



PREVALENCE OF METABOLIC SYNDROME AND IT'S COMPONENTS AMONG WOMEN WITH POLYCYSTIC OVARIAN SYNDROME

Gynaecology

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ABSTRACT

Introduction : The objective of this study was to provide an estimate of prevalence of metabolic syndrome and it's components among women with Polycystic ovarian syndrome in Eastern India.

Material and methods : The present study assessed the clinical, anthropometric and hormonal parameters including prevalence of metabolic syndrome in the patients with PCOS.

Results : The overall prevalence of metabolic syndrome according to the modified AHA/NHLBI ATP III (2005) criteria was 35%. 6.25 % cases were detected to have diabetes mellitus, 8.75% had impaired fasting glucose, and 8.75% had an impaired glucose test. Dyslipidemia was present in 70% cases of PCOS. Among all the risk factors, age and waist hip ratio ≥ 0.85 were strongly associated with the presence of metabolic syndrome.

Conclusion : women with PCOS, particularly those with age ≥ 25 years or with central obesity (a waist hip ratio of ≥ 0.85), are at a higher risk of developing metabolic syndrome and should be offered screening tests.

KEYWORDS

Metabolic syndrome, waist hip ratio, polycystic ovary syndrome, dyslipidemia.

INTRODUCTION

Polycystic ovary syndrome (PCOS) is the most complex and common endocrine disorder affecting 5 – 10 % of women in reproductive years[1]. In addition to irregular menstrual cycles, chronic anovulation, hyperandrogenism, and infertility, it has many metabolic manifestations such as dyslipidemia, hyperinsulinemia, insulin resistance, hyperglycemia, increased risk of cardiovascular disease or possibly endometrial cancer, which can be present in both lean and obese women with PCOS, and is associated with metabolic syndrome strongly.[2,3,4]

Metabolic syndrome is another group of endocrine disorder including insulin resistance, dyslipidemia, obesity, and hypertension.[5] It is associated with a two-fold increased risk of cardiovascular disease and a five-fold increased risk of type 2 diabetes.[6]

The original National Cholesterol Education Programme – Adult Treatment Panel III (NCEP – ATP III) criteria in 2001 defines metabolic syndrome as the co-occurrence of three or more of the following risk factors (i) central obesity with waist circumference ≥ 88 cm in women, (ii) elevated systolic and/or diastolic blood pressure of $\geq 130/85$ mmHg, (iii) impaired fasting serum glucose ≥ 110 mg/dL, (iv) elevated fasting serum triglycerides ≥ 150 mg/dL, and (v) fasting high-density lipoprotein (HDL) cholesterol < 50 mg/dL.[7]

The main changes in the modified American Heart Association/National Heart Lung and Blood Institute definition (ATP III 2005) include (i) defining the ethnic-specific difference in central obesity by using the World Health Organization recommendation for waist circumference ≥ 80 cm in Asian women, and (ii) and reducing the threshold for impaired fasting glucose to 100 mg% in accordance with the American Diabetes Association revised definition.[6]

The prevalence of metabolic syndrome in polycystic ovary syndrome has been studied in different populations. Reported prevalence is 43% in U.S., 28.4% in Brazil, 24.9% in Hong Kong Chinese women, and only 1.6% in Czech women.[8,9,10,11]

This data from different studies indicate the need for evaluation of metabolic syndrome in different populations, to help in planning screening strategies to prevent long-term effects.

Therefore, the aim of our study was to estimate the prevalence of metabolic syndrome in women with PCOS presenting to our hospital.

MATERIAL AND METHODS

A prospective cross-sectional study was done on 80 women with PCOS who were being evaluated for infertility in a hospital over a period of 18 months. The diagnosis of PCOS was based on the 2003 Rotterdam consensus (the Rotterdam European Society for Human Reproduction and Embryology (EHSRE)/American Society for Reproductive Medicine (ASRM) – sponsored PCOS consensus workshop group) with at least two of the following features: (i) oligo-

ovulation or chronic anovulation, (ii) clinical and/or biochemical hyperandrogenism, and (iii) ultrasound appearance of polycystic ovaries. Other etiologies that could mimic PCOS were excluded by doing appropriate blood tests and clinical suspicion (late onset congenital adrenal hyperplasia, adrenal tumors and Cushing's syndrome). Women with steroid or oral contraceptive drug intake in the preceding 3 months were also excluded from the study.

Metabolic syndrome was defined according to the modified American Heart Association/National Heart Lung Blood Institute AHA/NHLBI (ATP III 2005) definition. It was diagnosed if at least three of the following five features were present (i) waist circumference of ≥ 35 inches (ii) blood pressure of $\geq 130/85$ mmHg (iii) fasting blood sugar of ≥ 100 mg/dL (iv) triglycerides of ≥ 150 mg/dL, and (v) HDL of ≤ 50 mg/dL.

