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Original article

Metabolic syndrome in women with and without polycystic syndrome, A case control study in Iran

Farzaneh Montazerifar[*,1], Marzieh Ghasemi[2], Nafiseh Arabpour[3], Mansour Karajibani[4], Narjes Keikhah[5]

[*,1] Pregnancy Health Research Center, Nutrition Department, School of Medicine, Zahedan University of Medical Sciences, Zahedan, Iran

[2] Pregnancy Health Research Center, Obstetrics and Gynecology Department, Zahedan University of Medical Sciences, Zahedan, Iran

[3] School of Medicine, Zahedan University of Medical Sciences, Zahedan, Iran

[4] Health Promotion Research Center, Nutrition Department, School of Medicine, Zahedan University of Medical Sciences, Zahedan, Iran

[5] Department of Anatomical Sciences, Faculty of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran

[6] School of Medicine, Zahedan University of Medical Sciences, Zahedan, Iran

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Abstract

Background: Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in women of fertility age. The aim of this study was to compare the prevalence of metabolic syndrome (MetS) in women with and without PCOS, who referred to infertility clinic.

Methods: In this case control study, 120 women with PCOS and 120 healthy controls, who had referred to infertility clinic, were selected for the purpose of this study. Polycystic ovarian disease was diagnosed according to the Rotterdam (2003) criteria, and the prevalence of MetS was assessed according to the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) criteria for both groups.

Results: Women with PCOS had markedly higher prevalence of the MetS than healthy controls (29.2% and 7.5%, respectively; P<0.0001). Among risk factors of MetS, the most prevalent components were low level of HDL cholesterol (97.5%), central obesity (86.7%), and high triglyceride (77.5%). The prevalence of MetS increased with age and BMI (P<0.0001).

Conclusion: The results suggest that the MetS was more frequent in PCOs infertile women, especially in upper age groups. Thus, the screening of these patients is suggested for preventive strategies in high risk individuals.

Keywords: Infertility, Metabolic syndrome, Polycystic ovary syndrome, Prevalence

Introduction

Polycystic ovary syndrome (PCOS) is the most common endocrine disturbance in women of reproductive age, leading to infertility (1). The prevalence of PCOS has been reported to be around 6–20% in different countries (2, 3). Studies have shown that women with PCOS are at high risk of metabolic disorders and type 2 diabetes (4, 5) and an increased risk of cardiovascular disease, which is seen in obese women with the disorder (1). Metabolic syndrome, one type of endocrine disorder and a cardiovascular risk factor, is mainly observed with insulin resistance, hyperinsulinemia, dyslipidemia, abdominal obesity, and hypertension (6, 7). Many disorders caused by PCOS are similar to MetS components (6, 7). A high

***Correspondence author:** Dr. Montazerifar: Department of Nutrition, School of Medicine, Zahedan University of Medical Sciences, Zahedan, Iran Tel: +98- 9155416903 Fax: +98- 54-33295728 E-mail: fmontazerifar@gmail.com

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prevalence of diabetes mellitus and impaired fasting glucose, hypercholesterolemia, high triglyceride and low HDL (8-10), the prevalence of obesity in women with PCOS (9-12), hypertension and infertility prevalence in obese women with PCOS compared to those with normal weight have been reported in several studies (12). Studies on the prevalence of MetS in Iranian women with PCOS and those of other countries have reported varied data from 19.7% - 46.4% in Iran (1, 5, 8, 13), 37.5% - 47.5% in India (9, 10) and 43-46% in the US (14, 15). There is, nevertheless, one study conducted on Iranian women reporting that metabolic syndrome in women with PCOS was no more common than in healthy controls (13). The contradictory results on the prevalence of MetS of women with PCOS in Iran and other countries demonstrate that more research is needed to be done in this area. Thus, this study was performed to determine the prevalence of MetS and its risk factors in women with and without PCOS, who had referred to infertility clinic in Zahedan, Iran.

Materials & Methods

This study was supported by the Research Deputy of Zahedan University of Medical Sciences, Zahedan, Iran (approval date: January 2018; number 8624). The protocol of the study was approved by the Ethics Committee of Zahedan University of Medical Sciences (Code No: IR.ZAUMS.REC.1396.308).

