Association of Polycystic Ovarian Syndrome with Metabolic Disorders

Saba Khan, Sana Rehman, Geeta Chughani, Memoona Rehman, Erum Majid, Farheen Amir, Khadija Bano

ABSTRACT

Objective: To determine the association of Metabolic Disorders in women of reproductive age with polycystic ovarian syndrome (PCOS)

Study Design and setting: Cross Sectional Study conducted in the Department of Gynecology and Obstetrics, Ward 9, Jinnah Postgraduate Medical Center, Karachi.

Methodology: The study was conducted from November 2021 to February 2022. A total of 227 diagnosed patients of PCOS were included in this study. Five components of Metabolic syndrome were assessed: Body Mass Index (BMI), blood pressure, central obesity, fasting blood sugar and lipid profile. Informed consent was obtained from all participants. Patients' history, physical examination and laboratory investigations in terms of symptoms and findings relating to MS were recorded and assessed using SPSS version 21. Descriptive statistics were calculated and stratification was done. Chi-square test used post stratification and p-value =0.05 were considered significant.

Results: Mean age was 27.05±4.51 years. Mean symptom duration was 11.26±3.02 months. Central obesity, hypertension, hypertriglyceridemia, HDL-cholesterol <50 mg/dl and fasting glucose >100 mg/dl were found in 44.9%, 31.7%, 38.3%, 27.3%, and 38.8% patients, respectively. A total of 47 (20.7%) study subjects were identified with two or more above components of MS. Significant association of MS with age (>27 years; p<0.000) and duration of disease (>12 months; p<0.000) was observed.

Conclusion: A higher prevalence of MS was observed when participants aged more than 27 years and had symptoms for more than a year. Higher BMI was also found nearing statistical significance.

Keywords: Central obesity, Hypertension, lipid profile, Metabolic Syndrome, Polycystic Ovarian Syndrome

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INTRODUCTION:

Polycystic ovary syndrome (PCOS) is one of the most common reproductive health problems and endocrine disorders afflicting approximately 5-8% of premenopausal women. [1,2] Recently, a local study has quoted the prevalence of PCOS among Pakistani women as 52%.[2] It is associated with a broad range of clinical presentation including hirsutism, menstrual irregularities and infertility. Most women with PCOS have hyperandrogenemia, elevated luteinizing hormone (LH) and normal or decreased follicle stimulating hormone.[2]

PCOS is characterized by insulin resistance and compensatory hyperinsulinemia and women are often over weight. Furthermore, it is associated with dyslipidemia, systolic hypertension and hyper fibrinogenaemia. Thus women are at an increased risk of type 2 diabetes mellitus, gestational diabetes, atherosclerosis and other risks. [3] Overall, it is believed that both PCOS and metabolic syndromes are common in reproductive-aged women in the general population and that there is a substantial overlap between them. [4,5]

In the present study, PCOS is defined based on the Rotterdam classification (ESHRE/ASRM), 2003 [6] and MS is defined based on the International Diabetes Federation (IDF) definition

(Fig. 1). [7]

Rotterdam Classification of PCOS include two of the following three criteria:

1. Oligo/or anovulation

2. Clinical and /or biochemical signs of hyperandrogenism

3. Polycystic ovaries on Ultrasound exam

Metabolic syndrome (MS) is another cluster of endocrine disturbances with similar adverse outcomes as PCOS. Metabolic syndrome (MS) is a constellation of cardiovascular risk factors, including impaired fasting glucose, central obesity, dyslipidaemia and raised blood pressure (Figure.1)[1,2,5] Its clinical significance, although still debatable, lies in the fact that MS may predict a higher risk for cardiovascular events than the sum of the risks imparted by its individual components. According to one careful estimate, around 25% of world population has symptoms clearly indicative of MS. [7] Not surprisingly; untreated MS increases the risk of coronary and cerebro-vascular complications including death. MS in the presence of Type 2 Diabetes Mellitus and uncontrolled obesity further compounds the risk of long term disability as well as increases risk of mortality at an early age among the untreated population. [2, 7] Therefore, it is extremely important that risk factors of MS be identified in target populations like women with PCOS to reduce their incidence of adverse life events due to these risk factors. Researchers have identified Insulin resistance (IR) as the common denominator present in these abnormalities. [1, 2] MS has exponentially increased in prevalence during the last few years and women have seen a particularly larger share of this increase, especially in the younger age group.[5, 8, 9] The rationale of this study is to determine the frequency of MS in patients with PCOS in order to establish the local perspective as there is paucity of local data. In a recent study, the prevalence of PCOS was found to be higher in Pakistani women (52%) than among Western Caucasian women (20%–25%) in the UK.[2, 9] Therefore, the current study is planned to ascertain the prevalence and to identify it through regular screening of suspected patients to prevent adverse outcome.

METHODOLOGY:

This cross sectional study was carried out from mid-November 2021 to February 2022. A total of 227 diagnosed patients of PCOS (Rotterdam Criteria) [1,6] were recruited for this study. All had the diagnosis established for more than 6 months, or had history of repeated miscarriages or infertility and were not on any medication.

Patients were excluded from our study when their presenting symptoms did not meet the criteria for diagnosis of PCOS, or they were on various medications for other endocrine or systemic illness.

Five components of MS were assessed: Body Mass Index (BMI), blood pressure, central obesity, fasting blood sugar levels and lipid profile. Before the actual data collection, study design and data collection protocols were approved by the Institutional Review Board (IRB) via letter NO.F.2-81/2021-GENL/3727/JPMC. Informed consent was obtained from all participants in a language they could fully understand. Patients were reassessed for their suitability for the study in terms of the diagnosis of PCOS and presence of symptoms. Patients' history, physical examination and laboratory investigation in terms of symptoms and findings relating to MS were recorded and assessed using SPSS version 21. Descriptive statistics were calculated and stratification was done. Chi-square test used post stratification and p-value =0.05 were considered significant.

The sample size was estimated by considering the prevalence of MS in PCOS as 18% [10], margin of error as 5% and Confidence Interval (C.I.) as 95%. Sample size was calculated to be 227. Non probability consecutive sampling was used for the study.

RESULTS:

A total of 227 patients were included in the study with mean age of 27.05±4.51 years. The mean duration of disease of study subjects was 11.26±3.02 months. Mean height, weight and BMI of study subjects was 147.06±7.85 cm , 52.26±6.75 kg and 24.34±3.81 kg/m^2, respectively. Patients with BMI=25 kg/m^2 were considered as overweight. The mean waist circumference of study subjects was 76.92±6.71cm. The mean systolic and diastolic blood pressure of study subjects was 115.88±14.24 mmHg and 75.60±8.49 mmHg, respectively. The mean triglycerides, HDL-cholesterol and fasting plasma glucose of study subjects was 147.64±22.10 mg/dl, 56.50±10.46 mg/dl and 99.03±20.06 mg/dl, respectively.

We determined the frequency of MS in 47 patient as represented by figure 2. Stratification with respect to age, duration of disease and BMI was done to observe effect of these modifiers on outcome i.e. metabolic syndrome. P-value =0.05 was considered as significant. Metabolic syndrome was associated significantly with higher age (p=0.000) and duration of disease (p=0.000). The detailed results of frequency and associations are presented in Table1.

In our study, central obesity was seen in 102(45%) patients followed by fasting glucose (>100mg/dL) in 88 (39%).Figure 3 represents distribution of various features associated with MS.

