Cardiovascular status and metabolic syndrome among young women with polycystic ovarian syndrome in a rural area in Egypt

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Abstract

Objective: To evaluate the cardiovascular status and risk factors among active non smoker young PCOS women, in a rural community in Egypt, with or without features of MS. Materials & Methods: A case control study comprised of 312 PCOS women who were recruited from the Outpatient Clinics, Mansoura University Hospitals fulfilling the Rotterdam consensus criteria (2003) of PCOS. They comprised of 122 women who fulfilled the definition criteria of MS according to National Cholesterol Education Program and the Adult Treatment Panel III, 2001.The remaining 190 cases did not fulfill the definition criteria (non- MS PCOS). A healthy age-matched control group of 50 women free of PCOS were also included. All cases and control underwent ECG-QTc interval analysis, echocardiography for interventricular septum diameter (IVSD) and ejection fraction (EF) estimation, and carotid intima media thickness (cIMT) by ultrasound Doppler study.

Results: Cardiovascular abnormalities were significantly higher among the MS-PCOS cases compared to non- MS PCOS, significant prolongation of QTc interval (P 0.03) with evident QT dispersion (P 0.018), significant increase in IVSD (P 0.03), insignificant decrease in EF and significant increase in cIMT (P 0.046) in PCOS cases with MS. On the other hand, the non- MS PCOS cases showed significant prolongation of QTc interval (P 0.049), significant increase in IVSD (P 0.004) significant decrease in EF (P 0.039) and significant increase in cIMT (P 0.018) when compared to the healthy control women.

Conclusion: Many cardiovascular risks are frequent and evidence of premature atherosclerosis is existent among young women with PCOS, being even more exaggerated if there is associated MS. Early intervention to ameliorate cardiovascular risks for these cases is an important health care demand.

Keywords: Polycystic ovary syndrome, metabolic syndrome, cardiovascular risks.

Introduction

The new millennium has brought intense focus on the risk of cardiovascular disease (CVD) in women especially those with features of metabolic syndrome (MS) (1). PCOS is the most common endocrine disorder worldwide being not only a reproductive disorder but a multifaceted syndrome with insulin resistance (IR), substantial metabolic and long term cardiovascular (CV) consequences (2). Serial CV risk factors in MS are present at early age in PCOS women and IR appears to be the key factor linking these risk factors (3). Ehrmann and coworkers (4) reported that MS and PCOS have many features in common and usually have the same pathogenesis. However, Cusson et al (1) reported that the real increase of CVD in PCOS women remains unclear and definitive data are lacking and more studies are needed to define the magnitude of CV risk and CV disease in PCOS with or without MS (3). The aim of this work was to detect the CV risk factors and the CV manifestations present in women with PCOS with and without MS in a case control study.

Patients & methods

The studied cases included 312 women who were enrolled from patients attending the outpatient clinics, Mansoura University Hospital because of obesity, oligomenorrhea, amenorrhea and/or hirsutism after confirmation of the presence of PCOS according to the Rotterdam criteria (5). The study protocol was approved by the ethical committee and informed consents were obtained.

Clinical examination and laboratory investigations were carried out stressing on symptoms and signs of MS according to National Cholesterol Education Program and the Adult Treatment Panel III (NCEP- ATP III) (6); namely 3 or more of the following conditions; waist circumference >88 cm, BP >130/85mmHg, TG >150 mg/dl, FPG >110 mg/dl, HDL-C <50 mg/dl.

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Waist circumference was assessed in the standing position midpoint between the highest point of iliac crest and the lowest point of the costal margin in the mid axillary line. BMI was calculated as weight (kg)/height (meter)2. Blood pressure was measured twice at 30 minutes intervals by using a standard mercury manometer and the mean of two readings was used for analysis (7).

