An Observational Study on the Prevalence of Metabolic Syndrome in Reproductive Aged Women with PCOS

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Abstract

Background: Polycystic Ovarian Syndrome (PCOS) is a heterogeneous, multifactorial, polygenic endocrine condition seen in women of reproductive age group. The diagnosis of PCOS is made based on Rotterdam's criteria 2003 (Any two out of the following three-Oligoovulation and/or Anovulation, Hyperandrogenism, Polycystic ovaries). Hyperinsulinemia and Insulin resistance contribute to the basic pathogenesis of PCOS. *Aims:* The present study aims to study the prevalence of metabolic syndrome in PCOS in reproductive aged women. *Settings and Design:* Observational study. *Materials and Methods*: All the women aged 15 to 40 years attending the gynaecology OPD diagnosed with PCOS based on Rotterdam's criteria during the study period of one year with a sample size of 146 were included in this observational study. After getting informed written consent from these patients,detailed history of age, parity, socioeconomic status, menstrual, marital, obstetric, past, personal and family history were obtained. They were screened for metabolic syndrome according to the modified American Heart Association / National Heart Lung Blood Institute modified ATP 111 definition 2001 which 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 ≥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. *Statistical Analysis used:* Statistical analysis was done using SPSS version 25. Continuous variables were summarized as mean with standard deviation and analyzed using sample t-test. Categorical variables were expressed as proportions and analyzed by Chi-square test. *Results*: The prevalence of metabolic syndrome in PCOS was 38.4%.The occurrence of metabolic syndrome was more in the age group 26 to 35 years (62.33%). Central obesity with waist circumference ≥ 88 cm in women, elevated systolic and/or diastolic blood pressure of ≥130/85 mmHg,impaired fasting serum glucose ≥110 mg/dl, elevated fasting serum triglycerides ≥150 mg/dL, and fasting high-density lipoprotein (HDL) cholesterol <50 mg/dl and the ultrasound features of PCOS were observed to be statistically significant.No significant association was observed with hyperandrogenic clinical features and PCOS in USG in our study. *Conclusion:* The prevalence of metabolic syndrome in our study was 38.4%, which obviates the necessity of routine screening for metabolic syndrome in women with PCOS attending the gynaecology outpatient department. The study outcome can be utilised to prepare a screening protocol for metabolic syndrome, especially in low resource centres.

Keywords: Hyperandrogenism; Metabolicsyndrome; Polycystic Ovarian Syndrome; Central Obesity; hypertension.

Introduction

Polycystic ovary syndrome (PCOS) is the most common endocrinologicaldisordersaffecting about 12% to 20% of reproductive aged women. PCOS characterises with chronic anovulation, amenorrhea/oligomenorrhea, hyperandrogenism, and polycystic ovarian morphology on USG pelvis.The metabolic components in PCOS are hyperinsulinemia and insulin resistance. PCOS is seen in lean as well as obese women and it is strongly associated with high cardiovascular risk.

Polycystic Ovarian Syndrome (PCOS) is a heterogeneous,multifactorial,polygenic endocrine condition seen in the women of reproductive age group. The diagnosis of PCOS is made based on Rotterdam's criteria 2003 (Any two out of the following three-oligoovulation and/or anovulation, Hyperandrogenism, Polycystic ovaries). Hyperinsulinemia and Insulin resistance contribute to the basic pathogenesis of PCOS. A lot of studies have shown that metabolic syndrome is very closely linked to PCOS [1].

Metabolic syndrome is characterised by insulin resistance, hyperlipidemia, obesity, and hypertension which is associated with increased risk of cardiovascular disease and type 2 diabetes mellitus. This potentiates the importance of early detection of hyperinsulinemia, insulin resistance and metabolic syndrome which can be utilised as preventive measures in women with polycystic ovary syndrome.

The original National Cholesterol Education Programme – Adult Treatment Panel III (NCEP - ATP111) 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 ≥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.

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.

Both PCOS and metabolic syndrome are common risk factors for the occurrence of cardiovascular problems and type 2 diabetes mellitus. Hence there is need to conduct further research in this to identify the association between these two endocrinopathies so that the complications can be identified early and primary prevention is possible thereby lifestyle modification can be made to prevent future longterm sequelae in reproductive aged women in India [2,3,4].

