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Evaluation of potential association of metabolic syndrome in obese and non-obese PCOS women

Raminder Kaur^{1*} and Maninder Kaur¹

Abstract

Background Polycystic ovary syndrome is an escalating endocrinal and reproductive disorder among women of reproductive age and is considered the foremost health burden. Therefore, the present study is an attempt to estimate the potential association of metabolic syndrome in obese and non-obese PCOS women. A total of 250 PCOS women ranging in age from 18 to 45 years and living in the Chandigarh Capital Region were selected from the OPD, PGIMER, Chandigarh, (North India). Rotterdam Criteria (2003) was employed to diagnose polycystic ovary syndrome among women.

Results The prevalence of metabolic syndrome (MS) as assessed by the National Cholesterol Education Program Adult Treatment Panel (NCEP ATP III) was found to be 30% (4% in non-obese and 26% in obese) in PCOS women. Waist circumference > 88 cm is the most prevalent feature in PCOS women (67.2%) followed by HDL < 50 mg/dL (56.8%). The multivariate logistic regression analysis exhibited that visceral adiposity index (VAI) was a significant determinant of metabolic syndrome in obese (OR = 1.17, p < 0.01) and non-obese (OR = 1.2, p < 0.01) PCOS women. Results of ROC analysis further established visceral adiposity index as a potential determinant in metabolic syndrome in both the groups of PCOS women. In obese PCOS women, the W/H ratio also depicted accuracy in predicting metabolic syndrome risk.

Conclusions Visceral adiposity index is a significant tool to assess the metabolic syndrome in both groups, i.e., obese and non-obese. However, the waist/hip ratio can be considered as a predictive tool in obese women only. Thus, it could be used as a significant and inexpensive tool in clinical practices for early detection of metabolic syndrome in PCOS women.

Background

Polycystic ovary syndrome (PCOS) is considered a prevalent endocrinal disorder among women which is characterized by reproductive as well as metabolic disturbances [1]. This disorder shows variability in the presentation of symptoms in women ranging from oligo-anovulation, hyperandrogenism, and polycystic ovary morphology to

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metabolic dysfunctions such as obesity, hyperinsulinemia, hypertension, and dyslipidemia [1].

Metabolic syndrome is a cluster of disorders like hypertension, visceral obesity, glucose intolerance, elevated triglycerides, and low levels of high-density lipoprotein cholesterol in PCOS women of different regions and ethnicities [2, 3]. It has been frequently identified that insulin resistance is considered as main determinant of metabolic syndrome among PCOS women. The prevalence of metabolic syndrome among PCOS women is as high as 33% and is associated with various long-term health consequences such as cardiovascular diseases, diabetes, and cancers [4]. Obesity is a cardinal characteristic among



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PCOS women, so past studies [5, 6] have described that metabolic syndrome is more prevalent in obese PCOS women than in their non-obese counterparts. It is further observed that abdominal obesity or central fat accumulation are common features witnessed among PCOS women [7]. Despite the fact that there are variations due to ethnicity and geographical region, metabolic syndrome and PCOS have similar symptoms, exhibiting an increased risk for cardiovascular disease and a higher prevalence of obesity. However, the link between their pathophysiology is still ambiguous.

In India, due to the swift transition from underweight to overweight/obese population, the prevalence of PCOS is soaring, as urban women of India have a higher prevalence of obesity (44.1%) [8]. Previous research [9–11] in this domain has witnessed that VAI is considered a potential risk factor for assessing metabolic syndrome among different populations. However, there is an inconsistency in these results. The present study is an attempt to predict which anthropometric indices will more significantly gauge the metabolic syndrome among PCOS women. Therefore, the present study aims to evaluate the anthropometric and adiposity indices to predict the potential association of metabolic syndrome in obese and non-obese POCS women.

Methods

The present cross-sectional study was carried out on 250 PCOS women, within the age range of 18 to 45 years, of Chandigarh Capital Region (CCR). The women visiting the OPD of the Department of Gynecology and Obstetrics of the Postgraduate Institute of Medical Research and Education (PGIMER) from April 2018 to January 2020 were enrolled in the study. The women who met the Rotterdam criteria (2004) were identified as having PCOS. The Institutional Ethical Committee of Panjab University, Chandigarh (PUIEC/2018/109/A/09/01) gave their approval to the study. Before being enrolled in the study, each participant signed a written informed consent form. A strict protocol was followed throughout the study to ensure the internal as well as external validity of the research.

