at increased risk.³ An association between PCOS and

metabolic and cardiovascular risk factors has been rather well established, though the basic mechanisms underlying that association remain to be fully elucidated. In the face of the high prevalence of PCOS and its relations to metabolic and cardiovascular health risks, there is an urgent need to outline these associations to improve strategies of prevention, diagnosis, and management.

Recognized as a major risk factor for CVD, MetS consists of a group of interrelated conditions, namely insulin resistance, abdominal obesity, elevated blood pressure,



and dyslipidemia.⁴ Women with PCOS seem particularly vulnerable for MetS, as several studies have reported higher MetS prevalence rates in PCOS patients when compared to the general population.^{3,4} Studies have identified that women with PCOS have a two- to four-fold increased risk of MetS, independently of age and body-mass index (BMI).⁵ The association between PCOS and MetS is further complicated by the high prevalence of insulin resistance in PCOS patients. Insulin resistance is present in 50-70% of women with PCOS irrespective of obesity and is felt to play a key role in the development of both MetS and CVD in the PCOS patients.⁶

Besides metabolic disturbances, dyslipidemia, manifested by high triglycerides, low high-density lipoprotein (HDL) cholesterol, and elevated low-density lipoprotein (LDL) cholesterol, is also commonly found among women with PCOS.⁷ All these disturbances in the lipid profile perpetuate the risk of developing CVD by enhancing atherogenic changes which may eventually lead to arterial plaque formation.⁸ Previous studies reported comparable lipid profiles in women with PCOS and specified that the management of disturbed lipid is the most important factor for the reduction of long-term cardiovascular risk in these patients.⁹ Dyslipidemia, despite being well documented in PCOS, often remains poorly addressed in clinical practice due to lack of awareness about the long-term consequences.⁸

Other critical factors for CVD commonly seen in PCOS include hypertension. Studies reported higher blood pressure in PCOS women, suggesting possible chronic sympathetic activation and underlying endothelial dysfunction.¹⁰ Hypertension is an established cause of cardiovascular morbidity, and its association with PCOS would suggest the indication for its management in this population.^{4,10} In addition, there are new indications that PCOS may be associated with a chronic low-grade pro-inflammatory state, as supported indirectly by increased levels of inflammation markers such as C-reactive protein (CRP) and interleukin-6 (IL-6) within women with PCOS.¹¹

The present study, therefore, aims to present the overall comparative analysis of MetS prevalence and cardiovascular risk factors in women both with and without PCOS. In this regard, the investigation encompasses a wide variety of parameters for insulin resistance, lipid profile, blood pressure, and inflammation markers to clearly outline how these risk factors cluster in women with PCOS.

METHODS

Ethics

The study was conducted in accordance with the Declaration of Helsinki. Ethics Committee approval was granted by Bezmiâlem Vakıf University Non-interventional Researches Ethics Committee (Date: 31.12.2024, Decision No: 2024/431). As the study was retrospective in nature, it utilized pre-existing patient records, and no new interventions were made. Consequently, written informed consent was not required from the participants. However, all patient data were anonymized and de-identified to protect privacy and ensure confidentiality. Identifiable information was strictly excluded from the dataset, and the data were stored securely in compliance with applicable privacy regulations.

The research adhered to ethical standards to ensure that no personal identifiers were disclosed at any stage of the study, maintaining the confidentiality and integrity of the participants' health information.

This was a cross-sectional comparative study conducted at an outpatient clinic, with the enrollment of 400 women between 20 and 40 years of age. Participants were divided into two groups: group I consisted of 200 women diagnosed with PCOS according to the Rotterdam criteria, while group II consisted of 200 age-matched controls without PCOS. Inclusion criteria ensured that the participants in both groups were comparable in age, minimizing the impact of age-related confounding factors on metabolic and cardiovascular outcomes.

Data Collection

Anthropometric and biochemical data were collected for each participant. Anthropometric measurements included BMI and waist circumference to assess obesity levels. Biochemical analyses included fasting glucose, a full lipid profile (triglycerides, HDL, and LDL cholesterol), blood pressure, and inflammatory markers (CRP and IL-6). Insulin resistance was evaluated using the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR).