Several studies have given varied data that indicate the necessity for evaluation of metabolic syndrome in various populations, as it would be usefulin planning screening protocols to prevent future long-term complications in the patients with PCOS.

The aim of this study was to identify the prevalence of metabolic syndrome inwomen of reproductive age with polycystic ovarian syndrome.

Methods

An observational study was conducted in the female patients attending the gynaecology outpatient department of Karpagam Faculty of Medical Sciences and Research, Othakkalmandapam, Coimbatore, for a period of one year with a sample size of 146 with the following inclusion and exclusion criteria.

Inclusion Criteria

1. Ultrasound diagnosis of PCOS
2. History of menstrual irregularities-amenorrhoea/oligomenorrhoea
3. Presence of hirsutism
4. Presence of acanthosis nigricans
5. Age between 15 to 40 years
6. Consented women to take part in the study

Exclusion Criteria

1. Women with steroid drug intake in the preceding 3 months
2. Women with previously diagnosed diabetes.
3. Women with oral contraceptive intake in the preceding 3 months
4. Pregnant women
5. Women already diagnosed with hyperprolactinemia, hypothyroidism, cushings syndrome, congenital adrenal hyperplasia.
6. Women aged less than 15 years and more than 40 years

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7. Women who have not consented to take part in the study.

Oligo-ovulation and/or anovulation was characterized by oligomenorrhea (intermenstrual intervals of ≥ 35 days) and amenorrhea (intervals >3 months). Clinical hyperandrogenism was defined as the presence of hirsutism (Ferriman-Gallwey score of ≥ 8) and/or acne.Polycystic ovary on ultrasound was defined as the presence of at least one ovary 10 cm³ or more in volume and/or at least one ovary with 12 or more follicles measuring 2–9 mm in diameter.

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 ≥ 88 cm or more (ii) blood pressure of ≥ 130/85 mmHg (iii) fasting blood sugar of ≥ 100 mg/dL (iv)fasting triglycerides of ≥ 150 mg/dL, and (v) HDL of ≤ 50 mg/dL.

A standard questionnaire was used to document the age, parity,socioeconomic status, length of menstrual cycles,obstetric history, personal, medicaland family history of diabetes, hypertension, obesity and ischemic heart disease. Signs of androgen excess (hirsutism-Ferriman-Gallwey score of ≥8, acne, and alopecia) and insulin resistance were noted in the physical examination. Anthropometric measurements included a waist circumference in centimeters measured at the narrowest circumference, midway between the upper border of iliac crest and the lower rib margin. Height was recorded in centimeters and weight in kilograms and body mass index was calculated. Sitting blood pressure was measured after a 5-minute rest using a standard sphygmomanometer.The following biochemical investigations like fasting triglyceride levels,high density cholesterol levels and fasting blood glucose levels were done in all the patients.

Statistical analysis was done using SPSS version 25. Continuous variables were summarized as mean with standard deviation and analyzed using sample t-test. Categorical variables were expressed as proportions and analyzed by Chi-square test.

Results

The prevalence of metabolic syndrome in PCOS was 38.4%. PCOS was commonly seen between 26 to 40 years. Educational qualification, socioeconomic status have no statistical association in the prevalence of PCOS.

Table 1 shows that among the 146 PCOS patients, majority, about 31.5% were of the age group 26 to 30 years followed by 31 to 35 years (30.8%).

Table 2 shows 42.5% of the study participants belong to class 1 socioeconomic status and PCOS is almost equally distributed among class 2 and class 3 socioeconomic class.

Table 3 shows that majority of the PCOS had 2 children (65.8%) and about 20.6% were of P1 category and 13.6% of the PCOS patients had 3 and more children.

Table 4 says thet about 116 patients out of 146 study participants ie about 79.5% had bilateral PCOS in the ultrasound and in 30.5% of patients USG was within normal limits indicating that USG findings of PCOS was commonly seen when compared to hyperandrogenic features and menstrual irregularities in PCOS.

As per table 5, 56 study participants had waist circumference more than 88cm i.e. more than a third of the study participants had central obesity and about 90 patients had waist circumference upto 88cm indicating that 61.6% had waist circumference upto 88cm.