The age of all the participants was recorded from their date of birth, which was then converted into decimal age following the Decimal age calendar given by Tanner et al. [12]. The height (cm) and weight (kg) of the participants were measured nearest to 0.1 cm and 0.1 kg with the standard technique of Weiner and Lourie [13] using an anthropometric rod and weighing machine respectively. The waist and hip circumference (cm) was measured with Freeman's steel tape with a nearest of 0.1 cm. The percent body fat and visceral fat were estimated by using the Bioelectrical Impedance method (Karada Scan HBF-375)

because it is one of the rapid, non-invasive, and relatively inexpensive methods for evaluating body composition.

The fat mass and fat-free mass were calculated using the formula; $FM = (Body fat/100) \times weight)$ and FFM = (Body)weight - Fat mass) respectively. The blood pressure of each participant was evaluated after a rest of 10-15 min with a digital sphygmomanometer (Omoron BP monitor). The subjects were asked to sit relaxed on a chair and free from any stressful activities. The high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and triglycerides (TG) of PCOS women were recorded from their history (from the patient's OPD card as well as blood test reports). The following adiposity indices, i.e., W/H ratio derived from Waist Circumference (cm)/Hip Circumference (cm), W/Ht ratio=(WC) (cm)/height (cm), $VAI = WC/36.58 + (1.89 \times BMI)] \times (TG$ $(0.81) \times (1.52/\text{HDL})$, BAI=(HC (cm)/height (m)^{1.5}) – 18, FFMI=(Body weight – Fat mass), FMI=Fat mass/height² (m^2) and ASBI = WC/BMI^{2/3}Height^{1/2} were calculated for each participant.

All the participants were stratified into three categories according to the body mass index (BMI) as per the WHO [14] cut-off values for the Asian population. The participants with body mass index less than 18.5 kg/m² were assigned to the underweight category, participants having a BMI between 18.5 and 22.9 kg/m² were placed in the normal weight category and BMI > 23 kg/m² comprised the overweight/obese category. The first two groups were considered as non-obese groups and the third was the overweight/obese group.

Non-obese and obese PCOS women were further stratified on the basis of the presence or absence of Metabolic Syndrome (MS) assessed as per the National Cholesterol Education Program Adult Treatment Panel (NCEP ATP III) [15]. According to the guidelines, Metabolic Syndrome (MS) is defined as the presence of three or more following conditions: waist circumference > 88 cm, fasting serum triglycerides > 150 mg/dl, serum HDL-C < 50 mg/dl, blood pressure \geq 130/85 mm Hg and fasting serum glucose < 110 mg/dl. However, we used fasting insulin \geq 25 uU/ml which is considered a predictor of insulin resistance.

Statistical analysis

The data analysis was performed using Statistical Package for the Social Science version 20 (SPSS 20 Inc.). The prevalence has been presented as percentages (%). The univariate logistic regression was applied to assess the association of anthropometric and adiposity indices with metabolic syndrome in obese and non-obese PCOS women. Indices with significant results were further subjected to multivariate logistic regression. The strength of the associated variable has been explained in terms of odd ratios with a 95% confidence interval. A receiver operating characteristic curve or (ROC) was used to determine cut-off values for predicting anthropometric and adiposity indices to assess the metabolic syndrome. The area under the curve (AUC) represents how well the model predicts and implies their optimal cut-off points. All *p* values were two-tailed, and statistical significance was defined as *p* < 0.05.

Results

Prevalence of metabolic syndrome characteristics

In the present study, non-obese and obese PCOS women were stratified on the basis of the presence or absence of metabolic syndrome (MS) assessed as per the National Cholesterol Education Program Adult Treatment Panel (NCEP ATP III). It was observed that 4% of non-obese and 26% of obese PCOS women demonstrated the presence of metabolic syndrome.