Secondary causes of hyperandrogenism were excluded by appropriate clinical and laboratory tests. Women with known diabetes mellitus, hypertension, hepatic or renal disorders and women receiving antihypertensive, lipid lowering drugs were also excluded. The studied women were not desiring pregnancy and were not receiving oral contraceptives. Fasting plasma glucose level was measured by autoanalyzer by the glucokinase method. Insulin measurements were performed by using a polyethylene glycol accelerated double antibody radioimmunoassay method. TG was measured enzymatically on a chemistry autoanalyzer and free testosterone was assessed together with HDL-C estimation (8). Twelve lead electrocardiographies were undertaken with stress on ischemia, arrhythmia, QTc, QTd. Echocardiographic assessment was carried out with stress on IVSD, EF, together with measurement of cIMT for the studied cases and the reference groups.

Statistical analysis

Statistical analysis was performed by using SPSS statistical package for social science program version "16". The qualitative data were presented as frequency and percentages. The quantitative data were examined by using Kalmogrov-Smirnov test to test for normal distribution of the data when parametric, expressed as mean and standard deviation. Student t test was used, to test for difference in normally distributed quantitative data between the two groups. Mann-Whitney-μ test was used for comparison between two groups when data were not normally distributed. Significance was considered when P value was less than 0.05.

Results

Out of the 312 women with PCOS, 122 cases fulfilled the NCEP and the modified ATP III for the diagnosis of MS making the prevalence of MS among PCOS women to be 39.11%. The prevalence of MS increased significantly with age, BMI, IR and free testosterone plasma level (table II). The most dominant component of MS was the increased waist circumference (>88 cm) being present in 77.87% of PCOS women, followed by lowered HDL-CL plasma level (75.41%). Hypertriglyceridemia was present in 28.69% and BP elevation was present in only 20.5%. Elevated FPG was detected in only 17.21% of women with PCOS (table III).

Among the studied CV variables, QTc and QTd were significantly higher among the MS PCOS cases compared to non- MS PCOS: significant increase in IVSD, insignificant decrease in EF and increase in cIMT in PCOS cases with MS. On the other hand, the non- MS PCOS cases showed significant prolongation of QTc interval, significant increase in IVSD and significant increase in cIMT (P 0.018) when compared to the healthy control women (table IV). In the present study higher left ventricular mass (LVM), higher left atrium size, and lower LVEF and early to late mitral flow velocity were observed in both groups of PCOS in comparison to control (table IV).

Table (I): Demographic characters of the studied PCOS women.

	No. of cases	Percentage
Age		
≤30 years	125	40.07%
>30 years	187	59.94%
BMI		
< 25	125	40.07%
25-30	94	30.13%
>30	93	29.81%
Insulin resistance		
FBG/FI ≤4.5	190	60.9%
FBG/FI >4.5	122	39.11%
Free testosterone		
< 2 mmol/L	78	25%
≥2 mmol/L	234	75%

Table (II): Prevalence of metabolic syndrome according to age, BMI, IR, free testosterone

Risk parameters		PCOS without MS (n=190)	PCOS with MS(n=122)	P
Age	≤30 years	95 (50%)	30 (24.59%)	<0.001
	>30 years	95 (50%)	92 (75.41%)	
BMI	<25	120 (63.1%)	5 (4.09%)	<0.001
	25-30	64 (33.6%)	30 (24.5%)	
	>30	6 (3.1%)	87 (71%)	
Insulin resistance	FBG/FI ≤4.5	98 (51.6%)	92 (75.41%)	<0.001
	FBG/FI >4.5	92 (48.4%)	30 (24.59%)	
Free testosterone	≥2 mmol/L	134 (70.5%)	100 (81.9%)	0.023
	<2 mmol/L	56 (29.5%)	22 (18.1%)	

Table (III): Prevalence of individual components of metabolic syndrome in PCOS patients

Components of metabolic syndrome.	PCOS withMS (total no. 122 cases)	% of cases
HDL <50 mg/dl	92	75.4%
Waist circumference ≥88 cm	95	77.87%
TG ≥150 mg/dl	35	28.69 %
BP≥130/85 mmHg	25	20.5%
FPS ≥110 mg/dl	21	17.21%

Table (IV): Demographic characters of studied groups versus the control group.

