

Correlative Association between Insulin Resistance and Consequences of Metabolic Syndrome among Female Patients with Polycystic Ovary Syndrome (PCOS) in Tripura: North East India

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Received: 25-02-2024 / Revised: 23-03-2024 / Accepted: 26-04-2024

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Conflict of interest: Nil

Abstract:

Background: Polycystic Ovary Syndrome or PCOS is one of the most prevalent disorders of endocrine metabolic system affecting women of reproductive age group. This disorder is specialized with hyperandrogenism, dysfunction of ovulation along with polycystic ovarian features. Both insulin resistance and metabolic syndrome have several overlapping features in PCOS that produce linking factors between both of the diseases. Here in this study we implicate it to search for the prevalence of insulin resistance and metabolic syndrome among women diagnosed with Polycystic Ovary Syndrome (PCOS) in the North Eastern part of India.

Aims and Objectives: To obtain the occurrence of insulin resistance and metabolic syndrome among women diagnosed with Polycystic Ovary Syndrome (PCOS) in North East India.

Materials and Methods: 100 female patients collected from Gynecology OPD diagnosed with PCOS were selected and observed for the presence of clinical and biochemical characteristics of metabolic syndrome. The duration of this study was from December 2018 to November 2020 in Tripura Medical College, Agartala, Tripura, India.

Results: Metabolic syndrome was associated with women with PCOS among 31% of cases. Among these, 93.5% had HDL level < 50 mg/dl; while 90.3% had fasting glucose \geq 100 mg/dl; 87% of women are associated with obesity and 69% PCOS women are accompanied with insulin resistance.

Conclusions: PCOS itself is highly associated with prevalence of insulin resistance and metabolic syndrome. Both blood glucose and lipid parameters should be frequently checked for screening of women with PCOS in the clinical laboratories to delay or prevent the long term consequences of metabolic syndrome.

Keywords: Insulin Resistance, PCOS, Metabolic Syndrome, HOMA-IR, Hyperinsulinemia.

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Introduction

The Polycystic Ovary Syndrome (PCOS) is considered to be the most prevalent disorder of endocrine system found among females of reproductive age that consists upto 15% worldwide. [1]

The clinical features of PCOS consist of acne, abnormal skin and facial hair growth and menstrual disturbances. [2] Though the causes of PCOS are not totally known, complex interactions between environmental and genetic factors are considered to play a role, turning it to be a multifactorial disease with various causes. [3] Insulin resistance (IR) is present among 70% of women with PCOS, 4 which is considered to be main causative factor, producing Hyperandrogenemia leading to menstrual disturbances. [5] It is also be presented

as the factor associating glucose intolerance, hypertension, obesity, coronary artery disease and lipid abnormalities seen in various women with metabolic syndrome. [6,7] There are many experiments that project the women with PCOS were usually associated with the consequences of metabolic syndrome. [8,9]

The comorbidity accompanied by metabolic syndrome causes PCOS as a risk factor for the early production of cardiovascular disease and type 2 diabetes mellitus.

Though PCOS itself is presented with various endocrinal, reproductive and metabolic consequences, there was lacking of studies being conducted among North Eastern population of India. So, our study was conducted to portray the

presence of insulin resistance, metabolic syndrome and PCOS in North Eastern population of India.

Aims & Objectives

To measure the efficacy of metabolic syndrome and insulin resistance and their correlation for the production of PCOS among women of North East India.

Material and Methods

The aforementioned study was cross-sectional and observational in nature conducted in the Department of Biochemistry in collaboration with Department of Obstetrics and Gynecology which consists of 100 women of the age group of 15-45 years, who were attending Gynecology OPD and were diagnosed with PCOS as per Rotterdam criteria (2003). PCOS was confirmed if 2 of the 3 particular conditions were fulfilled; a) ovulation abnormalities, b) hyperandrogenemia or c) 12 or more cysts or one ovary or ovarian volume >10 ml.⁴ All the patients were examined for the presence of clinical or biochemical features of metabolic syndrome as per modified NCEP ATP III criteria. Plasma insulin estimation was performed by using Calbiotech ELISA kit produced by Thermofisher Scientific. Plasma fasting glucose and serum lipid profile were estimated by Automated Analyzer Siemens ADVIA 2400. Fasting blood glucose levels were estimated by using glucose oxidase-peroxidase method, triglyceride levels were estimated by using enzymatic end point method, and HDL cholesterol level was calculated by cholesterol oxidase method. Insulin resistance was calculated by HOMA-IR (Homeostatic measurement assessment-Insulin Resistance) manually, depicted as fasting plasma insulin ($\mu\text{IU/ml}$) X fasting plasma glucose (mg)/405. Blood pressure was estimated in sitting position in left arm. Waist circumference was

measured while standing, measured midway between the iliac crest and lower ribs. Patients on dyslipidemia, ovulation inducing agents and oral contraceptives were excluded. Among others, patients with thyroid dysfunction and other metabolic and systemic diseases, diagnosed diabetes were also excluded in this study. Ethical clearance has been obtained from Research Ethics Board, Tripura.

