Original article

Overweight/Obesity and metabolic syndrome in women with polycystic ovary syndrome

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Abstract

Introduction: Polycystic ovary syndrome (PCOS) is a common problem among women in south Asia. It is closely associated with metabolic syndrome (MetS) that is characterized by a cluster of co-morbidities. The aim and objective of the study was to evaluate the prevalence of the MetS and its features in women with PCOS in a small population from south India and classify them on the basis of body mass index (BMI).

Methods: Women affected with PCOS as assessed by ESHRE/ASRM criteria, were grouped into normal, underweight and overweight/obese groups based on BMI. Central obesity was assessed by measuring the waist circumference (WC). Blood pressure measurements and biochemical variables such as fasting blood glucose and lipid profile required for assessing the MetS were carried out.

Results: Our study has established that a considerable portion of nearly 30% of the PCOS women was suffering from MetS who were also overweight or obese. The results also showed that nearly 80% of the PCOS subjects had abdominal obesity that was supported by high WC and a good number of the subjects had exhibited hypertension, low high density lipoprotein and hypertriglyceridemia.

Conclusion: The suggestion that, PCOS may represent the manifestation of the MetS due to a strong link with obesity appears very appropriate.

Key words: Obesity, polycystic ovary syndrome, metabolic syndrome

Introduction:

Polycystic ovary syndrome (PCOS) has been variously described as a heterogeneous, polygenic endocrine disorder of unexplained hyperandrogenic chronic anovulation in women of reproductive age and is considered as a metabolic, cosmetic and multifactorial reproductive problem with features of amenorrhea, infertility and bilateral enlarged polycystic ovaries [(1)]. PCOS also involves a complex pathophysiology of various organ systems that puts women at a higher risk for a number of illnesses, including high blood pressure, diabetes, heart disease and other cardiovascular problems and cancer of the uterus, ovary, liver, colon and breast [(2)]. The world wide prevalence of PCOS is 6-10% and in its classical form may affect 5 - 7% of women [(3)]. PCOS is quite common among Asian women. A high prevalence of up to 35% reported for the Indian women is a great concern [(4, 5)]. Gynecologists believe from their experience that 25-30 % of the south Indian women visiting them do suffer from PCOS and a recent report puts the figure at 9.3% [(4, 5, 6)]. The incidence and prevalence of PCOS in overweight and obese (ow/ob) women is greater than 20%[7]. Several studies have shown a modest increase in the prevalence of PCOS with increasing body mass index (BMI) and up to 50% of women affected with PCOS may develop obesity

[7, 8, 9]. It is also of interest that the pattern of distribution of body fat plays a role in PCOS and it has been suggested that global adiposity rather than abnormal regional fat characterizes women with PCOS [10]. Most investigators have found that obese PCOS women tend to have an increased waist-hip ratio (WHR) suggesting abdominal (visceral) obesity that is directly associated with cardiovascular diseases and metabolic syndrome (MetS) [11, 12] and thus a close association between WHR > 0.8 and higher androgen levels, insulin resistance (IR), diabetes mellitus and MetS is well established in PCOS [13, 14, 15]. It is interesting to note that even lean women with a healthy body weight are also vulnerable to PCOS and MetS. And, obesity-associated disturbances in glucose and insulin metabolism leading to impaired glucose tolerance (IGT) or type 2 diabetes in PCOS affected women may, however, be different from lean women with PCOS [16]. Women with MetS and PCOS are also at greater risk of developing gestational diabetes [17].

Aims and objectives:

Due to a strong link between obesity and PCOS that leads to the development of MetS is an important clinical condition associated with several co-morbidities. Based on this fact we designed this study to establish the prevalence of MetS in PCOS women.

Material and methods:

By convenient sampling, 85 post-pubertal female subjects, diagnosed with PCOS were inducted for this descriptive, cross sectional study. Institute's research ethical committee approved the study. Written consent was obtained from each participant. The diagnosis of PCOS was made according to the ESHRE/ASRM criteria [18] based on the presence of two of the three following criteria: oligo- and/or anovulation, clinical and/or biochemical signs of hyperandrogenism and polycystic ovaries at ultrasonogram with the presence of 12 or more follicles measuring 2-9 mm and an increased ovarian volume of >10 cm^3.

All patients were questioned in detail regarding birth history, menstrual, obstetric and medical history. A standard questionnaire was used to document personal history. In addition, all PCOS patients were subjected to general physical examination. Height and weight for BMI, waist circumference (WC) (at the midpoint between the lateral iliac crest and the lowest rib margin), and blood pressure (BP) were noted. Systolic and diastolic blood pressure (SBP and DBP) was measured using a mercury sphygmomanometer after a 5-minute rest in a relaxed sitting position.