(mean ± SD)	PCOS with MS (n=122)(1)	PCOS without MS (n=190) (2)	Control (n=50) (3)	P(1- 3)	P(2- 3)	P (1- 2)
Age	29.2± 4.3	28.9± 4.5	29.91± 3.3	0.80	0.244	0.55
BMI	28.4± 2.2	28.8± 2.5	28.5± 2.1	0.389	0.780	0.138
Insulin resistance (FBG/FI)	3.9± 1.7	4.3± 1.8	4.6± 0.1	0.023	<0.001	0.048
Free testosterone (mmol/L)	1.8± 0.9	1.6± 0.8	1.1± 0.6	<0.001	<0.001	0.046
HDL(mg/dl)	45.5± 12.9	48.8± 13.5	54.7 ± 11.2	<0.001	<0.001	0.031
Waist circumference(cm)	88.5± 01.2	75.5± 1.1	74.5± 2.4	0.004	<0.001	<0.001
TG (mg/dl)	126.8± 12.9	121.8±20.1	116 ±16.2	0.033	<0.001	0.007
SBP(mmHg)	125± 15.5	120 ± 13.6	116 ± 9.2	0.015	<0.001	0.003
DBP(mmHg)	83± 9.9	80 ± 8.8	76.6 ± 9.9	0.028	<0.001	0.006
FPS (mg/dl)	95.1± 9.8	93.2± 9.9	89.2± 8.9	0.006	<0.001	0.097

Table (V): Cardiovascular abnormalities in studied groups versus the control group.

(mean ± SD)	PCOS with MS (n=122) (1)	PCOSwithout MS(n=190) (2)	Control (n=50) (3)	P(1-3)	P(2-3)	P(1-2)
QTc interval (ms)	456± 30	445± 50	435± 20	<0.001	0.031	0.016
QT dispersion (sec)	0.05±0.04	0.04 ±0.03	0.03±0.02	0.005	<0.001	0.018
IVSD	11.1 ± 0.8	10.9 ± 0.8	10.5 ± 0.9	0.004	<0.001	0.03
EF	69.8± 2.9	70.2± 2.8	71.2± 3.1	0.039	0.006	0.229
cIMT(cm)	0.845± 0.21	0.798±0.19	0.765±0.01	0.018	<0.001	0.046

Discussion

The prevalence of MS among women with PCOS in the present study is 39.11. This is nearly similar to many previous studies (4, 9), but lower than the findings of Dokras et al (10), Carmina (11) who reported that nearly 50% of women with PCOS have MS. While the results of Hahn et al (12) are much lower (31.5%). The differences in the prevalence of MS among women with PCOS could be due to racial or ethnic characteristics and/or differences in the diagnostic criteria adopted for the diagnosis of PCOS and MS. Carmina and coworkers (13) utilizing the ATP III criteria found the prevalence of MS to be 8.2% and by using the WHO criteria to be 16% in Italian women with PCOS.

The prevalence of MS increased with age from 24.59% in the group below 30 years to 75.41% in the group >30 years (P <0.001). This is contradictory to Dokras et al (10), Trevor et al (7) and Orchard et al (14) who found that the incidence of MS did not vary substantially by age. However, the present findings are in agreement with the result of Grant and Meigs (15) which revealed an increasing prevalence of IR in elderly populations.

The prevalence of MS in the studied women was positively related to BMI. This confirms the results of Coviello et al (9) who found none of the girls of normal BMI having MS, whereas 63% of obese PCOS were having MS.

The increased IR in the studied group of PCOS is in agreement with Orio et al, (16), Carmina et al (13). In Hahn et al (12) study, IR was the most common metabolic abnormality in PCOS being present in 71%. In our series IR was present in 75.4%.