The prevalence of different metabolic parameters among non-obese and obese PCOS women has been displayed in Fig. 1. The prevalence of WC>88 cm was the most prevalent feature observed in PCOS women with 61.6% in the overweight/obese group and 5.6% in the non-obese group. The second most prevalent feature was HDL < 50 mg/dl, with a frequency of 39.6% in the overweight/obese women group and 17.2% in the non-obese group. The prevalence of SBP \geq 130 mm of Hg in overweight/obese women was 21.2% and 3.6% in non-obese women. The prevalence of DBP \geq 85 mm of Hg was observed in 16.4% overweight/obese PCOS, whereas 5.2% in non-obese PCOS women. Triglycerides > 150 mg/ dl were present in the 13.6% overweight/obese group, while 7.6% were in the non-obese group. The prevalence of fasting insulin (>25 uU/ml) was noted to be very meager (1.6%) in overweight/obese women and 0.8% in nonobese women.

The univariate regression analysis was applied to examine the relationship between metabolic syndrome and various anthropometric variables as well as adiposity indices of obese/overweight and non-obese PCOS women (Table 1). The variables exhibiting significant association between metabolic syndrome and different indices in this analysis were further used to predict the associations of metabolic syndrome in multivariate logistic regression analysis. In the univariate regression model, VAI and W/H ratio were identified as significantly associated with metabolic syndrome (MS) in obese PCOS women.

 Table 1
 Univariate logistic regression for predicting occurrence

 of
 metabolic syndrome using anthropometric and adiposity

 indices in non-obese and overweight/obese PCOS women

Variable group		В	Wald	Significance	Exp B (95% Cl)	
VAI	NO	0.16	7.66	0.06	1.17 (1.04–1.32)	
	0	0.14	25.33	0.00	1.14**(1.08-1.21)	
ASBI	NO	0.30	0.00	0.99	1.35(0.00-8.63)	
	0	- 9.85	0.15	0.69	0.00(0.00-9.26)	
BAI	NO	0.05	0.17	0.67	1.05(0.81–1.36)	
	0	-0.01	0.13	0.70	0.98(0.92-1.05)	
FFMI	NO	-0.22	0.37	0.54	0.80(0.39–1.63)	
	0	0.04	0.38	0.53	1.05(0.90-1.22)	
FMI	NO	0.55	3.38	0.06	1.73(0.96–3.13)	
	0	0.05	0.85	0.35	1.05(0.94–1.47)	
WHt ratio	NO	12.45	2.30	0.12	2.57(0.02–2.53)	
	0	2.62	1.20	0.27	13.79 (0.12–5.02)	
W/H ratio	NO	6.06	1.43	0.23	4.2(0.21-8.59)	
	0	6.51	5.00	0.02	6.7*(2.2–20.44)	

Level of significance = $p < 0.05^*$; $p < 0.01^{**}$

NO Non-obese, O Overweight/obese, W/H Ratio = waist/hip ratio, WHtRatio Waist/height ratio, FMI Fat mass index, FFMI Fat-free mass index, BAI Body adiposity index, ABSI A body shape index, VAI Visceral adiposity index

PREVALENCE OF METABOLIC FEATURES



However, in non-obese PCOS women, only VAI was considered as a predictor of metabolic syndrome.

The multivariate logistic regression analysis (Table 2) presented that visceral adiposity index (VAI) was significantly associated with metabolic syndrome in obese (OR = 1.17, 95% CI 1.04–1.32, p < 0.01) and non-obese (OR = 1.2, 95% CI 1.08–1.21, p < 0.01) PCOS women. The model depicted a good fit of data, using Hosmer and Lemeshow test (chi-square = 3.41, p = 0.90), in non-obese PCOS women with explained variation between 19.9% (Cox and Snell R^2) and 37% (Nagelkerke R^2) in metabolic syndrome. Similarly, in obese women, the model demonstrated a good fit of data (chi-square = 8.93, p = 0.34) with total variation in explaining metabolic syndrome between 22.4% (Cox and Snell R^2) and 30.5% (Nagelkerke R^2).

Further, the ROC analysis was performed to predict the sensitivity and specificity of the variable group. The ROC curve (Figs. 2 and 3) revealed that the visceral adiposity index had significantly higher accuracy in predicting MS in non-obese women than obese women (AUC=0.81, 95% CI 0.66–0.96 vs AUC=0.72, 95% CI 0.64–0.80). In obese PCOS women W/H ratio also depicted accuracy in predicting metabolic syndrome risk with AUC=0.60 (95% CI 0.51–0.69).

