

# Prevalence of Metabolic Syndrome among Reproductive-aged Women with Polycystic Ovarian Syndrome: A Study from West-Central India

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## ABSTRACT

**Introduction:** Polycystic ovarian syndrome (PCOS) is the most common hormonal disorder prevailing in premenopausal women. These patients are 11 times more likely to encounter metabolic syndrome (MetS). There is a substantial overlap into the components of these two syndromes, which in turn leads to increased risk of type-2 diabetes mellitus (T2DM) and cardiovascular diseases (CVD) in the foreseeable future. In this perspective, the present study was planned to evaluate the prevalence of MetS and its individual components in PCOS in Indian scenario.

**Study design:** This cross-sectional study included 150 women diagnosed with PCOS between 18 and 38 years age. Demographic variables including age, education, occupation, inhabitant area, history of infertility, and family history of diabetes mellitus and hypertension were collected. Anthropometric parameters like weight, height, body mass index (BMI), waist circumference (WC), and systolic/diastolic blood pressure (SBP/DBP) were measured. Fasting venous blood samples were collected and analyzed for biochemical parameters like glucose, total cholesterol (TC), triglycerides (TG), and high-density lipoprotein (HDL) cholesterol.

**Result:** The prevalence of MetS in women with PCOS was 38.67%. The most prevalent component was decreased HDL (84.67%), followed by increased WC (75.33%), followed by raised TG (42%).

**Conclusion:** The analogy of PCOS with MetS implicates that it is crucial to analyze the emerging trend of MetS in patients with PCOS. Recognition of this high-risk group will aid in the enforcement of preventive strategies including therapeutic lifestyle modifications and risk factor management. This will have a promising impact on women's health and will prevent or delay the outset of varying cardiometabolic complications in PCOS.

**Keywords:** Metabolic syndrome, Polycystic ovarian syndrome, Prevalence.

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## INTRODUCTION

Polycystic ovarian syndrome, also usually noted as Stein–Leventhal syndrome, is one of the most conventional gynecological endocrinopathies.<sup>1</sup> This ovarian dysfunction syndrome affects nearly 5 to 8% women of reproductive peer group.<sup>2</sup> This heterogeneous disorder encompasses an all-embracing spectrum of clinical signs and symptoms. The prototypical stigmata of PCOS are elucidated by chronic anovulation, hyperandrogenism, and polycystic ovaries. While absolute comprehension of intrinsic pathophysiology of PCOS is still lacking, it is supposed to be a result of an interplay between genetic, epigenetic, metabolic, and neuroendocrine interactions as well as environmental factors.<sup>1</sup> It is acknowledged not merely as a systemic disorder with reproductive, cosmetic, psychological, and oncologic consequences, but over and above, it has facets of metabolic disorder, extending all through the women's lifetime.<sup>3</sup> It is a paramount burden which, if left unrestrained, substantially augments the risk of a variety of cardiometabolic complications, such as Insulin Resistance (IR), T2DM, hypertension, dyslipidemia, and CVD. This perplexing health issue has profound implications from financial standpoint on public health care system. By virtue of this, timely diagnosis and management of the syndrome should be accentuated.<sup>4</sup>

Insulin resistance with compensatory hyperinsulinemia is evident in a noteworthy subset of PCOS women (65–80%). Insulin resistance is speculated to be the unifying root cause in the interrelationship amid central obesity, glucose intolerance, lipid abnormalities, hypertension, and cardiovascular involvement in PCOS. Each one of these risk factors concomitant with PCOS is furthermore the pivotal component of what is designated as metabolic syndrome, Insulin Resistance Syndrome, or syndrome "X."<sup>4</sup>

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Metabolic syndrome is a kind of endocrine disruption, characterized by a constellation of metabolic derangements that embraces IR, hypertension, dyslipidemia (low HDL and elevated TG), and central or visceral obesity.<sup>1</sup> Metabolic syndrome is worth caring about, as it confers a 2-fold enhanced risk of CVD and a 5-fold enhanced risk of T2DM (which in itself magnifies the risk for CVD).<sup>5</sup> The pathophysiology of MetS is very intricate and has been only partially elucidated. Insulin resistance with ensuing hyperinsulinemia seems to be the foremost mediator of MetS.<sup>6</sup>

