

# Metabolic Syndrome among Polycystic Ovarian Syndrome: A Cross Sectional Study

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## Abstract

**Background:** The metabolic syndrome (MS) is a constellation of interrelated abnormalities. Polycystic ovarian syndrome (PCOS) is the most common cause of anovulatory infertility. PCOS is associated with insulin resistance and significantly higher ratio for the development of various cardiovascular risk factors and a significantly greater risk of MS. **Aim:** (1.) To find out the prevalence of metabolic syndrome (MS) in females with polycystic ovary syndrome (PCOS). (2.) Assess the metabolic risk factors in PCOS as per the definition of IDF criteria of metabolic syndrome. **Study design:** Descriptive and cross sectional hospital based study. **Materials and methods:** This study was conducted in the department of obstetric and gynecology at tertiary care center. Study duration 1 year. **Statistical analysis:** It was done using SPSS version 22.0 using Karl Pearson Chi Square Test, Paired T test. **Results:** MS was diagnosed in 35.45% of cases (39/110) with 33.33% in adolescents (14/42) and 36.77% in adults (25/68). **Conclusion:** we should change the attitude towards the polycystic ovarian syndrome -PCOS patients should be screened for Metabolic Syndrome and also should be offered prevention and further treatment.

## Introduction

Polycystic ovarian syndrome is the most common cause of anovulatory infertility. It's association with menstrual disturbance and altered hormonal parameters leads many affected women of reproductive age to attend gynaecology or infertility clinic. Principal factors underlying this disorder is insulin resistance, with the resultant hyperinsulinaemia stimulating excess ovarian androgen production. These women exhibit a characteristic dyslipidemia and a predisposition towards diabetes and cardiovascular disease in later life. Thus, polycystic ovarian syndrome seems to have many of the hallmarks of the metabolic syndrome.

The metabolic syndrome (MS) is a constellation of interrelated abnormalities. The importance of diagnosing MS in the general population lies in its association with a two-fold increased risk of cardiovascular disease and a five-fold increased risk of type 2 diabetes mellitus.

Prevalence of MS in women with PCOS appears to be significantly higher than estimated in their age matched

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counterparts from general population. Recent studies estimate the prevalence of MS in women with PCOS varying between 34% and 46%, it is at least twice than in age matched control women [1,2].

#### *Why is it important to do this study?*

- It is evident that polycystic ovarian syndrome is not a pure gynecological disorder, but a Gynecologic Endocrine disorder.
- It is important to identify women with PCOS and metabolic syndrome for an early intervention.
- They may be benefited from early screening for cardiovascular risk factors, particularly glucose intolerance.
- Early interventions prevent the future complication of endocrine and metabolic disturbances and reduce the risk of vascular diseases. It may change the approach of therapy from individual component of PCOS to combined PCOS & MS.

#### *Aims and Objectives*

- ❖ To find out the prevalence of metabolic syndrome (MS) in females with polycystic ovary syndrome (PCOS).
- ❖ Assess the metabolic risk factors in PCOS as per the definition of IDF criteria of metabolic syndrome.

#### **Materials and Method**

*Study design:* Descriptive and cross sectional hospital based study.

*Study area:* The study was carried out in the Gynaecology OPD of the Department of Obstetrics and Gynaecology at Tertiary Care Centre.

*Study duration:* 1 year

*Study population:* Patients of Polycystic ovarian syndrome in Gynaecology OPD of tertiary care centre.

*Sample size:* 110

*Inclusion criteria for PCOS:*

ESHRE/ASRM (Rotterdam) criteria (2003) [3]

Two or more of the following criteria are required

1. Polycystic ovarian (PCO) morphology on ultrasound scan

2. Hyperandrogenic features (defined biochemically and/or clinically)
3. Oligomenorrhoea or amenorrhoea.

ESHRE- European Society for Human Reproduction and Embryology;

ASRM- American Society for Reproductive Medicine.