Statistical analysis: Statistical analysis along with data entry was done by using SPSS version 21.0 software. Student's t test was used to obtain the association among continuous variables and metabolic syndrome of the subjects. P value of < 0.05 was considered as significant.

Results

31% of the study subjects consist of the features of the metabolic syndrome (Table 1 and Figure 1). 27.9 \pm 5.8 years are the mean age of the study group. Metabolic syndrome was considered to be more common among the age group of 15-35 years (31.3%) (Table 3 and Figure 2).

There is no significant association between age distribution and metabolic syndrome (Table 2). 80.4 \pm 8.6 cm was the mean waist circumference of the study group where women had significantly higher waist circumference (87.7 \pm 8.6 cm)(p value=<0.01) as compared to the women without metabolic syndrome. The women with metabolic syndrome had significantly higher (p value<0.01) systolic and diastolic (p value=0.009) blood pressure. Mean BMI of the study group was observed as 27.5 \pm 5.7. Higher BMI was observed among the women with metabolic syndrome (p value<0.01). 87% of the subjects were with obesity as compared to only 52.2% of the women without any essence of metabolic syndrome (Table 4 and Figure 3).

Table 1: Incidence of Metabolic Syndrome among PCOS women

Metabolic syndrome	Women with PCOS (n=100)	Prevalence %
Present	31	31%
Absent	69	69%

Table 2: Comparison between various variables in PCOS women with or without metabolic syndrome

Variables	Total (n=100)	With MBS (n=31)	Without MBS (n=69)	p-value
Age in years (mean \pm SD)	27.9 \pm 5.8	27.6 \pm 5.8	28 \pm 5.8	0.8
WC (cm) (mean \pm SD)	80.4 \pm 8.6	87.7 \pm 8.6	77.1 \pm 6.3	<0.01
FBS(mg/dl) (mean \pm SD)	93.7 \pm 13.9	106.9 \pm 9.9	87.7 \pm 11.2	0.008
FIN (m IU/L)	20.5 \pm 10.5	25.7 \pm 9.9	18.2 \pm 9.9	<0.001
HOMA-IR (mean \pm SD)	4.9 \pm 2.8	6.9 \pm 2.7	4 \pm 2.3	<0.001
SBP (mm Hg) (mean \pm SD)	123.7 \pm 12	130.7 \pm 9.1	120.9 \pm 11.7	<0.01
DBP (mm Hg) (mean \pm SD)	78.4 \pm 8	81.3 \pm 8.4	77.1 \pm 6.3	0.009
TG (mg/dl) (mean \pm SD)	119.2 \pm 37.4	146.4 \pm 29.6	107 \pm 34.1	0.0003
HDL (mg/dl) (mean \pm SD)	47.7 \pm 15.6	42.1 \pm 10	50.3 \pm 17.1	0.02
BMI (mean \pm SD)	27.5 \pm 5.7	30.5 \pm 5.7	26.2 \pm 5.2	<0.01

Table 3: Age distribution along with prevalence of metabolic syndrome in the women with PCOS

Age group	With metabolic syndrome	Without metabolic syndrome
15-30 years (n=67)	21 (31.3%)	46 (68.7%)
31-45 years (n=33)	10 (30.3%)	23 (69.7%)
Total (n=100)	31	69

Table 4: Correlative association of metabolic syndrome and Body mass index

BMI category	Metabolic syndrome		Total N=100
	Present (n=31)	Absent (n=69)	
Underweight (<18.5 kg/m ²)	1 (3.2%)	3 (2.8%)	4
Normal (18.5-22.9 kg/m ²)	1 (3.2%)	19 (8.8%)	20
Overweight (23-24.9 kg/m ²)	2 (6.4%)	11 (5.7%)	13
Obese (≥25 kg/m ²)	27 (87%)	36 (52.2%)	63