Direct quantitative evaluation of fasting blood sugar (FBS), postprandial blood sugar (PPBS), total cholesterol (TC), triglyceride (TG) and high density lipoprotein (HDL-C) was carried out on Roche-Hitachi fully automated random access chemistry analyser (RH model P-800).

The subjects were classified further into normal, underweight, and overweight/obese (ow/ob) categories on the basis of BMI for Asians [19] as shown in below. We also have used International BMI standards just for comparison at some places.

International BMI range	Group	Asian BMI Range	Group
<18.5	Underweight	<18.5	Underweight
18.5-24.9	Normal	18.5-22.9	Normal
25-29.9	Overweight	23-27.4	Overweight/Preobese
>30-	Obese	27.5 -34.9	Obese I
-	-	>35	Obese II

Accordingly, MetS was diagnosed in subjects presenting with at least three of five of the following criteria: increased WC >80 cm, low serum HDL-C (<50 mg/dl), increased serum TG (>150 mg/dl), increased blood pressure (>130/>85 mm Hg) and high FBS (>100 mg/dl) by adopting the modified NCEP-ATP III [20] criteria keeping in view that we followed the BMI classification for the Asians.

A statistical software package was used to analyse the numerical data (SPSS version 17.0). Descriptive statistics were calculated for each variable.

Results:

Physical characteristics of the PCOS patients are shown in Table 1. The average BMI was close to 28 kg/m^2, a clear indication of the ow/ob status in most subjects. This was also supported by a large WC of a mean value of nearly 85 cm. Based on the analysis of individual WC value over 80 cm, (as per modified NECP-ATPIII-2005) [20] 78% of the ow/ob subjects had clear central obesity and with WC >88 cm 33% subjects had developed central obesity (as per NCEP-ATPIII-2001) [21]. Similarly, blood pressure appeared to be in the high normal range and nearly 25% of the subjects had values suggestive of hypertension based mainly on diastolic blood pressure as per the cut-off levels for Mets.

Table 1. Physical characteristics and blood pressure of PCOS subjects.

Values are Mean ± SD. n= number of subjects= 85

Variable	PCOS subjects	Frequency/ (%)
Age (Yrs)	27.9 ± 7.1	-
Body Mass Index (kg/m^2)	27.1 ± 5.3	-
Waist circumference (cm)	84.7 ± 13.0	<80 = 19 (22%) >80 = 76 (78%)
Systolic blood pressure (mm Hg)	128.5 ± 12.7	<130 = 69 (81%) >130 = 16 (19%)
Diastolic blood pressure (mm Hg)	80.5 ± 8.4	<85 = 63 (74%) >85 = 22 (26%)

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Table2. Body mass index (BMI) defined waist circumference, systolic blood pressure (SBP) and diastolic blood pressure (DBP) of PCOS subjects. n=number of subjects, Values are Mean ± SD.

International BMI standard	**BMI**	**n**	**%**	**Age (Yrs)**	**Waist Circumference (cm)**	**SBP (mmHg)**	**DBP (mmHg)**
Under Weight	17.0 ± 0.8	3	3.5	26.0±1.7	63.7±8.0	110.0 ± 17.3	66.7 ± 11.5
Normal	22.4 ± 2.1	28	33	24.9±6.1	77.9±8.8	125.7 ± 7.9	78.6 ± 7.1
Overweight	27.5 ± 1.3	30	35	29.0±6.7	85.9±9.2	127.3 ± 11.4	80.0 ± 6.9
Obese	33.3 ± 3.6	24	28	30.2±7.9	93.5±14.8	135.4 ± 14.7	85.0 ± 8.8
p value	-	-	-	0.032	0.000	.021	.013
Asians BMI standard							
Under Weight	17.0 ± 0.8	3	3.5	26.0±1.7	63.7±8.0	110.0±17.3	66.7±11.5
Normal	20.9 ± 1.4	16	19	22.9±5.9	75.4±8.8	126.2±6.1	79.3±7.7
Overweight	25.6 ± 1.4	29	34	27.6±6.2	81.4±6.5	124.4±9.8	78.2±6.0
Pre-Obese	30.6 ± 1.8	32	38	30.9±6.2	90.0±9.4	133.0±12.7	83.1±8.5
Obese	38.9 ± 4.1	5	6	26.6±12.8	111.2±19.9	140.0±20.0	88.0±8.3
p value		-	-	0.032	0.000	0.001	0.001

Table 2 shows the age, frequency distribution of subjects based on BMI, WC and blood pressure. Accordingly, 78% and 63% of the subjects were ow/ob by Asian or International BMI standards respectively that was supported by high WC >80 cm. Similarly, there were some variations also in frequency distribution of hypertensive subjects (44% vs. 28%).