*Inclusion criteria for Metabolic Syndrome:*

IDF (International Diabetes Federation) (2005) [4]

Requires the presence of central obesity (waist circumference > 80 cm in women). (cut off value for South Asian women)

In addition, at least two of the following criteria should be met:

1. Elevated triglycerides (>150 mg/dl) (>1.7 mmol/l)
2. Reduced HDL cholesterol (< 50 mg/dl in women) (<1.3 mmol/l) or Specific treatment for lipid abnormalities
3. Elevated blood pressure ( $\geq$  130/85 mm Hg) or Specific treatment of previously diagnosed hypertension
4. Fasting plasma glucose (>100 mg/dl) (>5.6 mmol/l) or previously diagnosed type 2 diabetes mellitus

*Exclusion criteria*

- Women more than 40 years of age with irregular menstrual cycle.
- Females with diagnosed hypothyroidism or hyperprolactinaemia.
- Female who had used oral pills in the preceding three months.
- Secondary causes of androgen excess.

During clinical examination, body mass index (BMI) (kg/M<sup>2</sup>) will be calculated in each case. Height will be recorded to the nearest 0.5 cm and weight on a platform type (bathroom scale) machine. WC will be measured as the minimum value between the iliac crest and the lateral costal margin, using a 1-cm wide measuring tape.

Every female diagnosed with PCOS will undergo fasting plasma glucose (FPG) estimation. Fasting Plasma high density lipoprotein-cholesterol (HDL-C) and triglyceride (TG) levels, Serum TSH, Serum Prolactin and Serum testosterone.

- The primary outcome measure was to determine the prevalence of metabolic

syndrome in women with PCOS and secondary outcome included factors, which may predispose to the risk of development of metabolic syndrome.

- The study protocol was approved by the Institutional ethical and scientific committees.

Women were enrolled for the study only after an informed written consent.

#### Statistical Analysis

- Statistical analysis was done using SPSS version 22.0
- Descriptive statistics (Mean, Standard Deviation (SD), Percentages)
- Karl Pearson Chi Square Test
- Paired T test (Student t Test) to test the correlation between the intra group observations.
- Null hypothesis ( $H_0$ ): The parameters evaluated in the study have no effect in diagnosis of MS.
- Alternative Hypothesis ( $H_a$ ): The parameters evaluated in the study have effect in diagnosis of MS.

#### Result

- MS was diagnosed in 35.45% of cases (39/110) with 33.33% in adolescents (14/42) and 36.77% in adults (25/68).
- Females with metabolic syndrome had greater BMI (28.01 kg/m<sup>2</sup>) than those without MS (23.53 kg/m<sup>2</sup>).
- The Mean WC in total MS group was 100.69 cm. adolescent 101.35 cm and adults 100.32 cm.
- Prevalence of MS increases as increasing in the age of pcos patient (33.33% in 16-19 age groups to 42.30% in 26-30 age groups).
- TG and HDL abnormalities are more common than FPG and BP in PCOS with MS. It may be due to dyslipidemia is the primary process of MS.
- In present study out of 39 cases of MS, 38 cases had TG/HDL ratio more than 3.
- In the prevalence MS possibility of presence of five or four features of MS is lower than three and two features of MS. As the disease progresses BP and FPG levels derange.

That is why it is uncommon to get all five features of MS in PCOS patients, showing that identification of one risk variables in a female with PCOS should prompt the clinician to search for others.

#### Discussion

MS is a constellation of three main abnormalities (Dyslipidemia, Hypertension and Impaired FPG) which relate to a state of Insulin Resistance, and has been known for several decades [5].

The definition of MS laid down by the IDF [6] is new and the clinical criteria proposed by IDF are similar to those of NCEP-ATP III criteria [7] with identical thresholds for TG and HDL-C levels, BP and FPG. The IDF criteria difference in its inclusion of WC thresholds, which are adjusted for different ethnic groups.