On examination of given biochemical parameters, the mean plasma sugar level of the study group was 93.7±13.9 mg/dl. The plasma glucose levels were significantly higher (106.9±9.9 mg/dl) in the women with metabolic syndrome as compared to women without metabolic syndrome (87.7±11.2 mg/dl) (p value=0.008). On the other hand, the mean level of plasma insulin was obtained to be significantly higher among these women (p value <0.001). Similarly, HOMA-IR index was significantly higher among the women with

metabolic syndrome (p value <0.001). The cut-off value for HOMA-IR index was considered as 2.5, above which patients were taken as insulin resistant. [10] this study also shows the serum lipid profile, mean serum HDL level of the study group was 47.7±15.6 mg/dl. Mean HDL level was obtained to be significantly lower among women with metabolic syndrome (42.1±10 mg/dl) (p value=0.02). Mean serum triglyceride level was found to be significantly higher among women with metabolic syndrome (p value=0.0003).

Table 5: Occurrence of various individual components of metabolic syndrome among PCOS women

Components of Metabolic syndrome	Subjects with metabolic syndrome	Subjects without metabolic syndrome
Waist circumference ≥ 88 cm	12 (38.7%)	7 (10.1%)
HDL < 50 mg/dl	29 (93.5%)	39 (56.5%)
TGL ≥ 150 mg/dl	17 (54.8%)	3 (4.3%)
Hypertension ≥ 130/85 mm Hg	12 (38.7%)	3 (4.3%)
FBS ≥ 100 mg/dl	28 (90.3%)	8 (11.5%)

While occurrence of each component of metabolic syndrome was explained (Table 5), the waist circumference exceeded 88 cm in 38.7%, while triglyceride levels were ≥150 mg/dl among 54.8%, HDL levels were <50 mg/dl among 93.5%, blood pressure was ≥130/85 mm Hg among 38.7% and fasting blood sugar levels were ≥100 mg/dl among 90.3% of all women accompanied by metabolic syndrome, 93.5% of women with metabolic syndrome also were suffered from insulin resistance while only 57.9% of these women

without metabolic syndrome had insulin resistance (Table 6).

On the other hand, Table 7 portrays the occurrence of individual metabolic syndrome criteria fulfilled by women associated with or without metabolic syndrome. 48.4% of the women with metabolic syndrome fulfilled at least 3 criteria and 50.7% of the women without metabolic syndrome fulfilled at least 1 criteria of metabolic syndrome.

Table 6: Occurrence of insulin resistance among PCOS women with MBS

Insulin resistance	PCOS with MBS (n=31)	PCOS without MBS (n=69)	Total (n=100)
HOMA ≥ 2.5	29 (93.5%)	40 (57.9%)	69
HOMA < 2.5	2 (6.4%)	29 (42%)	31
Total	31	69	100

Table 7: Total No of individual criteria of metabolic syndrome fulfilled by the women associated with or without metabolic syndrome

No. of criteria fulfilled	PCOS with metabolic syndrome (n=31)	PCOS without metabolic syndrome (n=69)
5	2 (6.5%)	0
4	14 (45.1%)	0

3	15 (48.4%)	0
2	0	10 (14.5%)
1	0	35 (50.7%)
0	0	24 (34.7%)