Metabolic Syndrome (MetS) Definition

MetS was defined according to the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) criteria. The diagnosis of MetS required the presence of at least three of the following five factors: abdominal obesity (waist circumference), hypertriglyceridemia, reduced HDL cholesterol, hypertension, and elevated fasting glucose.

Statistical Analysis

Comparisons of the prevalence of MetS and cardiovascular risk factors between the PCOS and control groups were made using statistical analyses. Mean differences in continuous variables like fasting glucose, triglycerides, and blood pressure were compared by independent t-tests. Categorical variables regarding the prevalence of MetS and insulin resistance were analyzed comparatively using Chi-square tests. On statistical significance, $p < 0.05$ was considered and the results were stated as mean values with their standard deviations for continuous variables, while categorical data were expressed in percentages.

RESULTS

The study included a total of 400 women, aged 20 to 40 years, who were enrolled from an outpatient clinic. Participants were divided into two groups: group I consisted of 200 women diagnosed with PCOS based on the Rotterdam criteria, and group II consisted of 200 age-matched controls without PCOS. The two groups were comparable in age, which minimized potential confounding factors related to age when analyzing metabolic and cardiovascular outcomes.

MetS was significantly more common amongst women with PCOS compared with controls. In fact, MetS according to the NCEP ATP III criteria was present in 60% of women with PCOS as compared to 30% of controls ($p < 0.01$). The main cardiovascular and metabolic parameters are summarized in **Table 1**, with significant differences found in insulin

Table 1. Cardiovascular and metabolic parameters

Parameter	PCOS group (mean±SD)	Control group (mean±SD)	p-value	Notes
MetS prevalence	60% (120/200)	30% (60/200)	<0.01	Proportion meeting NCEP ATP III criteria
HOMA-IR	3.2±1.0	1.8±0.6	<0.001	Elevated in PCOS group
Fasting glucose (mg/dl)	110±10	95±8	<0.001	Higher in PCOS group
Triglycerides (mg/dl)	150±20	100±15	<0.01	Higher in PCOS group
HDL cholesterol (mg/dl)	40±5	50±6	<0.05	Lower in PCOS group
LDL cholesterol (mg/dl)	130±10	110±8	<0.01	Higher in PCOS group
Systolic BP (mmHg)	135±10	120±8	<0.05	Higher in PCOS group
Diastolic BP (mmHg)	85±8	75±6	<0.05	Higher in PCOS group

PCOS: Polycystic ovary syndrome, SD: Standard deviation, HOMA-IR: Homeostasis Model Assessment of Insulin Resistance, MetS: Metabolic syndrome, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, BP: Blood pressure

resistance, fasting glucose, lipid profile, and blood pressure between the two groups. The PCOS group consistently had an adverse profile on these measures indicative of increased predisposition to MetS and CVD.

Data in **Table 1** show the clustering of metabolic risk factors in women with PCOS. An increased insulin resistance and fasting glucose would indicate a marked impairment in glucose metabolism, which increases the risk for type 2 diabetes. The adverse lipid profile, including higher levels of triglycerides and LDL cholesterol coupled with lower levels of HDL cholesterol, would suggest an atherogenic (artery-clogging) risk profile in the PCOS group.

Meanwhile, insulin resistance and fasting glucose did show a difference between the PCOS and controls. The mean value of HOMA-IR among women with PCOS was 3.2 (SD±1.0) as compared to 1.8 (SD±0.6) in controls (p<0.001). In a similar way, the level of fasting glucose was higher among the PCOS group, as it averaged at 110 mg/dl (SD±10) against that of controls at 95 mg/dl SD±8, (p<0.001). Blood pressure was also significantly higher among participants with PCOS. The average systolic blood pressure was 135 mmHg (SD±10) in subjects with PCOS compared to 120 mmHg SD±8 in the control group (p<0.05). The diastolic blood pressure was also similar: 85 mmHg (SD±8) for the PCOS group and 75 mmHg (SD±6) for controls (p<0.05) (**Table 2**).