Prevalence of MS in patient with PCOS in varies studies

Study	Studied Populations	Prevalence of MS in PCOS
Present study (Table 1)	110 PCOS (R) Indian	IDF :35.45%
Kavita Mandrelle and cols. [8] (2012) Cross-sectional	120 PCOS (R) Indian	Modified ATP III : 37.5%
Bhattacharya [9] Cross-Sectional (2008)	117 PCOS(R) mBMI: obese Indian	IDF: 46.2%
Hahn and cols. Cross-Sectional (2008)	411 PCOS (R) German females	IDF: 33.8%
Park and cols. cross-sectional (2007)	113 PCOS (NIH), mBMI: lean Korean	NCEP: 14.5%
Dokras and cols. [10] Retrospective (2005)	129 PCOS (NIH), mBMI: obese Caucasian	IDF:47.3%
Ehrmann and cols. [2] retrospective (2006)	368 PCOS (NIH), mBMI: obese Multiracial	NCEP: 33.4%
Cussons and cols. Retrospective (2006)	168 PCOS (NIH), mBMI: obese	WHO: 33% IDF: 40%

The variation in the rates of MS reported by different studies may be attributable not only to anthropometric differences between diverse ethnicity, but also to differences in the criteria used for PCOS diagnosis.

As per table 2 & 3 PCOS female with MS have more BMI and WC compared to without MS, the difference is statistically significant. In present study population non-obese women did not exhibited metabolic syndrome (0% prevalence according to IDF criteria). These findings are similar to Faloia

E and colleagues study in lean patients with PCOS (0% prevalence of MS according to NCEP-ATP III criteria).

In present study 35.45% prevalence of MS detected in overweight and obese PCOS patients (mean BMI: 28.01 kg/m<sup>2</sup>). In comparison, Apridonidze and colleagues [1] reported high incidence of MS (43%) in obese women over a 3-year period. Dokras and colleagues [10] reported 47.3% prevalence of MS in obese PCOS. Bhattacharya [9] also found 46.2% prevalence of MS in obese PCOS. This shows that central obesity has been implicated in the pathophysiology of MS.

As in table 4 present study shows that prevalence of MS is more in adults (26-30 yrs: 42.30%) than in the adolescents (<20 yrs: 33.33%). Bhattacharya [9] had high prevalence of MS 48.6% in 26-30 yrs age group than 43.6% in adolescent. The difference is not statistically significant. Kavita Mandrelle and colleagues [8] also had high prevalence of MS 48.9% in 25-29 yrs of age group than 16.0% in less than 24 yrs of age.

As in table (5, 6, 7, 8) in present study abnormalities in lipids are common in MS. Abnormalities in both the lipids, HDL-C and TG together, were common in adolescents (78.57%) and adults (68%) both. Out of

**Table 1:** Distribution of study population according to MS

Group	With MS		Without MS	
	Number	%	Number	%
Whole Group	39	35.45	71	64.55
Adolescent	14	33.33	28	66.67
Adult	25	36.77	43	63.23

**Table 2:** Mean BMI (kg/m<sup>2</sup>) of the study sample

Group	With MS		Without MS		P value
	Mean BMI	SD	Mean BMI	SD	
Whole group	28.01	2.54	23.53	1.11	0.0001**
Adolescent	28.36	2.68	23.60	1.37	0.0001**
Adult	27.81	1.37	23.48	2.46	0.0001**

\*\*= Highly Significant (P<0.01)

(BMI < 25kg/m<sup>2</sup>: lean; BMI 25-30kg/m<sup>2</sup>: overweight; BMI > 30kg/m<sup>2</sup>: obese)

**Table 3:** Mean waist circumference and SD in PCOS

Group	With MS		Without MS		P value
	Mean WC	SD	Mean WC	SD	
Whole group	100.69	4.72	76.51	3.63	<0.000** (2.03485E-18)
Adolescent	101.35	4.39	72.21	3.77	<0.000**
Adult	100.32	4.94	72.76	3.53	<0.000**

\*\*= highly significant (p<0.01)

2.03E-18 = 2.03 X 10<sup>-18</sup> (0.000000000000000000203) can be interpreted as <0.000

**Table 4:** Age wise Distribution of metabolic syndrome in females with polycystic ovary syndrome

Age group	Total no of cases	Cases with MS	%
16-19	42	14	33.33
20-25	40	14	35.00
26-30	26	11	42.30
31-35	2	0	0