DISCUSSION:

The present study showed a high prevalence (47; 20.7%) of MS in PCOS. During the last decade, the prevalence of MS has increased in the general population – and this increase has been steeper in women, particularly in young ones.[2,5,9]

A cross sectional study done at the Gynecologic Endocrinology Unit in Bangkok enrolled 250 PCOS Thai women who were diagnosed using Revised Rotterdam 2003

Figure-1: Definition of Metabolic Syndrome for women (IDF criteria)

Central Obesity plus any two of the below four factors defined as Metabolic Syndrome (MS)	
Raised Triglycerides	>150 mg/dl
Low HDL	<50 mg/dl in women
High Blood Pressure	Systolic BP>130 or Diastolic >85 mmHg
High Fasting Blood Glucose	>100 mg/dl

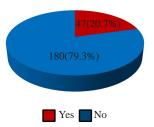Figure 2: Frequency of metabolic syndrome (n=227)

Table – 1: Frequency and Association of Metabolic Syndrome with Age, Duration of Disease and Body Mass Index (n=227)
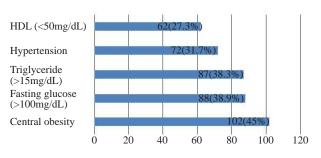
Factor	Metabolic syndrome		Total	P-value
	Yes (n=47)	**No** (n=180)		
AGE				
=27 years	12 (8.9%)	123 (91.1%)	135	P<0.000*
>27 years	35 (38%)	57 (62%)	92	
Total	**47**	**180**	**227**	
Duration Of Symptoms				
=12 months	14 (9.2%)	138 (90.8%)	152	P<.000*
>12 months	33 (44%)	42 (56%)	75	
Total	**47**	**180**	**227**	
Body Mass Index				
<25	13 (14.6%)	76 (85.4%)	89	P<0.069*
=25	34 (24.6%)	104 (75.4%)	138	
Total	**47**	**180**	**227**	

Chi Square Test was applied.
P-value = 0.05 considered as significant.
* Significant at 0.05 levels.

Figure 3: Distribution of observed features of Metabolic Syndrome (MS) in The Study Population (227) Of PCOS Patients

criteria and found the prevalence of MS by the definitions of NCEP ATP III to be 18.0%.[10] Several international studies showed variable frequencies. Deswal et al. in a meta-analysis of well conducted studies from around the world found the prevalence of PCOS based on the Rotterdam Criteria to be between 2.2% and 22.5%.[11] Brazilian and Chinese studies found the prevalence to be 28.4% and 24.9%, respectively.[12,13] Mandrelle et al and a German study found a prevalence of 37.5% and 33.8%, respectively.[14,15] A meta-analysis looking at the risk of MS in PCOS patients and controls concluded that there was a 2 fold risk of diagnosis of MS in women diagnosed with PCOS as compared with healthy controls.[1] Another study by Cheung et al. concluded that there is a five-fold increased risk of developing MS in women with PCOS.[13] Both PCOS and MS are closely related entities producing significant effect on fertility and having profound influence on cardiovascular morbidity and endocrine functioning.[1,5]

This persistent increase in the prevalence is a major concern due to the potential of adversely affecting cardiovascular health profile in terms of its morbidity and mortality in women. The Metabolic derangements are more obvious in obese as compared to non-obese PCOS counterparts.[2,13]

In the present study the relationship between a higher BMI (>25) does not reach statistical significance (table 2; p<0.069), but does show an obvious increased (1.5-fold) clinical association of a higher BMI with MS. This could be because of a smaller sample size of this study. Various studies[16,17] have identified that Metabolic Syndrome and its individual features are quite common among patients with the BMI on the higher side. In contrast, Akram and Roohi[9] and Shanmugham et al.[17] have reported obesity in only a third of their study patients. This finding can be interpreted as a normal variance in the incidence of obesity in different geographical regions and the social norms associated with weight of a person.[2,7]

The National Diabetes Survey of Pakistan (NDSP) reported the prevalence rate of obesity among PCOS patients as 62.1% during the years 2016-2017.[18]

This high prevalence of obesity may be responsible for the increased frequency of MS in our study population. So it is understood that MS is a common finding in obese women. However, obesity is only one of the putative denominators of MS, as the others are linked to the individual's metabolic susceptibility.[17]