This case control study was conducted on 120 women with PCOS and 120 healthy controls attending the infertility clinic in Zahedan, Iran. The study was carried out between March, 2018, and April, 2019. Informed consent forms were also given to all the participants. The control group comprised infertile women without PCOS, whose infertility was due to their husbands. All consecutive women with and without PCOS were matched based on age and body mass indices (BMI).

The Rotterdam criteria (2003), used for the diagnosis of PCOS, had at least two of the following features: (i) oligo-ovulation or chronic an ovulation, (ii) clinical and/or biochemical hyperandrogenism, and iii) ultrasound appearance of polycystic ovaries (9,16).

The inclusion criteria were as follows: 15-45 years of age, no use of steroid or oral contraceptive drugs within 3 months prior to the onset of the study, the history of diabetes, the use of anti-diabetic and anti-lipid medications, hypertension, androgen secreting tumors, thyroid and renal disorders, hyper-prolactinemia, and Cushing's syndrome.

The anthropometric measurements and the blood pressure of the participants were evaluated by a researcher right after obtaining the written consent forms. Their weight and height were also measured with light clothing without shoes. The BMI was calculated as weight (kg) divided by the square of height (m2) (kg/m2). Waist circumference (WC) was measured with a non-elastic tape at the narrowest circumference, midway between the top of iliac crest and the lowest rib margin. WC ≥ 88 cm was considered as central obesity. BMI was stratified into two groups as follows: (1) non-obese: BMI < 25 kg/m2 and (2) overweight /obese: BMI ≥ 25 kg/m2 (9). Age was also categorized into two subgroups: (1) < 30 year and (2) ≥30 years. Blood pressure was measured twice using a manual mercury sphygmomanometer on the right arm in a sitting position after 10 minutes rest. The mean of two measurements was reported (9).

Overnight fasting blood sample was obtained from all women. Blood tests, including fasting blood glucose (FBS) and lipid profile (total cholesterol, triglyceride, high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) levels, were measured using enzymatic calorimetric method by Pars Azmun kits, Tehran, Iran.

The diagnosis of MetS was according to the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III (criteria); thus, the presence of three or more of the following five criteria was necessary: (1) waist circumference of ≥88 cm or more, (2) blood pressure of ≥130/85 mmHg; (3) fasting blood sugar of ≥ 100 mg/dL, (4) triglycerides of ≥150 mg/dL and (5) HDL-C of ≤50 mg/dL (8). In addition, High LDL-C and high cholesterol were defined as LDL-C ≥130 mg/dL and (total cholesterol ≥200 mg/dL), respectively.

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Statistical analysis

The statistical analyses were performed using SPSS software version 21 (SPSS,Inc., Chicago, IL, USA). The data were presented as mean ± standard deviation (SD) and frequency (%). The Student's t-test and Chi-square test were used to compare the continuous and categorical variables, respectively. Kolmogorov-Smirnov test was used for evaluation of normality of distribution. Spearman's correlation coefficient was calculated to assess the association between MetS and other biomarkers. After controlling the significant variables identified by univariate analyses, a bionominal logistic regression analysis with calculation of the adjusted odds ratio (OR) and 95% confidence interval (CI) was performed for the identification of independent predictors of metabolic syndrome. A P-value of <0.05 was considered significant.

Results

The anthropometric and biochemical characteristics of participants are demonstrated in Table 1. The mean age and BMI of women with PCOS were 26.3±5 years and 27.9±6 Kg/m2, respectively, and the mean age and BMI of women without PCOS (control group) were 26.8± 5.4 years and 26.6±5.2Kg/m2, respectively. The prevalence of metabolic syndrome was found to be higher in women with PCOS compared to the control group (29.2% vs. 7.5%; P<0.0001). Also, the women with PCOS had significantly higher values of waist circumference (P<0.001) and triglyceride (P=0.04) and lower levels of serum HDL-C (P = 0.046) than the control group.

Table 2 demonstrates the distribution of metabolic syndrome according to different categorizes of age and body mass index. The results showed that the prevalence of MetS increased with age and BMI (P<0.001).