The PCOS patients have an eleven-fold augmentation in the prevalence of MetS and the risk is aggravated in spite of young age.<sup>6</sup> These patients may exhibit the attributes of MetS quite in advance than the actual manifestations of diabetes mellitus and cardiovascular disease.<sup>2</sup> Obesity, peculiarly visceral adiposity, and IR usually proceed hand in hand and culminate in the development of reproductive, endocrine, and metabolic derailments in PCOS as well as in the MetS. There is a school of thought that suggests that these two syndromes encompass two explicit clinical entities, wherein IR continues to be the unified culprit in their pathogenesis.<sup>4</sup> Since the anthropometric and metabolic aberrations encountered in PCOS converge with the components of MetS, the concern pertaining to evaluation of MetS in PCOS women has created enormous curiosity.<sup>7</sup> Accordingly, PCOS is occasionally specified as "MetS of gynecology" or as a "sex-specific variant of MetS."<sup>8</sup>

The uttermost troublesome concerns of PCOS patients alter with age, starting with cosmetic hassles like acne and hirsutism during teenage, to oligomenorrhea and infertility throughout their reproductive lives, and to cardiometabolic ailments after menopause.<sup>8</sup> Gynecologists many a time look at it as a reproductive issue and till very recently, these patients were treated based on this pronounced facet. PCOS is possibly appraised just as an early expression of MetS coupled with an array of derangements. Focusing out of the conventional reproductive perspective, directed toward well-timed screening and alleviation of various cardiometabolic risk components is obligatory in all PCOS patients.<sup>4</sup> Recognition of high-risk women beforehand in their lifetime will result in the enforcement of precautionary maneuvers inclusive of comprehensive lifestyle modifications and risk factor management. This will have a favorable influence on women's well-being and will mitigate the plausibility of cardiometabolic ramifications.<sup>6</sup> Consequently, it is imperative to ascertain the outlook of MetS among this at-risk community group. We ought to perceive PCOS and MetS under a new paradigm, which reinforces the horizon of PCOS.

In view of this background comprehension, we evaluated the prevalence of MetS and its individual components in PCOS women in the Indian scenario.

## MATERIALS AND METHODS

This was a cross-sectional study. After written and informed consent, total 150 patients with a diagnosis of PCOS, between 18 and 38 years age group were enrolled. Study protocol was approved by the institutional ethical committee.

Pregnant and lactating women, women who had previous surgery of at least one ovary, patients on oral contraceptive pills, lipid-lowering drugs, and any medications known to affect glucose metabolism or blood pressure for past 3 months, smoking and alcoholism were excluded from the study. The patients with any known endocrine disorder, diabetes mellitus, hepatic and renal diseases were not included in the study.

Demographic variables including age, education, occupation, inhabitant area, history of infertility, and family history of diabetes mellitus and hypertension were collected. Anthropometric parameters, such as weight, height, BMI, and WC, SBP, and DBP were measured.

Body weight (in kg) was measured using a standard weighing scale, with the participants barefoot with arms hanging freely at their sides and wearing light clothing. Height (in meter) was measured with each subject standing erect against wall without shoes with a wall-mounted ruler. Body mass index was calculated as weight in kilograms divided by the square of height in meters ( $\text{kg}/\text{m}^2$ ). Waist circumference was measured at a point midway between the upper border of iliac crest and the lowest rib margin using a soft nonstretchable tape and was taken at the end of a normal expiration in the mid-axillary line. Systolic and diastolic blood pressures (mm Hg) were measured twice in the right arm in a sitting position after a 10-minute rest, using a standard mercury sphygmomanometer, the average of the two readings was considered for analysis.

After 12 hours of fasting, venous blood samples were obtained. Fasting blood glucose (FBG), TC, TG, and HDL were measured. Blood glucose was measured by glucose oxidase-peroxidase end point method using commercial kits from ERBA Diagnostics. The TG level was measured by using the standard lipase-glycerokinase-glycerophosphate oxidase end point method using commercial kits from Reckon Diagnostics. The HDL was measured by modified polyvinyl sulfonic acid and polyethylene-glycol-methyl ether coupled classic precipitation end point method using commercial kits from Erba Diagnostics. Total cholesterol was measured by cholesterol

**Table 1:** Comparison of demographic characteristics between PCOS women with and without MetS

Variable	PCOS with MetS (n = 58)	PCOS without MetS (n = 92)	p-value
Age	31.17 ± 5.15	24.83 ± 4.08	<0.05
BMI (kg/m <sup>2</sup> )	30.04 ± 3.06	26.66 ± 2.41	<0.05
WC (cm)	97.41 ± 8.73	91.31 ± 6.93	<0.05
SBP (mmHg)	129.97 ± 13.75	113.42 ± 10.85	<0.05
DBP (mmHg)	88.45 ± 9.93	74.11 ± 7.81	<0.05

**Table 2:** Comparison of biochemical parameters between PCOS women with and without MetS

Variable	PCOS with MetS (n = 58)	PCOS without MetS (n = 92)	p-value
HDL (mg/dL)	39.91 ± 6.9	43.97 ± 8.79	<0.05
TG (mg/dL)	174.05 ± 35.79	131.41 ± 28.23	<0.05
FBG (mg/dL)	104.48 ± 13.74	85.25 ± 10.74	<0.05
TC (mg/dL)	194.64 ± 25.14	178.32 ± 17.01	<0.05
LDL (mg/dL)	119.91 ± 25.59	108.07 ± 19.08	<0.05

oxidase peroxidase end point method using commercial kits from Reckon Diagnostics.