**Table 5:** HDL Levels (< 50 mg/dl)

Group	With MS		Without MS		p value	Hypothesis
	Number	%	Number	%		
Whole Group	37	94.87	18	25.35	0.453	A
Adolescent	14	100	6	21.42		
Adult	23	92	12	27.90		

p=0.453, A= accepts the null hypothesis

Null hypothesis (H<sub>0</sub>): The parameters evaluated in the study have no effect in diagnosis of MS

**Table 6:** TG Levels (>150 mg/dl)

Group	With MS		Without MS		p value	Hypothesis
	Number	%	Number	%		
Whole group	30	76.92	6	8.45	0.493	A
adolescent	11	78.57	2	7.14		
adult	19	76	4	9.30		

**Table 7:** TG/HDL Ratio

TG/HDL Ratio	Whole group		Adolescent		Adult	
	With MS	Without MS	With MS	Without MS	With MS	Without MS
0-2	0	2	0	2	0	0
2-3	1	55	0	22	1	33
3-4	13	13	2	4	11	9
4-5	16	1	8	0	8	1
5-8	9	0	4	0	5	0

**Table 8:** High Fasting Plasma Glucose Levels (>100 mg/dl)

Group	With MS		Without MS		p value	Hypothesis
	Number	%	Number	%		
Whole group	9	23.07	0	0	0.114	A
Adolescent	2	14.28	0	0		
Adult	7	28	0	0		

**Table 9:** High Systolic BP ( $\geq$ 130 mmHg) Levels

Group	With MS		Without MS		p value	Hypothesis
	Number	%	Number	%		
Whole group	15	38.46	3	4.22	0.194	A
Adolescent	5	35.71	1	3.57		
Adult	10	40	2	4.65		

**Table 10:** High Diastolic BP (>85 mmHg) Levels

Group	With MS		Without MS		p value	Hypothesis
	Number	%	Number	%		
Whole group	8	20.51	2	2.81	0.094	A
Adolescent	2	14.28	0	0		
Adult	6	24	2	4.65		

these lipids abnormalities with MS, low HDL-C levels are more commonly associated. In adolescent with MS 100% of cases were found to have low HDL level and in adult 92% was recorded. Dokras et al. [10] found low HDL-C in 63.7% and elevated TG in 46.8% of adult females. Bhattacharya et al. [9] also found Dyslipidemia to be more common than other abnormalities of MS. Both lipids are deranged in 64.7% of adolescents and 47.2% of adults.

Despite known associations between PCOS and glucose intolerance, the present study shows that abnormalities in both HDL-C (94.87%) and TG (76.92%) are more common than FPG (23.07%) in whole group with MS. Bhattacharya [9] found 97.3% of dyslipidemia in compare to 27.77% of FPG

abnormalities. Dokras et al. [10] also found 63.7% of low HDL-C and 46.8% high TG compare to 12.6% of FPG abnormalities. The common presence of lipid abnormalities over FPG abnormality emphasizes the greater importance of screening for dyslipidemia, rather than FPG alone, in females with PCOS.

In our study TG/HDL ratio more than 3 was found in 97.43% (38/39) PCOS females with MS compared to 19.71% (14/71) without MS. Dokras and colleagues [10] Study found that triglycerides/HDL-C levels were significantly higher in PCOS women with metabolic syndrome (median 5.9; 25<sup>th</sup>-75<sup>th</sup> percentiles: 4-7.5) compared with women with PCOS not having metabolic syndrome (median

**Table 11:** Distribution of features of MS according to IDF criteria

Parameters	Adolescents with MS		Adults with MS		P value	Hypothesis
	N	%	N	%		
All five features	0	0.00	1	4	-	-
Any 4 features	1	7.14	2	8	0.001**	R
Any 3 features	4	28.57	8	32	0.001**	R
Any 2 features	9	64.28	14	56	0.032*	R

\*\*= highly significant (p<0.01),

**Table 12:** Prevalence of abnormalities in females with polycystic ovary syndrome and metabolic syndrome (Chi Square test)

Parameters	Adults with MS		Adolescent with MS		p value	Hypothesis
	N	%	N	%		
Low HDL - C	23	92	14	100	0.453	A
High TG	19	76	11	78.57	0.493	A
Both Abnormal	17	68	11	78.57	0.0001**	R
FPG abnormality	7	28	2	14.28	0.114	A
Increased SBP	10	40	5	35.71	0.194	A
Increased DBP	6	24	2	14.28	0.094	A
Both Raised	4	16	2	14.28	0.003**	R

\*\*= highly significant (p<0.01),

R= reject null hypothesis, A = accept null Hypothesis

2.1; 25<sup>th</sup>-75<sup>th</sup> percentiles: 1.3-2.8, p < .01). Dokras et al. [10] revealed that triglycerides/ HDL-C more than 3.2 had high sensitivity and specificity.