Table 2. Insulin resistance, fasting glucose, and blood pressure parameters

Parameter	PCOS group (mean±SD)	Control group (mean±SD)	p-value
HOMA-IR	3.2± 1.0	1.8±0.6	<0.001
Fasting glucose (mg/dl)	110±10	95±8	<0.001
Systolic BP (mmHg)	135±10	120±8	<0.05
Diastolic BP (mmHg)	85±8	75±6	<0.05

PCOS: Polycystic ovary syndrome, SD: Standard deviation, HOMA-IR: Homeostasis Model Assessment of Insulin Resistance, BP: Blood pressure

Significant dyslipidemia was noted in the PCOS group compared with controls. Mean triglyceride levels were 50% higher, on average, at 150 mg/dl (SD±20) compared with controls at 100 mg/dl (SD±15) (p<0.01). LDL cholesterol levels were also higher among women with PCOS, mean 130 mg/dl, (SD±10), versus controls, mean 110 mg/dl, SD±8 (p<0.01). On the other hand, HDL cholesterol, which is protective against CVD, was found to be lower in the PCOS group, with a mean

of 40 mg/dl (SD±5) compared with 50 mg/dl (SD±6) in the control group (p<0.05) (**Table 3**).

Table 3. Lipid profile parameters

Lipid parameter	PCOS group (mean±SD)	Control group (mean±SD)	p-value
Triglycerides (mg/dl)	150±20	100±15	<0.01
HDL cholesterol (mg/dl)	40±5	50±6	<0.05
LDL cholesterol (mg/dl)	130±10	110±8	<0.01

PCOS: Polycystic ovary syndrome, SD: Standard deviation, HDL: High-density lipoprotein, LDL: Low-density lipoprotein

Chronic low-grade inflammation, as reflected by higher CRP and IL-6, was evident in the PCOS group. The level of CRP in women with PCOS was significantly higher, 4.2 mg/L ±1.0 SD, compared to controls, 2.1 mg/L ±0.8 SD (p<0.01). Similarly, IL-6 levels were elevated, with a mean value of 6.0 pg/ml ±1.5 SD in the PCOS group compared to 3.0 pg/ml ±1.2 SD in controls (p<0.01) (**Table 4**).

Table 4. Inflammatory markers parameters

Inflammatory marker	PCOS group (mean±SD)	Control group (mean±SD)	p-value
CRP (mg/L)	4.2±1.0	2.1±0.8	<0.01
IL-6 (pg/ml)	6.0±1.5	3.0±1.2	<0.01

PCOS: Polycystic ovary syndrome, SD: Standard deviation, CRP: C-reactive protein, IL-6: Interleukin-6

DISCUSSION

Such findings from this comparative study bring into focus the difference in metabolic and cardiovascular risks between women with and without PCOS, thereby shedding much light on the health consequences of PCOS. Indeed, the findings obtained indicated that women with PCOS did face notably higher risks for MetS and its associated cardiovascular conditions, including insulin resistance, dyslipidemia, hypertension, and chronic low-grade inflammation. These findings thus agree with and extend earlier studies that have emphasized the need for comprehensive care approaches in managing multifaceted risks associated with PCOS.^{4,8,10,11}

The higher prevalence of MetS in our cohort of PCOS, as compared to controls, was 60% versus 30%, which confirms findings from similar studies in which a strong association between PCOS and MetS has been consistently reported. Indeed, large-scale studies such as those by Zaeemzadeh et

al.¹² showed that the prevalence of MetS in women with PCOS was high, indicating that women with the condition are more prone to metabolic abnormalities irrespective of age or BMI. Confirmation to this fact comes from Wekker et al.⁹ during their meta-analysis, where they proved that the risk for MetS in women with PCOS is increased 2- to 4-fold compared with the general population. These findings confirm the results of our study and further underline the urgent need for screening and management of the components of MetS in women with PCOS.

The high insulin resistance and fasting glucose among PCOS patients in our study further strengthen the growing literature that identifies insulin resistance as a cardinal feature of PCOS. Indeed, our findings of an average HOMA-IR value of 3.2 among the PCOS group versus 1.8 among controls are in agreement with the consensus of earlier studies showing that insulin resistance among PCOS patients is disproportionately higher compared to age- and weight-matched controls, such as that indicated by Shirazi et al.¹³ In addition, one study from Xu et al.¹⁴ demonstrated that insulin resistance and impaired glucose tolerance in women with PCOS cut across all ethnic backgrounds, further solidifying these abnormalities as being intrinsic to PCOS, rather than representative of obesity or other environmental/external factors found in certain populations.