The diagnosis of PCOS was established in accordance with the Rotterdam 2003 criteria. Presence of any two of the following three conditions confirmed the diagnosis: (i) Oligo- and/or anovulation, (ii) clinical and/or biochemical signs of hyperandrogenism, and (iii) polycystic ovarian morphology (on ultrasound).<sup>1</sup>

The MetS was defined as stated in the US National Cholesterol Education Program Adult Treatment Panel III criteria as the occurrence of at least three of the following risk factors: (i) Central obesity with WC >88 cm, (ii) elevated level of serum TG ≥ 150 mg/dL, (iii) decreased level of HDL < 50 mg/dL, (iv) elevated SBP/DBP ≥ 130/85 mm Hg, and (v) impaired FBG level ≥ 110 mg/dL.<sup>1</sup>

Thereafter, the study participants were classified into two groups: (i) PCOS women with MetS (58) and (ii) PCOS women without MetS (92).

## Statistical Analysis

All data were analyzed using the GraphPad Prism software, version 5. The results were interpreted as mean ± standard deviation. Student's unpaired t-test was used for comparison between groups. Categorical variables were presented as number and percentage. A p-value < 0.05 was considered statistically significant.

## RESULTS

In our study, the prevalence of MetS in women with PCOS was 38.67% (58/150).

All five features of MetS were present in 4 cases (2.67%), four features in 16 cases (10.67%), and three features were present in 38 cases (25.33%) of the studied PCOS population. The PCOS women without MetS (92) also had one or two components of MetS by the time of recruitment into this study. Of these, 68 (45.33%) women had two features, while 24(16%) women had one feature of MetS.

Demographic characteristics of PCOS women with and without MetS are shown in Table 1. Mean values of

**Table 3:** Prevalence of individual components of MetS among women with PCOS

Components of the MetS	Prevalence in PCOS (n = 150) n (%)
HDL < 50 mg/dL	127 (84.67%)
WC > 88 cm	113 (75.33%)
TG ≥ 150 mg/dL	63 (42%)
SBP/DBP ≥ 130/85 mm Hg	37 (24.67%)
FBG ≥ 110 mg/dL	18 (12%)

age, BMI, WC, SBP, and DBP in PCOS patients with MetS were significantly higher than PCOS women without MetS.

Laboratory findings including FBG, TG, TC, and LDL were significantly higher in PCOS women with MetS than in those without MetS. On the contrary, HDL in PCOS women with MetS was significantly lower than in women without MetS (Table 2).

Prevalence of individual components of MetS in PCOS women is shown in Table 3. The most prevalent isolated abnormality of MetS in PCOS women was decreased HDL (84.67%), followed by increased WC (75.33%), followed by raised TG (42%).

## DISCUSSION

Polycystic ovarian syndrome, a cluster of variform etiologies belonging to unique syndromic annotation, is the utmost important reproductive endocrinopathy in women.<sup>1</sup> It is the preeminent cause attributed to female infertility. Nevertheless, PCOS should no longer be taken into account as a merely gynecological disorder, owing to the fact that these women appear to be furthermore susceptible to develop MetS. Consequently, there is heightened risk of diabetes mellitus and CVD in these women. This detrimental association of PCOS with MetS gives rise to serious cardiometabolic outcomes apart from the traditional worrisome concerns of a PCOS patient.<sup>5</sup> This draws attention to the prerequisite for prevention of these long-term complications by means of proper screening, diagnosis and intervention. In this facet, we have conducted the present study to determine the prevalence of MetS among reproductive-aged PCOS women from India.



In this study, the prevalence of MetS in PCOS women was 38.67%. This finding is analogous to the prevalence in numerous other studies. In a study by Sharma and Majumdar,<sup>9</sup> the prevalence of MetS in PCOS was 39.16% in India. Avila et al<sup>10</sup> found 36% prevalence. Pourteymour Fard Tabrizi et al<sup>7</sup> found 39.5% prevalence in Iran. Ishak et al<sup>4</sup> found 43.4% prevalence in Malaysia. Likewise, other studies found the prevalence of MetS in PCOS to be 37.5% by Mandrelle et al,<sup>11</sup> 42% by Ramprasad et al,<sup>12</sup> 36.02% by Pikee et al.<sup>13</sup> These variations in the prevalence in different studies might be attributed to age, genetic factors, sample size, diagnostic criteria, and population characteristics.