As table 9 & 10 in present study shows SBP and DBP were raised in 38.46% and 20.51% in whole group with MS, Compared to 4.22% and 2.81% without MS respectively. Dokras and colleague [10] found 29.3% prevalence of high BP in female with PCOS. Bhattacharya [9] found raised SBP in 66.66% and high DBP in 40.74% in whole group with MS.

As table 11 among the five additional features of MS as per IDF criteria, none of the adolescents showed all five features whereas only one adult showed all five features. The majority of adolescents (64.28%) and adults (56%) showed the presence of two additional features. Dokras and colleague [10] also found that 2% had all five components, 8.1% had four components and 37.2% had three components. Bhattacharya [9] also found that 8.1% had all five features, 14.81% had four components, 35.18% had three components, 44.44% had two components.

It shows in the prevalence MS possibility of presence of four or five features of MS is lower than three and two features of MS. It is because Dyslipidemia is more common as the primary process of MS. As the disease progresses BP and FPG levels derange. That is why it is uncommon to get all five features of MS in PCOS patients, showing that identification of one risk factor in a

female with PCOS should prompt the clinician to search for others [9,10].

In table 12 abnormalities of HDL & TG together were found in 68% (17/25) of adults and 78.57% (11/14) of adolescents. The difference was statistically significant (p value =0.0001), and null hypothesis was rejected. Bhattacharya [9] also found 64.7% (11/17) of adults and 47.2% (17/37) of adolescents. It shows dyslipidemia is common in MS.

In present study both SBP & DBP were raised in 16% (4/25) of adults and 14.28% (2/14) of adolescent with MS. The difference was statistically significant (p value =0.003), and null hypothesis was rejected. Bhattacharya [9] also found 37.8% in adult and 23.5% in adolescent.

In our study FPG abnormalities were found in 28% of adult and 14.28% adolescents. Bhattacharya [9] found 35.1% in adult and 11.8% in adolescent. Dokras and colleague [10] found 12.6% of cases had elevated FPG levels.

In comparison with our study Kavita Mandrelle and colleagues [8] found 8.3% had impaired fasting glucose, high blood pressure of  $\geq 130/85$  mmHg was recorded in 20% cases. Dyslipidemia was present in 93.3% cases of PCOS with a low HDL (<50 mg/dL) being the commonest feature seen in 91.7% cases.

According to above discussion lipid abnormalities are more common than FPG, SBP and DBP in PCOS females with MS.

### Limitation

The present study also had limitations. No control group has been studied and it is a clinic-based cross sectional study. There is a need for prospective long-term well-controlled cohort studies, preferably starting from the teen ages.

There was also an inadequate number of published data from the Indian subcontinent using the IDF criteria (Bhattacharya [7]), so comparison of the present study's data to other research from this country was limited.

### Conclusions

Metabolic syndrome mostly asymptomatic at early stage but PCOS presents with overt symptoms of menstrual irregularity, infertility, hirsutism, and acne. These are the problems that bring women to health care providers. Their presence affords providers the opportunity to intervene early.

Present study highlights the need for comprehensive screening and educational programs for females with PCOS of all ages. Finding one risk factor should prompt the clinician to search for other risk factors. Though there are no guidelines for the best screening test or frequency with which to screen these females after the initial evaluation, the present study suggests that obese females with PCOS should be screened at frequent intervals and intervene early with counseling and, if needed, medications to alter the risk profile for later development of the metabolic syndrome.

Lifestyle modification in term of diet and exercises is the primary approach which has to be introduced in adolescence and practiced life long to get long term benefits.

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