The polycystic ovary syndrome (PCOS), the commonest endocrinopathy of women, has been associated with such a metabolic susceptibility, mainly attributable to the recognized association of the syndrome with insulin resistance (IR). Insulin resistance, as well as central adiposity, appears to affect not only obese but also lean PCOS women. Therefore, these women may be predisposed to develop MS, independently of obesity *per se*.[1 - 4, 17, 18]

An exhaustive meta-analysis by Hallajzadeh et al [1] reported the prevalence of MS in PCOS as 37.9% and 47.5%, utilizing the NCEP III and IDF criteria, respectively. In the same NCEP III criteria a BMI in excess of 32 kg/m^2 was used as a surrogate for a waist circumference greater than 88 cm.

In our study obesity incidence was reported as 44.9% (Table 3; 102 patients) and mean waist circumference was 76.92±6.71cm (65-98 cm).

An increased waist circumference is typically highly correlated with hyper-insulinemia and is thought to reflect an increase in the proportion of total body fat that is deposited in the visceral compartment compared with the subcutaneous space. [2, 8, 19]

In our study raised fasting blood sugars of more than 100mg/dl was seen in 88 patients i.e. 30.8%. Women with PCOS are at an increased risk of developing dysglycemia due to Insulin resistance (IR). [2, 8] However, in contrast to our findings, Amato et al. noted impaired fasting glucose/T2DM in 12% of women with PCOS. [20] The observed diversity may be due to the variance in the prevalence of diabetes in different parts of the world due to various factors like dietary habits, culture of physical exercise and pre-diabetic surveillance.

Forty seven (20.7%) out of 227 patients of PCOS had at least one component of MS at presentation (Table 1). Of the individual metabolic components of MS, the most prevalent in women with PCOS was decreased serum high-density lipoprotein (HDL) cholesterol level (27.3%) followed by obesity (44.9%) and hypertension (31.7%). Out of the total study population (227 patients), 38.3 % had raised Triglycerides (Table 3). In our study, high triglycerides contributed more as compared to low HDL (27.3%) to MS. Similarly, Celik et al.[21] revealed significantly high triglyceride levels in PCOS women as compared to control.

In our study one third (72; 31.7%) of the participants with PCOS were hypertensive, and similar finding was observed in other studies.[1,2,7,9] In contrast to our finding, one study reported the frequency of hypertension in only 10.7% of study participants.[22] This disparity in data is reflective of varied lifestyles, dietary habits and medication use in different study populations representing different geographical areas.

In the present study we found a statistically significant association of MS with increasing age (p<0.000). MS was seen in 35 out of 92 patients (38%) of age above 27 years as compared to 8.9% in women less than 27 years (Table 2). Recent studies also reported a higher age group (above 25 years) having a higher incidence of MS in women attending infertility clinics due to PCOS. [2, 18]

In a recent study from Brazil (2020) a higher incidence of MS was reported among women with a median age 25 (21-29) and with a median BMI of 28.7. These results are in agreement with our results (Table 2). [22] It was also observed that longer the duration of symptoms of PCOS, the higher was the incidence of MS (Table 2). When the duration of PCOS was more than 12 months the prevalence of MS was 44% (33 patients) in comparison to 9.2 % when the duration of symptoms was less than 12 months.

There are some limitations to this study. The present study included a single-center experience and nonrandomized study design. It was conducted with small sample size and in an urban environment therefore, the results might not be generalizable to larger populations.

CONCLUSION:

A high frequency of MS (n=47; 20.7%) was observed in women of higher age group having a BMI above 25 and with longer duration of symptoms (>12 months) of PCOS. The findings support the inference that PCOS should be considered a general health disorder with serious public health implications and indicate that physicians should comprehensively screen all women with PCOS for the metabolic syndrome to avoid adverse health outcomes.

Authors Contribution:
Saba Khan: Concept, Design
Sana Rehman: Interpretation of data
Geeta Chughani: Design, interpretation of data
Memoona Rehman: Concept, analysis
Erum Majid: Design
Farheen Amir: Analysis
Khadija Bano: Final approval, concept

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