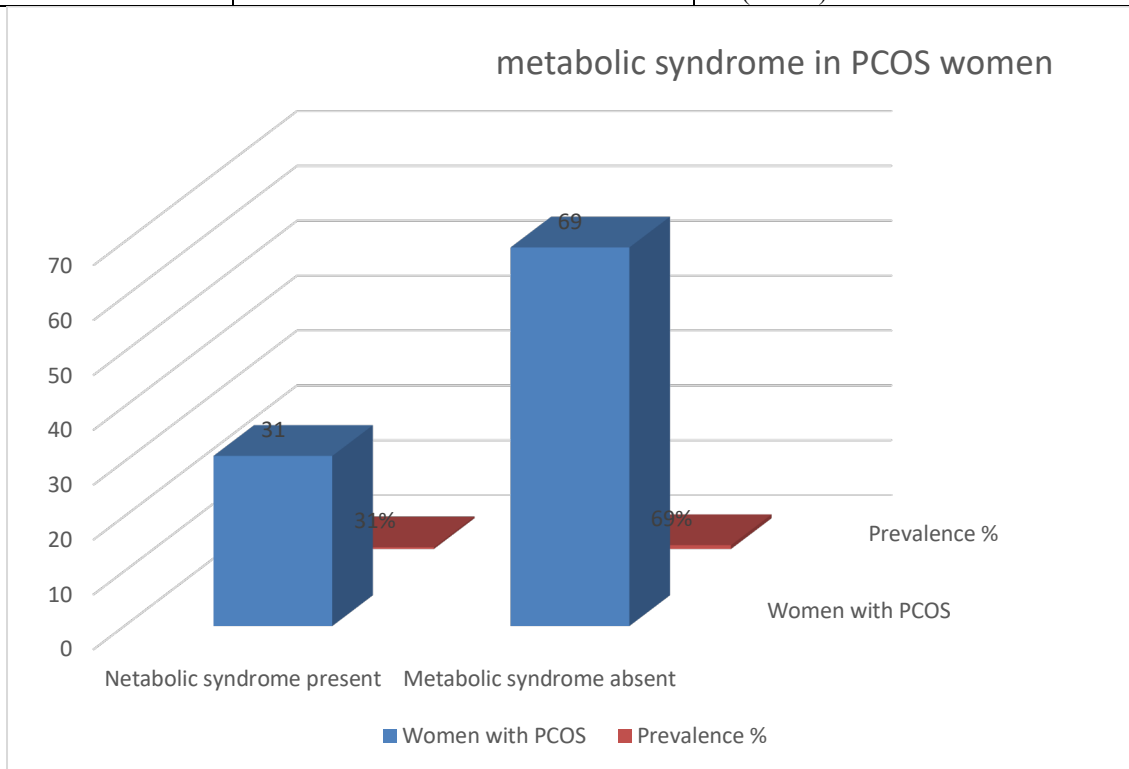


Figure 1: Prevalence of Metabolic Syndrome in PCOS women

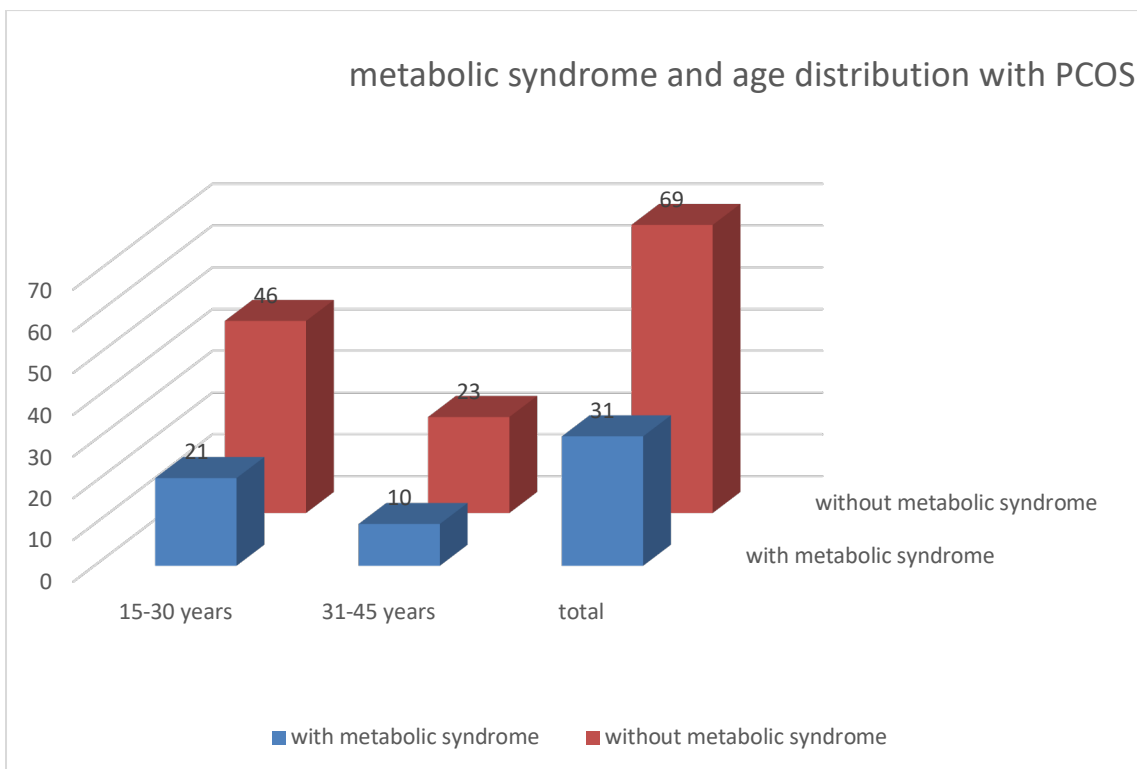


Figure 2: Prevalence of metabolic syndrome and age distribution among women with PCOS