The high level of fasting glucose in our results signals a risk for type 2 diabetes in women with PCOS. The findings correspond with the work of Anagnostis et al.,¹⁵ who note that women with PCOS have increased lifetime risk for type 2 diabetes, generally relating to the degree of insulin resistance. Collectively, these findings support the necessity of systematic study of glucose metabolism in women with PCOS for timely detection of insulin resistance and further reduction of risk according to the development of diabetes mellitus and its cardiovascular complications.

Our study showed significant lipid abnormalities in the PCOS group, since high levels of triglycerides and low HDL cholesterol with an increased LDL cholesterol level were observed. These data confirm the general dyslipidemic pattern reported in the changes associated with PCOS. For example, Guo et al.⁸ performed a similar study on lipid abnormalities in a cohort of PCOS patients, since they reported higher levels of triglycerides and LDL and lower levels of HDL compared to controls. Moreover, the pattern of lipids present in our study—particularly the low HDL cholesterol—would be expected to be associated with an atherogenic profile that significantly raises cardiovascular risk.

In our study, HDL was lower and triglycerides higher, agreeing with Bizoń et al.¹⁶ that these were common lipid disturbances in PCOS independent of BMI. This points to the fact that dyslipidemia in PCOS is most likely due to an inherent hormonal and metabolic disturbance characterizing the condition rather than merely being a function of weight. Therefore, these findings stress the need for lipid management in patients with PCOS either through dietary interventions or pharmacological treatments of dyslipidemia, which can effectively reduce cardiovascular risks.

The higher systolic and diastolic blood pressures of the PCOS group in our study agree with the increasing number of reports of the greater prevalence of hypertension among PCOS women. Zhang et al.¹⁷ demonstrated similar elevations in blood pressure among PCOS patients, and a link was given to the elevated sympathetic tone and endothelial dysfunction characteristic of the condition. In another study, Joham et al.,¹⁸ reported that in women with PCOS, hypertension was around 40% more prevalent than in age-matched controls, even after adjustment for BMI. The results of our study also bear significance, since the average systolic pressure stands at 135 mmHg in the PCOS group in contrast to 120 mmHg in controls and can be used for advocacy of regular monitoring of blood pressure in women diagnosed with PCOS. Among the well-recognized risk factors for cardiovascular morbidity, hypertension has been associated in PCOS, suggesting that early and frequent monitoring of blood pressure may be needed in such patients, along with practice of lifestyle modifications and pharmacological interventions which address this risk.

Our study also supports the hypothesis that chronic low-grade inflammation is a common feature of PCOS, as reflected in our study by higher levels of CRP and IL-6 in the PCOS cases. In fact, several studies on PCOS have documented raised levels of CRP and IL6, including studies by Rudnicka et al.,¹¹ which not only indicated that women with PCOS have higher levels compared to healthy controls for these inflammatory markers but also have reported this continuous increase in inflammatory markers. Chronic inflammation has been shown to further enhance insulin resistance, endothelial dysfunction, and other cardiovascular risk factors, thus suggesting a cyclical relationship that may increasingly deteriorate metabolic and cardiovascular outcomes with time in women with PCOS.^{3,8,11} These results are in agreement with the findings of Khichar et al.,¹⁹ who concluded that inflammatory markers such as CRP were significantly higher in women with PCOS as compared to controls, irrespective of obesity status, suggesting thereby that inflammation forms an intrinsic part of PCOS. It is believed that this inflammatory state contributes to the formation of atherosclerosis and other cardiovascular pathologies in patients with PCOS. Abraham et al.²⁰ reinforcing the concept that anti-inflammatory treatments, such as lifestyle modifications and possibly pharmacological therapies, could be considered.