The length of the menstrual cycles; personal and family history of diabetes; hypertension; obesity; and ischemic heart disease was documented. Anthropometric measurements included a waist circumference and the hip circumference in centimeters. Height was recorded in centimeters and weight in kilograms. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters (kg/m^2). Blood pressure was measured after a 5-min rest using a standard Sphygmomanometer. Signs of androgen excess (acne, hirsutism and alopecia) and signs of insulin resistance were noted in the physical examination. Overnight fasting blood sample and a 75 g oral glucose tolerance test obtained in all the women. Impaired fasting glucose, impaired glucose tolerance test, and diabetes were defined in accordance with the American Diabetes Association revised definition. Blood tests also included a thyroid stimulating hormone (TSH) level, total testosterone and a fasting lipid profile, which included total cholesterol, triglycerides, HDL, and low-density lipoprotein levels.

Patients in whom the complete panel of physical examination, ultrasound, and laboratory data for the classification of PCOS and metabolic syndrome was available were considered for the analysis.

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.

Study was conducted according to the modified AHA/NHLBI (ATP III 2005) criteria for the metabolic syndrome. The prevalence of metabolic syndrome has been reported to be 46.2% in Indian women with PCOS according to the International Diabetes Federation criteria.[14] Women were enrolled in the study only after an informed and written consent.

RESULTS

A total of 80 consecutive women with PCOS were recruited. The prevalence of metabolic syndrome was found to be 35% in the study

population. Three features were present in 23% cases, four features in 9% cases, and all five features were present in 3% cases.

The age of the women in our study ranged from 18 to 38 years with a mean age of 26.05 years SD $\pm$ 4.75. The prevalence of metabolic syndrome increased with age as shown in **Table 1**. The mean age of women was significantly higher in women with metabolic syndrome than those without metabolic syndrome (29.33 $\pm$ 5.40 vs. 23.75 $\pm$ 2.84, P value <0.001) [**Table 3**].

Majority of them (83.7%) presented with primary infertility while the rest had secondary infertility. Mean duration of infertility was 1 year to 15 years. Except for 3.75% cases who had regular menstrual periods, most of the study cases had menstrual irregularity with 86.25% having oligomenorrhea and 10% with amenorrhea.

A family history of diabetes mellitus was present in 32.5% cases, hypertensive disorders in 28.75%, family members with obesity in 21%, and a history of ischemic heart disease in the family in 10%.

Mean BMI in the study group was 26.55 kg/m² with a range of 18.6 to 40 kg/m². We found that the prevalence of metabolic syndrome increased with increasing BMI [**Table 2**]. The mean BMI in those with metabolic syndrome was significantly higher than those without metabolic syndrome (29.03 $\pm$ 4.1 vs 24.02 $\pm$ 3.2) [**Table 3**]. A waist-hip ratio of ≥ 0.85 was found in 46.25% cases. The mean waist-hip ratio was significantly higher in those found to have metabolic syndrome than in those without metabolic syndrome (0.87 $\pm$ 0.05 vs 0.81 $\pm$ 0.05, P value <0.05) [**Table 3**].

Clinical features of hyperandrogenism such as hirsutism was present in 28.75%, and acne in 7.5%. Acanthosis nigricans was seen in 16.25% cases. A significantly greater number of patients had hirsutism (43% vs 21%) and acanthosis (28.5% vs 9.6%) in those with metabolic syndrome than in whom metabolic syndrome was not present. The calculated free testosterone level was also higher in those with metabolic syndrome than those without the syndrome (1.93 $\pm$ 0.5 vs 1.60 $\pm$ 0.50) [**Table 3**]. As hirsutism and free testosterone levels are markers of hyperandrogenism and acanthosis nigricans for insulin resistance, it was found that both hyperandrogenism and insulin resistance were strongly associated to metabolic syndrome.

A total of 6.25% cases were detected to have diabetes mellitus, 8.75% had impaired fasting glucose, and 8.75% had an impaired glucose test. High blood pressure of $\geq 130/85$ mmHg was recorded in 25% cases. Dyslipidemia was present in 70% cases of PCOS with a low HDL (<50 mg/dL) being the commonest feature seen in 67.5% cases. Among all the risk factors, age and waist-hip ratio ≥ 0.85 were strongly associated with the presence of metabolic syndrome.