Discussion

Polycystic ovarian syndrome (PCOS) is an emerging endocrine-metabolic condition among women in reproductive span marked by abnormal fat distribution. In the present study, 30% of participants had metabolic syndrome (MS), out of which 4% were in the non-obese category and 26% were obese women. Similarly, a study carried out on Brazilian women by De Medeiros et al. [16] noticed a higher prevalence of metabolic syndrome (MS) in obese PCOS women (44.4%) as compared to their lean counterparts (6%). Many researches carried out on different populations were consistent with our

Table 2 Multivariate logistic regression and ROC analysisfor predicting the occurrence of metabolic syndrome usinganthropometric and adiposity indices in non-obese andOverweight/obese PCOS women

Variable group	В	Wald	Sig	Exp B (95% CI)	AUC (95% CI)			
Obese								
VAI	0.16	26.54	0.00	1.17(1.1–1.25)	0.72(0.64-0.80)**			
W/H Ratio	24.22	0.45	0.50	3.3(0.00-12.33)	0.60(0.51-0.69)*			
Non-obese								
VAI	0.17	6.92	0.00	1.20(1.04–1.35)	0.81(0.66-0.96)**			
Level of significance level = p values < 0.05*; p < 0.01**								

VAI Visceral adiposity index, WHRatio Waist/hip ratio

PCOS Group: Non-obese 1.0 Source of the Curve 0.8 WHratio Sensitivity WHtRatio VΔI 0.6 Reference Line 0.4 0.2 0.0 0.6 0.2 0.4 0.8 1.0 0.0

ROC Curve

1 - Specificity

Fig. 2 ROC curve showing probabilities in predicting metabolic syndrome in the non-obese group

findings and recorded an increased prevalence of metabolic syndrome with an increased rate of obesity [16, 17].

The presence of metabolic syndrome was 39.5% in Iran [17] and 46% in the American population [18]. The prevalence of metabolic syndrome seemed to be low in European populations, exhibiting 1.6% in the Czech Republic [19] and 8.2 to 16% in Italy [2]. This may be due to a lower prevalence of obesity, thus, attributing to lifestyle factors [20].

Results of the present study depict that WC>88 cm was the most prevalent feature with a frequency of 61.6% in obese women and 5.6% in non-obese women. Most of the studies indicated a strong association between obesity and metabolic syndrome [21, 22]. It is well known



Fig. 3 ROC curve showing probabilities in predicting metabolic syndrome in the obese group

that waist circumference increases with central obesity and has superseded BMI as a more accurate indicator of obesity-related metabolic disorders [23].

The prevalence of dyslipidemia is common among PCOS women. In our study, the occurrence of HDL < 50 mg/dl was higher among overweight/obese PCOS women than their non-obese counterparts. Another researcher Iuhas et al. [24] reported that PCOS women had lower HDL levels and high total cholesterol and LDL-C levels. In divergence with these findings, Macut et al. [25] observed no difference between the lipid profile of PCOS and healthy population. However, the features of dyslipidemia such as decreased HDL-C and increased triglycerides were observed in PCOS women only. The influence of hyperandrogenism and insulin resistance, which are common in PCOS women, as well as nutrition, exercise, and genetic predisposition, contributed to different forms of dyslipidemia in women with PCOS. It was observed in a systematic review that alteration in triglycerides and HDL-cholesterol occurred among PCOS women, irrespective of BMI [26].

Apart from PCOS, excess central fat distribution is a key requirement in the classification of the metabolic syndrome, and it is inherently linked to both glucose intolerance and Type 2 Diabetes, as well as lipid diseases and hypertension. In the present research, the prevalence of increased SBP (21.2%) and DBP (16.4%) were also higher among obese PCOS women than non-obese women. The prevalence of hypertension has been reported in numerous studies [27–29] among PCOS women. A study [30] revealed a higher relative risk of developing hypertension among reproductive age of PCOS women only (1.7-fold, 95% CI 1.43–2.07).

Similarly, an increased level of triglycerides among obese women (13.6%) than their non-obese counterparts was observed in our study. The prevalence of hypertriglyceridemia was 24.6% in Chinese PCOS women [31], which is in convergence with the findings of the present study. Another cross-sectional research performed by Yildrim et al. [32] depicted significantly higher triglyceride concentration in PCOS women than in control women $(130.5\pm25.6 \text{ vs } 82.0\pm11.8)$. It is evident that increased lipid level in combination with hyperinsulinemia suppresses the secretion of FSH, which is ultimately associated with a detrimental metabolic environment. Hence, there are endocrinal disorders and ovulation dysfunction in PCOS [31].