Table 1: Age distribution of PCOS patients

Age	Number of Patients	Percentage
15-25 Years	30	20.6
26-30 Years	46	31.5
31-35 Years	45	30.8
36-40 Years	25	17.1
Total	146	100

Table 2: Socioeconomic status of PCOS patients

Class	Number of Patients	Percentage
Class 1	62	42.5
Class 2	46	31.5
Class 3	38	26.0
Total	146	100

Table 3: Parity of the PCOS patients

Parity	Number of Patients	Percentage
P1	30	20.6
P2	96	65.8
P3 and Above	20	13.6
TOTAL	146	100

Table 4: Ultrasound features of PCOS patients

USG Findings	Number of Patients	Percentage
Bilateral PCOS	116	79.5
NAD	30	20.5
TOTAL	146	100

Table 5: Waist circumference of PCOS patients

Waist Circumference	Number of Patients	Percentage
UpTo 88 cm	90	61.6
More than 88 cm	56	38.4
Total	146	100

Table 6 shows HDL cholesterol was more than 50mg/dl in 56.2% of the study participants and 43.8% of the PCOS patients had HDL cholesterol less than 50mg/dl.

Table 7 shows about 16 PCOS patients out of 146 had FBS less than or equal to 110mg/dl and 130 patients had FBS level more than 110mg/dl.

Table 8 shows about 85 PCOS patients (58.2%) out of 146 had fasting triglyceride levels less than 150mg/dl and only 61 patients (41.8%) had fasting triglyceride level more than 150mg/dl.

There was no significant association between acne, alopecia and the presence of PCOS in the present study (Table 9).

Table 10 explains the prevalence of metabolic syndrome in PCOS is 38.4%.56 patients had metabolic syndrome and 90 patients did not have metabolic syndrome.

Table 11 shows that 87.2% of the patients with metabolic syndrome had fasting blood sugar more than 110mg/dl and 12.8% of the patients with metabolic syndrome had FBS levels less than 110mg/dl and the association is statistically significant.

Table 6: HDL Cholesterol levels of the PCOS patients

HDL levels	Number of Patients	Percentage
Less than 50mg/dl	64	43.8
More than 50mg/dl	82	56.2
Total	146	100

Table 7: Fasting blood sugar levels of the PCOS patients

FBS	Number of Patients	Percentage
Less than or equal to 110mg/dl	16	11.0
More than 110mg/dl	130	89.0
Total	146	100

Table 8: Fasting Triglyceride levels of the PCOS patients

TGL	Number of Patients	Percentage
Less than 150mg/dl	85	58.2
More than 150mg/dl	61	41.8
Total	146	100

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Table 12 shows that 84.3% of the patients with metabolic syndrome had HDL cholesterol less than 50mg/dl and 15.7% of the patients with metabolic syndrome had HDL levels more than 50mg/dl and the association is statistically significant

Table 13 shows that 100% of the patients with metabolic syndrome had fasting triglyceride more than 150mg/dl indicating the association is statistically significant

Table 14 shows that 100% of the patients with metabolic syndrome had BP higher than 130/85mmHg and the association is statistically significant

Table 15 shows that 100% of the patients with metabolic syndrome had waist circumference more than 88cm and the association between waist circumference and metabolic syndrome is statistically significant.

Discussion

The prevalence of metabolic syndrome in PCOS in our study is 38.4% and it is comparable with the study by Ehrmann et al. (33.4%) and Dokras et al. (47.3%) [5,6]. In comparison, a study done on

Table 9: Blood Pressure measurements in PCOS patients

BP	Number of Patients	Percentage
>=130/85 mm Hg	62	42.5
<130/85mm Hg	84	57.5
Total	146	100

Table 10: Metabolic Syndrome among PCOS patients

Metabolic syndrome	Number of Patients	Percentage
Present	56	38.4
Absent	90	61.6
Total	146	100

Table 11: Association of Metabolic Syndrome with Fasting Blood Sugar level

FBS	Metabolic Syndrome			Chi square	P value
	Present	Absent	Total		
<=110mg/dl	8(12.8%)	8(91.1%)	16	12.1	0.001
>110mg/dl	48(87.2%)	82(8.9%)	130		
Total	56	90	146		

Table 12: Association of Metabolic Syndrome with HDL Cholesterol level

HDL	Metabolic Syndrome			Chi square	P value
	Present	Absent	Total		
<=50mg/dl	47(84.3%)	17(18.9%)	64	61.45	0.0001
>50mg/dl	9(15.7%)	73(81.11%)	82		
Total	56	90	146		