The present results illustrated that the prevalence of MS is increased in PCOS cases having higher free testosterone. This is in accordance with Apridonidze et al (17) who concluded that women with PCOS and MS differ from their counterparts lacking the MS in terms of increased hyperandrogenemia and more severe IR.

The significant elevation of free testosterone plasma level in women with PCOS (75%) are confirmatory to those of Chang et al (18) who found that the clinical phenotypes of PCOS have frank hyperandrogenemia and also in agreement with the Consensus Development Conference ADA in 1998 (19). The latter stressed on the biochemical criteria particularly hyperandrogenemia to diagnose PCOS.

Despite the known association between PCOS and glucose intolerance (20), the present study shows that abnormalities in both HDL-C and TG together are more common than FPG. Dokras et al (10) found similar results on white females with PCOS. The common presence of lipid abnormalities over FPG abnormalities emphasizes the greater importance of screening for dyslipidemia together with FPG in women with PCOS. The infrequent "hyperglycemia" in the present series is against the WHO criteria for diagnosing MS (21), where DM, impaired glucose tolerance (IGT) are prerequisites plus any two clinical or biochemical abnormalities (high BP, dyslipidemia, central obesity, microalbuminuria).

In spite of the significant increase in CV risk factors in PCOS with MS and those without MS in relation to matched control groups, there was no clinical manifestation of CV changes. Dokras (22) described PCOS as a silent preclinical CV disorder that has to be screened and managed early to guard against manifest atheroscle-

rosis. Increased cIMT which is a surrogate marker of early subclinical atherosclerosis (23) was observed more in the group of PCOS with MS than PCOS alone groups and both in relation to the control group. Although the present finding is confirmatory to many previous studies (24, 25, 26), yet it is not in accordance with Meyer et al (27) who found no difference in the mean cIMT between PCOS and control in spite of significant increase in CV risk factor, lipids, insulin resistance and increased pulse wave velocity (PWV). Also it is not in agreement with Costa et al (28) who found no difference in PCOS versus control. However, Talbott and coworkers (29) found that the PCOS remained associated with increase cIMT independent of insulin resistance or visceral fat. Lackhani et al (25) advised the development of new strategies like cIMT for screening PCOS cases even in young aged women < 35ys.

Calculating the QTc interval and the QTd which is the difference between the maximum and the minimum QTc interval revealed significant prolongation in PCOS with MS followed by PCOS group in comparison to the control groups and the QTd was significantly more frequent among the two groups in relation to the control group. These results are in accordance with Seyfeli et al (30), who found that obese women had higher maximum P wave duration and QTd and concluded that obese women may not only be at risk of ventricular arrhythmia but also at atrial arrhythmia.

The prolonged QTc and increased QTd could point to silent CVD dysfunction. However, Orio et al (31) reported the lack of electrocardiographic changes in women with PCOS and the QTc, QTd were not significantly different in relation to the controls. Meden Vertovec et al (32) found that the QTc intervals were even shorter. Shroff et al (33) concluded that young obese women with PCOS have a high prevalence of early asymptomatic coronary atherosclerosis compared with obese control and they advised to screen and aggressively counsel and treat PCOS women to prevent symptomatic CVD.

Echocardiographic study revealed that all systolic function parameter were comparable in the PCOS with or without MS to the control group except that patients with PCOS had significantly lower ratio between the early and late peak mitral flow velocities and longer isovolumic relaxation time representing a trend for non restrictive type of diastolic dysfunction with higher LVM. Our results are confirmatory to Tiras et al (34). On the other hand, Yarali et al (35) showed evidences of restrictive cardiomyopathy.

Conclusion

Many cardiovascular risk factors are frequent with evidence of premature atherosclerosis which exists among young women with PCOS being more exaggerated if there is associated MS. Early intervention to ameliorate the CV risks for these cases is an important health care demand.

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