In the current cross-sectional study, visceral adiposity index acts as a significant predictor of metabolic syndrome risk in non-obese (OR 1.20, 95% CI 1.04– 1.35) and obese PCOS women (OR 1.17 times, 95% CI 1.1–1.25). In convergence with the finding of the present study, Iranian obese PCOS women exhibited a two-fold higher probability of occurrence of metabolic syndrome [17]. Adiposity plays an important role in the development of PCOS and strongly influences the clinical and endocrine characteristics in various women [33]. A study conducted on Thai women [34] reported that the visceral adiposity index was the best indicator in predicting metabolic syndrome (MS) followed by BMI and WHtR.

Another study conducted by Bil et al. [35] also portrayed VAI as an independent factor in assessing the metabolic syndrome risk among PCOS women using logistic regression analysis (p=0.002). They further noted that VAI was a sex-specific indicator of visceral adiposity and visceral to subcutaneous fat ratio.

In the present study, VAI demonstrated a one-fold higher risk for the prediction of metabolic disorders. The VAI is a biomarker for adipose tissue malfunction and aberrant distribution. Obesity plays a key influence in the development of hyperandrogenism and other PCOS symptoms via insulin resistance and compensatory hyperinsulinemia. In comparison to the control group, PCOS women have similar amounts of total and trunk fat but have more visceral fat [36]. VAI has been connected to low-grade inflammation in PCOS women and can affect the adipose tissue's endocrine activity. The findings of Amato and Giordano [10] revealed a strong association between VAI and adipocytokines in comparison to other anthropometric tools. Past literature [3, 37, 38] also highlighted a strong association between obesity and metabolic syndrome.

There are specific established effects of visceral fat on metabolic dysfunction through adipokine and fatty acid release. It is vital to explore the possible role of visceral fat preponderance as a contributor to the pathophysiology of insulin resistance which is central to PCOS [39]. Therefore, our study suggests that VAI should be considered a simple and useful tool to predict metabolic syndrome in PCOS women with and without obesity.

Strengths and limitations

The present study is an attempt to comprehend the metabolic profile of PCOS women while focusing on obesity. The current topic of research was less explored in the Northern region of India with the present sample size. The use of various anthropometric indices to assess the association of metabolic disorders among PCOS women is one of the major strengths of the study. While lack of a control group due to financial restrain as well as the unavailability of serum glucose levels were the limitations of the present study.

Conclusion

The present research demonstrates a high prevalence of metabolic syndrome in obese PCOS women. The features of metabolic syndrome showed waist circumference as the most prevalent characteristic among PCOS women. The multivariate test showed VAI as an important predictive tool to assess the metabolic syndrome in both groups i.e., obese, and non-obese. However, the waist/hip ratio can be considered as a predictive tool in obese women only. So, it could be used as a significant tool in clinical practices for early detection of metabolic syndrome in PCOS women. Prior screening of metabolic disorders through simple tools could be beneficial for women to prevent further aggravation of PCOS symptoms and complications.

Already known implications of the study

It is well known that metabolic syndrome is more prevalent among PCOS women than their non-PCOS counterparts. Obesity is an independent risk factor in the development of metabolic syndrome. However, previous studies assessed the association between metabolic syndrome and body mass index of PCOS and control population. Our study implied how BMI categorization among PCOS women showed significant differences in assessing metabolic syndrome using different anthropometric indices. Further studies need to be done in this domain to validate the findings of the present study.

Abbreviations

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Authors' contributions

The authors RK and MK are involved in study conception, research design, and manuscript drafting. RK is involved in the collection of data. RK and MK analyzed and interpreted the data. All authors read and approved the final manuscript.

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Availability of data and materials

The data generated/analyzed during the research study are not publicly available due to ethical declaration. However, could be available on reasonable request.

Declarations

Ethics approval and consent to participate

The Institutional Ethical Committee of Panjab University, Chandigarh, India (PUIEC/ 2018/109 /A /09/ 01) gave their approval to the study. Before being enrolled in the study, each participant signed a written informed consent form.

Consent of publication

Not applicable.

Competing interests

The authors (R.K. and M.K.) declare that they have no competing interests.

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