Table 13: Association of Metabolic Syndrome with TGL level

TGL	Metabolic Syndrome			Chi square	P value
	Present	Absent	Total		
<=150mg/dl	0	85(94.4%)	85	170.2	0.0001
>150mg/dl	56(100%)	5(5.6%)	61		
Total	56	90	146		

Table 14: Association of Metabolic Syndrome with Blood pressure

BP	Metabolic Syndrome			Chi square	P value
	Present	Absent	Total		
Normal	0	84(93.3%)	84	171.67	0.0001
Elevated	56(100%)	8(6.7%)	62		
Total	56	90	146		

Table 15: Association of Metabolic Syndrome with Waist circumference

Waist Circumference	Metabolic Syndrome		Total	Chi square	P value
	Present	Absent			
Up to 88 cm	0	90(100%)	90	162.81	0.0001
>88cm	56(100%)	0	56		
Total	56	90	146		

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 [7].

Metabolic syndrome characterises three main abnormalities: elevated blood glucose, hyperlipidemia, and elevated blood pressure, which directly contribute to a pro-thrombotic and pro-inflammatory state, predisposing to the development of atherosclerotic cardiovascular disease and type 2 diabetes mellitus. 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.

The age adjusted prevalence of metabolic syndrome in our study shows that women between 26 and 35 years have the highest prevalence 70.3% which is comparable to the study by DeyRamprasad et al. (71.5%)[8]. Majority of the PCOS had 2 children (65.8%) and about 20.6% belonged to P1 and 13.7% of the PCOS patients had 3 and more children in our study. Socioeconomically 42.5% belonged to class 1 and 31.5% belonged to class 2 and 26% belonged to class 3 indicating that PCOS and metabolic syndrome are more prevalent in class1 group according to modified Kuppusamy scale. In our study, 100% of the patients with metabolic syndrome had waist circumference more than 88cm and the association between waist circumference and metabolic syndrome is statistically significant in PCOS patients indicating more than one third were obese. 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 [9]. The prevalence of metabolic syndrome has been found to be higher in weight-matched PCOS women compared to non-PCOS women. 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. 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.

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 [10]. 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 [11]. In our study, the prevalence of metabolic syndrome also increased with increased waist circumference.

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 [12].

Age and central obesity (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.[13], who concluded that waist circumference is closely related with obesity-related risk factors as compared with the BMI.

In our study, 87.2% of the patients with metabolic syndrome had fasting blood sugar more than 110mg/dl and 12.8% of the patients with metabolic syndrome had FBS levels less than 110mg/dl and the association is statistically significant. About 84.3% of the patients with metabolic syndrome had HDL cholesterol less than 50mg/dl and 15.7% of the patients with metabolic syndrome had HDL levels more than 50mg/dl and the association is statistically significant. 100% of the patients with metabolic syndrome had fasting triglyceride more than 150mg/dl indicating the association is statistically significant. 100% of the patients with metabolic syndrome had BP higher than 130/85mmHg and the association is statistically significant.

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Screening all reproductive aged women with PCOS for metabolic syndrome would be ideal but is not always practical, especially in a low-resource settings. Identifying risk factors for screening would be an alternate strategy. Our results suggest that women having any of the following risk factors: age more than 25 or with central obesity are at a greater risk of having the metabolic syndrome and for developing diabetes mellitus type 2 and cardiovascular problems. However, the results need to be cautiously interpreted as the present study has certain limitations. The study was done at a tertiary care centre without use of a control group of non-PCOS women.

Conclusion

We found a prevalence of metabolic syndrome of 38.4%, which constitutes more than a third of the PCOS women. The present study highlights the need for comprehensive screening for metabolic syndrome in women with PCOS attending Gynaecology OPD. In our study, age >25 years and presence of central obesity (waist circumference more than 88cm)were identified as risk factors for metabolic syndrome.

There is a significant association between elevatedcentral obesity with waist circumference e"88 cm in women, elevated systolic and/or diastolic blood pressure of ≥130/85 mmHg, impaired fasting serum glucose ≥110 mg/dL,elevated fasting serum triglycerides ≥150 mg/dL and fasting high-density lipoprotein (HDL) cholesterol <50 mg/dl. The findings can be used to formulate a screening protocol for metabolic syndrome, particularly in low resource settings in our country.

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