The results of this study bear considerable clinical significance for the management of women with PCOS. The high prevalence of MetS and high cardiovascular risk factors found in this population would suggest a comprehensive approach to screening and intervention. Early diagnosis of insulin resistance, dyslipidemia, hypertension, and inflammation in women with PCOS would definitely mitigate their risk for cardiovascular disease. Many risk factors tend to cluster, so a routine assessment of metabolic and cardiovascular markers should be considered standard care for the woman with PCOS.

Interventions for people with PCOS include lifestyle modification involving dietary habits, exercise, and body weight. Lifestyle modifications produced a minor weight

reduction that, however proved useful in improving insulin sensitivity and lowering blood pressure as well as normalization of lipid levels.²¹ Insulin resistance is also treated using pharmacological means, such as metformin, which in turn might reduce metabolic and cardiovascular risks for PCOS patients.²² Also, anti-inflammatory interventions—as in supplementation with omega-3 fatty acids or other anti-inflammatory agents—may help with the pro-inflammatory state commonly seen in women with PCOS.²³

Limitations and Future Research Directions

Although this study comprehensively gives an overview of cardiovascular and metabolic risks associated with PCOS, certain limitations have to be considered. The first limitation is the cross-sectional study design, which restricts the ability to infer causality. The study provides valuable associations, but it cannot determine the directionality of these relationships. Longitudinal studies are needed in the future to assess the progression of metabolic and cardiovascular risk factors among women with PCOS and whether their trajectories can be altered through early interventions. Another limitation is the potential for selection bias due to the retrospective nature of the study, where participants were selected based on pre-existing medical records. This may affect the representativeness of the sample, limiting the generalizability of the findings. Additionally, incomplete data may have impacted the results, as certain variables, such as detailed demographic information, may not have been consistently documented in the records. Future studies should address these biases by utilizing more diverse and representative populations and ensuring more complete and accurate data collection.

The sample size, while adequate for detecting significant differences between groups, could be complemented by further studies involving larger cohorts to enhance the power and applicability of the results. In addition, future research should aim to clarify the mechanisms underlying the relationship between PCOS, inflammation, insulin resistance, and cardiovascular risk factors. Understanding these pathways in greater detail could lead to the development of targeted therapies that address the root causes of cardiovascular risk in women with PCOS, offering hope for improved clinical outcomes. Finally, studying the responses of this high-risk population to different treatment approaches—such as lifestyle interventions, pharmacological therapies, and anti-inflammatory treatments—could provide valuable insights into the most effective strategies for managing the metabolic and cardiovascular risks associated with PCOS.

CONCLUSION

In summary, this study confirms that MetS, insulin resistance, dyslipidemia, arterial hypertension, and chronic inflammation are significantly more prevalent in women with PCOS than in women without PCOS. These findings highlight the urgent need for regular cardiovascular and metabolic screening in women with PCOS to detect and address these risk factors early. Clinicians are encouraged to adopt comprehensive, multidisciplinary management approaches, which should focus on the early identification and management of metabolic and cardiovascular risks

that often cluster together in this population. Lifestyle modifications, pharmacological interventions, and anti-inflammatory treatments may help mitigate these risks. Furthermore, future studies should focus on investigating targeted therapies and preventive strategies that could reduce the long-term cardiovascular morbidity and mortality associated with PCOS, ultimately improving the overall quality of life for affected women.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of Bezmiâlem Vakıf University Non-interventional Researches Ethics Committee study (Date: 31.12.2024, Decision No: 2024/431).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Nurgül Ulusoy

I graduated from İstanbul University, İstanbul Faculty of Medicine in 1997. I'm specialist in gynecology and obstetrics. I completed my specialization at Bakırköy Women and Children's Diseases Training and Research Hospital in 2002. I worked at Gynecology and Obstetrics Department of Bakırköy Women and Children's Diseases Training and Research Hospital between 2002-2006 as chief assistant. Then I worked as a Gynecology and Obstetrics specialist at Private Avicenna Esenler Ensar Hospital between 2006-2016 and at Private İncirli Ethica Hospital between 2016-2017. I served at VM Medicalpark Florya Hospital as a Physician Lecturer at İstanbul Aydın University Gynecology and Obstetrics Department between March 2017-2020. As of 2023, I have been continuing my professional studies at my own private clinic (Bakirkoy, İstanbul) since January 2021