The prevalence of metabolic risk factors is shown in Table 3. The most prevalent risk factors were the low level of HDL-C (97.5%), the central obesity (86.7%), high LDL-C (80.8%), and high triglyceride (77.5%). A significant correlation was found between metabolic syndrome with WC (r= 0.2, P=0.02), FBS (r=0.21, P=0.02), triglyceride (r= 0.59, P<0. 001), high LDL-C (r= 0.21, P=0.02), and low HDL-C (r= - 0.19, P=0.03).

In a logistic regression analysis, low HDL-C (OR = 3.05, 95% CI: 1.76–5.51), high triglyceride (OR= 3.54, 95% CI: 1.57-7.99) and high WC (OR= 2.01, 95% CI: 1.01-3.88) were markedly associated with MetS (Table 4).

Table1. Demographic, anthropometric, and metabolic characteristics in studied groups

Variables	With PCOS (n=120) Mean± SD	Without PCOS (n=120) Mean± SD	P-value
Metabolic syndrome n (%)	35(29.2%)	9 (7.5%)	<0.001
Age (years)	26.3±5	26.8± 5.4	0.478
Body mass index (Kg/m^2)	27.9±6	26.6±5.2	0.065
Waist Circumference (Cm)	99.3±11.1	90.4±9	<0.001
Systolic pressure (mmHg)	116.6±7.5	114.6±8.3	0.500
Diastolic pressure (mmHg)	79.6±5.8	78±6.7	0.250
Fasting blood sugar (mg/dL)	95.2±14.9	94.3±7.3	0.320
Cholesterol (mg/dL)	197.1±22.8	191.2±22.9	0.130
Triglyceride (mg/dL)	141±73	120.8±58.5	0.040
LDL-C (mg/dL)	110.6±21.1	105.4±12	0.450
HDL-C (mg/dL)	39.2±3.4	49.3±7.4	0.046

PCOS: polycystic ovary syndrome; LDL-C: low density lipoprotein cholesterol; HDL-C: high density lipoprotein cholesterol

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Table2. Distribution of metabolic syndrome according to age and body mass index categorizes

Variables	With PCOS n / Total (%)	Without PCOS n / Total (%)	P-value
Age (years)			
<30	10 / 61 (16.4%)	8 / 67 (11.9%)	0.450
≥30	25 / 59 (42.4%)	1 / 53 (1.9 %)	< 0.0001
Body mass index (Kg/m2)			
<25	7 / 33 (21.2%)	3 / 39 (7.7%)	<0.010
≥25	28 / 87 (32.2%)	6 / 81 (7.4%)	<0.0001

PCOS: polycystic ovary syndrome

Table3. Prevalence of metabolic risk factors in studied groups

Variables	With PCOS n (%)	Without PCOS n (%)	P-value
Overweight/Obese (BMI ≥25 Kg/m^2)	87(72.5%)	81(67.5%)	0.390
Central obesity (WC ≥ 88 cm)	104(86.7%)	28(23.3%)	<0.0001
Hypertension (BP ≥130/85 mmHg)	6(5%)	1(0.8%)	0.010
High FBS (≥ 100 mg/dL)	13(10.8%)	5(4.2%)	0.050
High Cholesterol (≥200 mg/dL)	64(53.3%)	32(26.7%)	<0.0001
High Triglyceride (≥150 mg/dL)	93(77.5%)	5(4.2%)	<0.0001
High LDL-C (≥130 mg/dL)	97(80.8%)	78(65.0%)	0.006
Low HDL-C (≤50 mg/dL)	111(97.5%)	3(2.5%)	<0.0001

PCOS: polycystic ovary syndrome; BMI: Body mass index; WC: waist-circumference; BP: Blood pressure; FBS: fasting glucose blood sugar; LDL-C: low density lipoprotein cholesterol; HDL-C: high density lipoprotein cholesterol

Table 4. Logistic regression analysis showing the predictive association of studied variables and presence of metabolic syndrome in PCOS group

Model	Beta	P-value	Odds ratio	95% CI
Central obesity (WC ≥ 88 cm)	0.244	0.041	2.01	1.01~3.88
Hypertension (BP ≥130/85 mmHg)	0.072	0.540	0.69	0.43~1.56
High FBS (≥ 100 mg/dL)	0.222	0.089	0.66	0.48~1.09
High Cholesterol (≥200 mg/dL)	0.084	0.385	0.52	0.18~1.05
High Triglyceride (≥150 mg/dL)	0.569	0.0001	3.54	1.57~7.99
High LDL-C (≥130 mg/dL)	0.080	0.062	1.05	0.93~1.58
Low HDL-C (≤50 mg/dL)	0.007	0.001	3.05	1.76~5.51

PCOS: polycystic ovary syndrome; BMI: Body mass index; WC: waist-circumference; BP: Blood pressure; FBS: fasting glucose blood sugar; LDL-C: low density lipoprotein cholesterol; HDL-C: high density lipoprotein cholesterol.