DISCUSSION

Metabolic syndrome is characterized by three main interrelated abnormalities: elevated plasma glucose, dyslipidemia, and elevated blood pressure along with obesity, which directly contribute to a pro-thrombotic and pro-inflammatory state, predisposing to the development of atherosclerotic cardiovascular disease and type 2 diabetes mellitus.[6] Hyperinsulinemia and insulin resistance are the common underlying metabolic abnormalities seen in PCOS and metabolic syndrome. Insulin resistance with elevated circulating insulin levels induces unfavorable changes in the lipid metabolism and increased androgen production from the theca cells. Androgen excess may support the presence of an unfavorable metabolic state leading to dyslipidemia and central distribution of fat (android pattern). In obese women, excess insulin and androgens may contribute to the development of the PCOS and metabolic syndrome.[12] The android pattern of fat distribution may be the result as well as the cause of hyperandrogenism, setting up a vicious circle of hyperinsulinism, hyperandrogenism, central adiposity, and metabolic abnormalities.[13]

The present study shows that the overall prevalence of metabolic syndrome in women with PCOS presenting with infertility is 35%. In comparison, a study done on Indian women, which included both adolescent as well as adult women with PCOS, reported a prevalence of 46.2% by the International Diabetes Federation criteria.[14] A recent consensus definition incorporating IDF and AHA/NHLB (2004) risk factors has been introduced.[15] The main modification in the consensus definition is the incorporation of elevated waist circumference according to population and country-specific cut-offs

(for Asian women, waist circumference >80 cm). The main finding of our study (prevalence of metabolic syndrome in PCOS women with infertility - 35%) remains unchanged even after applying the new consensus definition.

Earlier studies have suggested that certain phenotypes of PCOS women have a higher risk of developing metabolic syndrome and consequently long-term risk of cardiovascular disease/type 2 diabetes mellitus.[16] The prevalence of metabolic syndrome has been found to be higher in weight-matched PCOS women compared to non-PCOS women.[17]

Hahn *et al.* established a prevalence of metabolic syndrome of 33.8% in German women with PCOS (International Diabetes Federation criteria) and found that the prevalence rate increased with obesity and age.[18] In a study on Brazilian women with PCOS, the prevalence of metabolic syndrome was found to increase with BMI: 3.2%, 19.2%, and 52.3% for normal, overweight, and obese women, respectively.[9] In our study, the prevalence of metabolic syndrome also increased with both age and BMI as shown in Tables 1 and 2.

In the present study, 6.25% women were found to have diabetes while the prevalence of dyslipidemia was 70%, stressing the need for screening women with PCOS for these derangements.

A Dutch study on anovulatory PCOS women has reported that a waist circumference of >83.5 cm along with biochemical evidence of hyperandrogenism was a powerful predictor of the presence of metabolic syndrome and insulin resistance.[19]

Study showed that age and central obesity (waist-hip ratio/waist circumference) were better predictors of metabolic syndrome in women with PCOS compared to other parameters including BMI. Our finding of central obesity correlating with presence of metabolic syndrome in women is in agreement with earlier study by Janssen *et al.*, who concluded that waist circumference is closely related with obesity-related risk factors as compared with the BMI.[20]

Ideal is to screen all infertile women with PCOS but the is not always practical. So risk factors identification for screening can be an alternate strategy. Our results suggest that women having any of the following risk factors: age more than 25 or with central obesity waist-hip ratio >0.85, are at a greater risk of having the metabolic syndrome.

The results has to be interpreted cautiously as the present study has certain limitations. The study was done at a hospital without the use of a control group of non-PCOS women for comparison and larger sample size will be required for a more precise estimation of the prevalence of metabolic syndrome in pcos women.

Conclusion

We found a prevalence of metabolic syndrome of 35%, which constitutes more than a third of the PCOS women who presented with infertility in our clinic. The present study highlights the need for comprehensive screening for metabolic syndrome in women with PCOS attending infertility clinic. In our study, age >25 years and presence of central obesity (waist-hip ratio >0.85) were identified as risk factors for metabolic syndrome. The findings can be used to formulate a screening policy for metabolic syndrome, in patients with polycystic Ovarian syndrome.

Table 1 Distribution of metabolic syndrome in pcos women with the age

Age in years	No. Of patients without metabolic syndrome	No. Of patients with metabolic syndrome (%)
< 25	27	3 (10%)
25 - 30	17	13 (43%)
30 - 35	7	7 (50%)
>35	1	5 (83.3%)
Total	52	28

Table 2 Distribution of metabolic syndrome in pcos women with the body mass index

BMI (kg/m2)	Without metabolic syndrome	Without metabolic syndrome (%)	Total
< 24.9	29	5 (14.7%)	34
25 – 29.9	18	20 (52.63%)	38

>30	3	5 (62.8%)	8
Total	50	30	80

Table 3 Clinical, anthropometric and hormonal parameters of polycystic ovarian syndrome in women with and without metabolic syndrome

	Without metabolic syndrome (n = 52)	With metabolic syndrome (n= 28)
Age (years)	23.75 +/- 2.84	29.33 +/- 5.40
Weight (kg)	58.30 +/- 9.1	68.63 +/- 9.70
BMI (kg/m ²)	24.02 +/- 3.2	29.03 +/- 4.1
Waist hip ratio	0.81 +/- 0.05	0.87 +/- 0.05
Hirsutism	11 (21%)	12 (43%)
Acanthosis	5 (9.6%)	8 (28.5%)
Acne	4 (7.6%)	2 (7.14%)
Free testosterone (%)	1.60 +/- 0.50	1.93 +/- 0.50

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