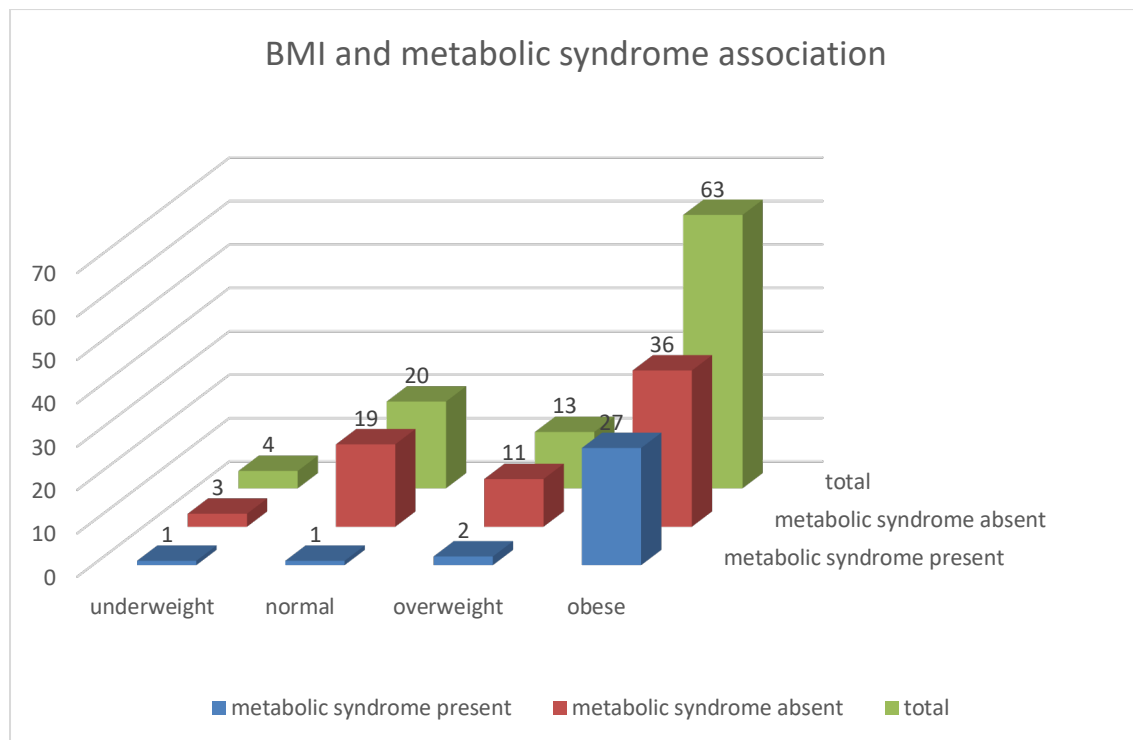


Figure 3: Association of Body mass index with metabolic syndrome

Discussion

Here in this study 100 PCOS diagnosed women were examined for the presence of biochemical or physical features of metabolic syndrome as per NCEP ATP III criteria which classifies metabolic syndrome as per the presence of at least three of these five criteria; 1) central or abdominal obesity with waist circumference ≥ 88 cm, 2) serum triglycerides ≥ 150 mg/dl, 3) serum HDL cholesterol < 50 mg/dl, 4) BP $\geq 130/85$ mm Hg and 5) fasting blood sugar (FBS) ≥ 100 mg/dl. [11] 31% of the PCOS patients fulfilled the criteria of metabolic syndrome in this study.