Biochemical variables (blood sugar and lipid profile), however, could not be evaluated in all patients due to certain constraints. The mean fasting sugar level was 104 mg% for 61 subjects which was higher than the normal range. Abnormal individual biochemical values with <50 mg% HDL, >150 mg% TG and >100 mg% FBS that was related to the MetS was recorded in 25%-67% of the subjects. Table 3 provides the results of blood sugar and lipid profile in relation to BMI standards for Asian population. There were no statistically significant differences in any variable in relation to BMI levels. However, ow/ob groups had higher FBS and LDL levels were slightly higher in all groups. PPBS level was slightly higher only in the obese group. TC and triglycerides were within the normal range in all groups. HDL was lower in all groups except the normal BMI group (Table 3).

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Table 3. Biochemical variables of PCOS subjects based on BMI for Asians.

Group/BMI	FBS	PPBS	TC	TGL	HDL	LDL
Under Weight <18.5	86.0±0.0 (1)	- -	- -	- -	- -	- -
Normal 18.5-22.9	90.1±9.2 (12)	105.6±22.7 (6)	171.0±18.9 (5)	67.4±26.9 (5)	55.8±10.6 (5)	101.0±11.2 (5)
Over Weight 23-27-27.4	111.0±38.1 (19)	130.7±63.8 (11)	174.1±37.5 (11)	120.0±45.6 (10)	40.7±7.5 (10)	113.7±33.8 (10)
Pre-obese 27.5-34.9	103.6±26.1 (24)	128.5±48.1 (14)	177.0±53.0 (16)	125.8±53.3 (15)	48.1±37.4 (15)	110.4±41.6 (14)
Obese >35	113.2±47.6 (5)	152.0±62.9 (5)	170.0±41.8 (4)	123.0±46.7 (4)	44.2±13.9 (4)	100.7±44.4 (4)
p value	0.38	0.55	0.98	0.135	0.761	0.89

FBS=Fasting blood sugar, PPBS=Postprandial blood sugar, TC=Total cholesterol, TGL=Triglyceride, HDL=High density lipoprotein, LDL=Low density lipoprotein. Figures in parentheses denote number of subjects.

Table 4 depicts the percent of PCOS subjects who had developed one or the other co-morbidities of MetS.

Table 4. Frequency of PCOS subjects with individual co-morbidities of MetS.

Similarly, Table 5 shows the prevalence of MetS in our study subjects, based on different criteria.

Characteristics	Percent	Characteristics	Percent
Impaired glucose tolerance	18	Systolic BP > 130 mm Hg	19
Type 2 diabetes mellitus	09	Diastolic BP >85 mm Hg	26
Fasting blood sugar >100 mg%	33	Waist circumference >88 cm	33
HDL-C <50 mg%	67	Waist circumference >80 cm	78
Triglyceride >150 mg%	26	Overweight/Obesity	78
LDL >100 mg%	60	--	--

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Table5. Prevalence (%) of individual Metabolic Syndrome (MetS) characteristics in PCOS subjects according to different criteria. (Three out of five characteristics will qualify for MetS).

Parameter	Modified ATP III (2005) [20]	Based on BMI >23 for Asians[19]	Based on WHO Criterion [32]
Waist circumference>80 cm	78	78	DM – 25% IGT – 18% Obesity – 44% HT – 20% Dyslip – 30%
Blood pressure >130/85	19/26	44/6	
HDL-C <50 mg%	67	85	
Triglyceride >150 mg%	26	-	
Fasting sugar >100 mg%	33	78	

WHO Criterion for metabolic syndrome: One major out of diabetes mellitus (DM), insulin resistance (IR), impaired glucose tolerance (IGT); Two minor out of Obesity (BMI>30), Hypertension (HT), Dyslipidemia (Dyslip) and Microalbuminuria. Figures in parentheses denotes reference numbers.

Discussion:

The etiology of PCOS is not well understood and its pathophysiological and molecular basis is still a puzzle. However, as described way back in 1921, androgen excess and IR leading to hyperinsulinemia are considered to be the basic defects in PCOS [22]. Furthermore, it is associated with type 2 diabetes, lipid disturbances, and cardiovascular diseases. Therefore, it has been suggested that PCOS mimics an early manifestation of MetS with a cluster of abnormalities where the combination of IR and compensatory hyperinsulinemia predisposes individuals to develop a high plasma triglyceride and a low high-density lipoprotein cholesterol concentration, high blood pressure and coronary heart disease [23].