Our study showed that demographic variables like age, BMI, WC, SBP/DBP, and biochemical parameters, such as TG, TC, and FBG were significantly higher in PCOS patients with MetS than in PCOS patients without MetS. HDL levels were significantly decreased in PCOS women with MetS than in those without MetS. These findings are supported by studies done by Zahiri et al,<sup>1</sup> Cussons et al,<sup>14</sup> Ramprasad et al,<sup>12</sup> and Soares et al.<sup>15</sup>

In this study, the most prevalent component of MetS was decreased HDL (84.67%) followed by increased WC (75.33%), followed by raised TG (42%). Zahiri et al,<sup>1</sup> Varghese et al,<sup>2</sup> Sharma and Majumdar,<sup>9</sup> Soares et al<sup>15</sup> reported similar findings in their studies. In a study by Pourteymour Fard Tabrizi et al<sup>7</sup> (Iran) and Moini et al<sup>16</sup> (Tehran), the most prevalent components were low HDL, followed by raised TG, followed by raised WC. Cussons et al<sup>14</sup> (Australia) and Ferdous Mehrabian et al<sup>6</sup> (Iran) found increased WC to be the most prevalent component followed by decreased HDL. This difference in the prevalence of individual components of MetS could be due to variances in race and dietary patterns of population.

On further analyzing MetS components in PCOS women, it was observed that in spite of absence of full-blown MetS, these women had one or two components of MetS by the time of enrollment into current study. Eventually, in the absence of specific interventions, they might develop full-blown MetS in the near future. Likewise, these women too are still at risk of cardiometabolic complications. Furthermore, it was found that PCOS women complied with the criteria for MetS at a relatively younger age. Accordingly, it is worthwhile in clinical practice to evaluate varied components of MetS in PCOS patients.

Thus, the relationship amidst PCOS and MetS is seemingly correlative. Plausible hypotheses concerning this association are: (i) IR, (ii) central obesity and related adipose tissue factors, and (iii) vascular and coagulation abnormalities, the principal mediators in the pathogenesis of both these syndromes. In PCOS, intrinsic IR along with compensatory hyperinsulinemia brings about unfavorable metabolic milieu with a propensity toward

dyslipidemia and increased androgen production from ovarian theca cells. Androgen excess in turn may act as an endocrine modulator of MetS, exacerbating the metabolic derailments and central fat distribution (android pattern). Ultimately, this culminates in setting up a vicious circle of hyperinsulinism, hyperandrogenism, central adiposity, and metabolic abnormalities, leading to the intriguing overlap between PCOS and MetS.<sup>11</sup>

The PCOS is not altogether a reproductive disease, but a systemic ailment as well, with more worrisome concerns past the reproductive age. The PCOS women oftentimes come up to gynecologists with menstrual irregularity, acne and hirsutism, and reproductive dysfunctions far ahead during their reproductive lifetime. This could be availed as a potential opportunity to make them aware regarding their long-standing threat of cardiometabolic complications, to evaluate and monitor these patients, and thereby to impede the various facets of MetS, by timely interventions. The comprehensive evaluation and therapy of PCOS women should extend over and above the target of transient symptom control. It should be carried through not only at once upon diagnosis, but longitudinally thereafter, with attention to the long-lasting devastating diabetic and cardiovascular ramifications. Health care professionals should motivate PCOS women in regard to harmonious lifestyle alongside proper diet and exercise plan. Earlier pharmacotherapy with insulin sensitizers and lipid-lowering agents may be advised if therapeutic lifestyle modifications are in vain.<sup>5</sup>

The limitation of our study is that this was a cross-sectional study with small sample size. Future long-term prospective studies with greater sample size are required to further understand the interplay between components of PCOS and MetS.

## CONCLUSION

In the present study, the prevalence of MetS in PCOS women was 38.67% besides decreased HDL being the most prevalent component. The PCOS women had at least one feature of MetS by the time of recruitment into the present study and thus, are at high risk of developing full-fledged MetS in foreseeable future. Hence, it is imperative to assess the emerging trend of MetS among the PCOS population. Recognition of MetS in PCOS antecedently in the disease process provides an individualized clinical perspective. This will aid in bringing the awareness and well-timed interventions to forestall long-term cardiometabolic sequelae in this population. Thus, PCOS and MetS should be perceived under a new paradigm, which expands the horizon of PCOS.

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