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Discussion

The metabolic abnormalities in women with PCOS directly contribute to the increased risk of MetS and the development of atherosclerotic cardiovascular disease (1,9). The present study demonstrated that the prevalence of MetS in women with PCOS was 29.2%, which was according to ATPIII criteria. The results of our study are close (28.8%) to that of Zahiri et al (1) in North of Iran. It was, nonetheless, lower than the reported rate in a study performed in an urban population of Tehran (46.4%) (17), and those of several other studies in the United States (33.4–46%) (14, 15). Also, in some Asian countries such as India and Brazil, the rates were 37.9% and 28.4% (9, 10), respectively. In contrast, in several studies in Iran (5, 8, 13, 18) and several European countries, like Turkey (11.6%) (19) and southern Italy (8.2%) (20), the prevalence of MS in women with PCOS was found to be lower compared to our results. The different prevalence rates of MetS are likely to be attributed to sample size, diagnostic criteria, race, age, body mass index, and lifestyle in various populations (1, 5, 8).

Advanced age was known as a vital risk factor for metabolic syndrome in the case of PCOS and in general population as well. Our study revealed that the risk of MetS in women with PCOS increased with age, and 42.4% of women the ages ≥ 30 years had metabolic syndrome. The results of several studies have also revealed that women with both PCOS and MetS were significantly older than others (1, 5, 22). It seems that the high prevalence of MetS in aging may be partly associated with hyperinsulinimia changes in body composition and increased body fat (8). It is also known that the pattern of fat distribution in obese women is associated with the increased risk of insulin resistance, hyperandrogenism, and metabolic disorders (1,8,9).

The relationship between MetS and BMI in general population (21) and in women with PCOS (22) was revealed in earlier studies. However, it has been reported that in women with PCOS, the age and central obesity are more powerful predictors for the presence of metabolic syndrome than BMI (9). In contrast, a meta-analysis result in Iran showed that there was no significant correlation between the MetS and waist circumference, BMI, and age (18). Our study showed that the risk of MetS increased in those with BMI ≥25 kg/m2, as 32.2% of women with PCOS who had BMI ≥ 25 kg/m2 were exposed to MetS. Similar to the findings of our study, other studies found that the prevalence of MetS increased with obesity (5, 9, 22). Also, our finding, the high value of waist circumference in women with PCOS compared to healthy controls, indicated that WC was closely correlated with MetS. This finding was consistent with those of the earlier studies (9,23).

Among the biochemical parameters that were measured in our study, the level of serum triglyceride was markedly higher and the HDL- C level was markedly lower in women with PCOS compared to healthy controls. Dyslipidemia was present with a low level of HDL-C in 97.5% of women with PCOS, followed by increased triglyceride in 77.5%.

In previous studies, the most prevalent components of MetS in women with PCOS were different. However, in line with our findings, several studies have reported that the most prevalent risk factors of MetS in women with PCOS were the low level of HDL-C, high triglyceride, and the increased WC (24,25). Low levels of HDL-C, as a component of MetS, has a crucial role in the development of cardiovascular diseases (1,5, 22). In our study, the multivariate logistic regression analysis showed that central obesity, low HDL-C, and high triglyceride were more powerful predictors of metabolic syndrome in women with PCOS compared to other risk factors of MetS.

The present study has some limitations. This study was performed with low sample size. For a more accurate estimate, a greater sample size is needed. Also, the evaluation of body composition, physical activity, and dietary intake are essential for preventive planning.

Conclusion

The results suggest that obese women with PCOS in upper age groups are at a greater risk of metabolic disorders. The identification of risk factors for screening can be a substitute strategy. Further

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investigations for the screening of metabolic syndrome in women with PCOS are highly required.

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Conflicts of Interest

The authors have no competing interests.

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