The prevalence of MetS in PCOS women shows a marked variation between countries and ethnic groups, probably due to differences in diet, lifestyle and genetic factors [24]. Although, the role of obesity in the development of PCOS is not very clear, it is a major feature of PCOS that may contribute to its pathogenesis by aggravating the intrinsic insulin resistance [25] that culminates as MetS [26]. Obesity in PCOS is not simply because the patients are eating more and exercising less. Food quality seems to play a more active role in metabolic abnormalities and individual's state of metabolism also may be responsible for the development of obesity in PCOS [27]. It may also contribute to the development of glucose and lipid metabolism disorders. Of course, the involvement of excess visceral fat is well known in cardiovascular risks since visceral fat is a source of many cytokines (adipokines) such as adinopectin, leptin, visfatin etc. [12]. Interestingly, a significantly higher prevalence of central obesity, hypertension and dyslipidemia has been reported for Asian Indians [28]. One study has reported a mean BMI of 26.5 kg/m^2 in south Indian women with PCOS [29]. In our study, the PCOS subjects had a mean BMI of 28 kg/m^2. As per the BMI for Asian population, it was noted in our study that 78% were either overweight or obese with a BMI of >23 kg/m^2 that correlated well with central obesity defined by a waist circumference of >80 cm (and BMI of >30 kg/m^2 correlated well with central obesity defined by a waist circumference > 88 cm in 28% of the

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subjects as per International BMI standard ratings), hypertension in 28% of the subjects with a systolic and diastolic blood pressure of >130/85 mmHg. This possibly could have contributed to a high percentage of PCOS subjects in that category and the remaining were lean PCOS subjects. More than 80% of the subjects in this study had gained extra body weight at puberty and thus obesity may be responsible for the development of MetS features. Natasha et al. [30] have tested the hypotheses that parental MetS would be related to the PCOS phenotype in their offspring and that MetS prevalence would be increased in adolescents with PCOS. Thirty-six adolescent girls with PCOS and their first degree relatives were evaluated for MetS characteristics in their study and they concluded that familial factors related to paternal MetS seem to be fundamental to the pathogenesis of PCOS.

Diabetes mellitus, IR, IGT and dyslipidemia are common in PCOS. Sundararaman and his coworkers [29] have reported an elevated fasting insulin levels in PCOS subjects, higher insulin resistance and greater intimamedial thickness. In our study, the mean FBS value was 104 mg% (cut-off level; 100 mg%). Of the 61 subjects in whom fasting blood sugar was estimated 33% had > 100 mg%. However, the PPBS was high in only about 25% of the subjects. When analysed further for correlation between BMI and biochemical profile, we found FBS and PPBS were higher than the recommended values in ow/ob subjects (115 mg% and 146 mg% respectively). HDL was lower in group with BMI >23 kg/m^2 whereas LDL was more than the recommended value (>100 mg%) in all the BMI groups.

Apridonidze et al. [31] have reported that 43% of women with PCOS in their study had features of MetS and according to ATPIII criteria MetS prevalence was 15% in PCOS women with a BMI of 26 kg/m^2. It has been reported that south Asia is a home to largest population of MetS and for example a report cites a waist circumference of 91 cm for South Asian women with PCOS along with 17% hypertensive tendency, 52% impaired glucose tolerance, 16% increased triglycerides, and 70% with low HDL levels increase the risk of developing MetS in PCOS [4, 32, 33]. A good number of our patients fell into the category of PCOS with MetS. Approximately > 30% of PCOS subjects in our study had characteristics of MetS. On the basis of BMI criteria for Asians, MetS cases in our study were at a higher level of > 45%. On WHO criteria the figure was about 25% (Table 5).

There are about half a dozen or more bodies that have set criteria for diagnosing MetS. For example, some important ones that can be considered include AHA/NHLBI definition (ATPIII 2005), NCEP-ATP-III, WHO criteria, Europina group for the study of insulin resistance (EGIR), International Diabetes Foundation (IDF), and NHA 04 [20, 21, 34-37]. However, most of them share a common ground of glucose, lipid abnormalities and hypertension but with some minor modifications. World Health Organization (WHO) [38] recommendations for waist circumference ≥80 cm in Asian women and reducing the threshold for impaired fasting glucose to 5.6 mmol/l in accordance with the revised definition of American Diabetes Association (ADA) [39] are just a few examples. For curiosity, we verified any differences in the frequency of MetS as defined above by some different criteria (Table 5).

In conclusion, the suggestion that due to a strong link with obesity, PCOS may represent the manifestation of the MetS with a cluster of abnormalities appears very appropriate.

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