This finding is similar with the study conducted by Kaur J et al (37%), Mandrelle et al (37.5%) and Kar S et al (37.5%). [12-14] The study conducted by Vietnamese PCOS women by Le MT et al; projects the prevalence rate of 10.4% only. [15] The main causative reasons for this difference may be due to ethnic background, diet, different lifestyle, methods used for definition of metabolic syndrome and variation among the study population. In this study it has been shown that women between age of 15-30 years have the higher occurrence of metabolic syndrome (31.3%) as compared to 30.3% of the age group of 31-45 years. But this difference is not statistically significant here. On the contrary, the study done by Dey R et al found the occurrence of metabolic syndrome to be more in the age group of 31-45 years. [16] Mean waist circumference in the patients with metabolic syndrome was obtained higher than those without it. Waist circumference \geq

88 cm is considered to be one of diagnostic criteria for metabolic syndrome and was obtained among 38.7% of patients with metabolic syndrome. This study is similar with the study conducted by Sheena Solti et al and Indu et al who observed similar findings among 37.8% and 37.3% of their study cohorts respectively. [17-18] this study also depicts that the patients without metabolic syndrome had mean systolic blood pressure of 120.9 ± 11.7 mm Hg as compared to women with metabolic syndrome which has higher systolic blood pressure (130.7 ± 9.1 mm Hg). This difference was statistically significant.

Diastolic blood pressure was also significantly higher among the women with metabolic syndrome (p value=0.009). This is similar to the study conducted by Indu NR et al; [18] that portrayed a significantly higher systolic and diastolic blood pressure in the women with metabolic syndrome. The mean BMI of this study was 27.5 ± 5.7 . Mean BMI was higher among both groups than the recommended specific cut off values.

Women with metabolic syndrome had significantly higher BMI levels compared to those who didn't have metabolic syndrome. 87% of the patients with metabolic syndrome also have obesity, which is similar to other studies. [16-19] In case of PCOS women with obesity, hyperandrogenemia and hyperinsulinemia may cause the development of PCOS and metabolic syndrome both. [18] As per the biochemical parameters, insulin, fasting blood sugar and the HOMA-IR were significantly higher in women with metabolic syndrome compared to

those without it. These findings are similar to the study conducted by Dey R et al. [16] Analysis of lipid parameters also projected significantly lower HDL levels and higher triglyceride levels among women with metabolic syndrome. As per the metabolic syndrome defining criteria, HDL cholesterol was <50 mg/dl in 93.5%, waist circumference was ≥ 88 cm in 38.7%, blood pressure was $\geq 130/85$ mm Hg in 38.7% and triglyceride levels were ≥ 100 mg/dl among 90.3% of all women with metabolic syndrome.

This study is similar to the study conducted by Dey R et al [16] in which HDL cholesterol was < 50 mg/dl in 50%, triglyceride levels were ≥ 150 mg/dl in 40%, waist circumference was ≥ 88 cm in 34%, blood pressure was $\geq 130/85$ mm Hg in 50% while fasting blood sugar levels were ≥ 100 mg/dl in 16% of women with presence of metabolic syndrome. 93.5% of women with metabolic syndrome are also associated with positive insulin resistance as compared to 57.9% of the patients without metabolic syndrome. As per table 7, 48.4% of the women with metabolic syndrome had at least 3 criteria fulfilled while majority of women without metabolic syndrome fulfill at least 1 criteria of metabolic syndrome (50.7%). This study is similar to the study conducted by Le MT et al [15] that found 69.7% of women with metabolic syndrome fulfilled at least 3 criteria for it.

Conclusion:

This study consists of 100 women with PCOS portrays the high percentage of association with metabolic syndrome (31%). Most of them had high fasting glucose levels (90.3%), low HDL levels (93.5%) and high TG levels (54.8%) which can put the patients at high risk of metabolic syndrome and its morbid consequences. Since there was a high association of metabolic syndrome in the reproductive age here, there is an urgent need for query of PCOS cases beside the reproductive outcomes. Insulin resistance was present among 93.5% of the women with metabolic syndrome and in 57.9% of the women without metabolic syndrome. Since insulin resistance was observed in 69% of the women associated with PCOS, with presence or absence of metabolic syndrome, we suggest the inclusion of insulin resistance as a part of diagnosis criteria of PCOS itself.

As PCOS is associated with many features of metabolic syndrome, we suggest full investigations of biochemical parameters especially of TG, sugar and HDL levels to be conducted among women with PCOS for predisposition to metabolic syndrome. The major limitations of this study were it has been done with a relatively small sample size, without a sizeable control group without any comparison of various phenotypes produced by PCOS women. We have not measured insulin

resistance by using euglycemic hyperinsulinemic clamp, the gold standard method for diagnosing insulin resistance. We have used HOMA-IR instead because it is less cumbersome and more convenient. So further experiments with various phenotypes associated with larger sample size with a suitable control group would be helpful for better comprehension of the potential ground for the progression of metabolic syndrome among women with PCOS.

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