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RESEARCH ARTICLE

Abdominal Fat Distribution, Insulin Resistance and Cardiovascular Risk Profiles in Women with Polycystic Ovary Syndrome

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ABSTRACT

Aim: To determine potential associations of abdominal fat distribution with insulin resistance and cardiovascular risk in women with polycystic ovary syndrome (PCOS).

Methods: Cross-sectional study that included detailed clinical examination, body mass indices (BMI), waist-hip ratio, insulin resistance and cardiovascular risk scores for 350 women registered between August 2008 and December 2009. Biochemical analysis included fasting blood glucose level, serum insulin level, triglycerides, total cholesterol and HDL cholesterol. Primary outcomes of interest included insulin resistance and cardiovascular risk score.

Results: The mean age of the subjects was 25.77 years. Oligoovulation was present in 99% of the women. Eighty-two (23.43%, 95% CI: 19.21%, 28.08%) women were obese and 100 (28.57%, 95% CI: 24.02%, 33.47%) women had android obesity. Insulin resistance was present in 136 (38.86%, 95% CI: 33.85%, 44.05%) women and 107 (30.57%, 95% CI: 25.91%, 35.55%) women had a cardiovascular risk >1. Women with a waist-hip ratio >0.85 were more likely to have insulin resistance (OR 2.70, 95% CI: 1.68, 4.35, $p < 0.001$) and at increased risk for cardiovascular events (OR: 1.82, 95% CI: 1.12, 2.97, $p = 0.02$). Obese women were more likely to have insulin resistance (OR 2.53, 95% CI: 1.53, 4.19, $p < 0.001$) and at increased risk for cardiovascular events (OR: 2.17, 95% CI: 1.30, 3.63, $p = 0.003$).

Conclusion: Long-term health hazards of PCOS have to be considered as these may be prevented to some extent by early identification and interventions, such as changing the lifestyle of the individual.

Keywords: Waist-hip ratio, Insulin resistance, Cardiovascular risk, Polycystic ovary syndrome.

INTRODUCTION

Polycystic ovary syndrome (PCOS) is a common endocrine and metabolic disorder that affects 5 to 10% of women in their reproductive life.[1] PCOS is associated with an endothelial dysfunction which is linked to insulin resistance and is a risk factor for cardiovascular disease.[2,3] Talbott et al demonstrated early atherogenic process as evidenced by thickening of carotid intima media in middle-aged women with PCOS compared with age-matched women without PCOS.[4] Metabolic disturbances, in particular, hyperinsulinemia lead to overproduction of ovarian androgens which cause chronic anovulation, menstrual disturbances and hirsutism.[5] Hyperinsulinemia evidently plays a role in the etiopathogenesis of hyperandrogenism by increasing ovarian androgen production and decreasing the serum sex hormone binding globulin (SHBG) concentration and augmenting luteinizing hormone-stimulated ovarian androgen biosynthesis.[6,7] The associated insulin resistance increases the risk of developing glucose intolerance, type 2 diabetes mellitus, gestational diabetes mellitus, hypertension, dyslipidemia and heart disease. This cluster of abnormalities associated with insulin resistance has been termed 'syndrome X' or the dysmetabolic syndrome.[8]

Obesity is a classic characteristic of PCOS and is observed in 35 to 60% of women with PCOS.[9] Central obesity is common and body fat distribution, i.e. waist-hip ratio appears to be more important in the pathogenesis of PCOS than total body weight.[10] We designed a cross-sectional study to explore the potential association of abdominal fat distribution with insulin resistance and cardiovascular risk profiles in a cohort of women with PCOS.

METHODS

The study protocol was approved by the Institutional Review Board of Fernandez Hospital, Hyderabad and adhered to the tenets of the declaration of Helsinki. The study population included a cohort of women attending the Gynecology Outpatient Department in Fernandez Hospital, between August 2008 and December 2009, who were diagnosed to have PCOS by Rotterdam criteria, i.e. who had any two of oligo (an) ovulation, hyperandrogenism and polycystic ovaries on

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ultrasonography. Women aged less than 18 years and above 40 years or with diabetes and hypertension (preexisting risk factors for cardiovascular diseases) or a prior history of cardiac diseases were excluded from the study.

Every woman presenting to the gynecology outpatient clinic undergoes a standardized clinical protocol that includes a detailed demographic, obstetric and medical history and clinical examination protocols specific for specific conditions. Systolic and diastolic blood pressures are measured for each woman in the sitting posture and height and weight measurements are recorded at each visit. The body mass index (BMI) is estimated from the height and weight measures. Additionally, a waist-hip ratio is also estimated for each woman. A waist-hip (W/H) ratio >0.85 was considered as android fat distribution. Biochemical analysis included estimation of fasting blood glucose level, serum insulin level, serum triglycerides, total cholesterol and HDL cholesterol. Insulin resistance was assessed by measuring the ratio of fasting glucose to fasting insulin levels and a ratio of <4.5 was considered as consistent with insulin resistance. Cardiovascular risk was calculated based on Framingham cardiovascular risk score using age, total and HDL cholesterol values, systolic blood pressure and history of smoking. The 10-year risk was calculated from the free internet based Framingham cardiovascular risk calculator available at http://hp2010.nhlbihin.net/atpiii/calculator.asp?usertype= prof%20.

Data was entered in Microsoft Office Excel (MS Excel version 2003) and exported to STATA version 8.0 (College Station, Tx, USA) for statistical analysis. The mean of continuous variables and frequency distribution of categorical variables was determined. The association of abdominal fat distribution with insulin resistance and cardiovascular risk was explored using a logistic regression model. Odds ratios (OR) and the 95% confidence intervals (95% CI) around the point estimates were derived.

RESULTS

The study included 350 women with a mean age (SD) of 25.77 (4.72) years. A total of 319 (91.14%) of the 350 women in the study were married and 261 (81.82%) of the 319 women were infertile (Table 1). The details of the biochemical analysis are presented in Table 2. Eighty-two (23.43%, 95% CI: 19.21%, 28.08%) women were considered obese based on a BMI cutoff of 30 and 100 (28.57%, 95% CI: 24.02%, 33.47%) women had android obesity based on a waist-hip ratio of >0.85. Insulin resistance was present in 136 (38.86%, 95% CI: 33.85%, 44.05%) of the 350 women with PCOS. A total of 107 (30.57%, 95% CI: 25.91%, 35.55%) women had a cardiovascular risk >1 based on the Framingham cardiovascular risk score. Among the 268 women with BMI < 30, 28 (10%) had android obesity. In this subset of 28 women, 21 had insulin resistance and seven had increased cardiovascular risk.

In a logistic regression model, women with a waist-hip ratio >0.85 were more likely to have insulin resistance (OR 2.70, 95% CI: 1.68, 4.35, p < 0.001) and were at increased risk for cardiovascular events (OR: 1.82, 95% CI: 1.12, 2.97, p = 0.02). Women with obesity (based on a BMI > 30) were more likely to have insulin resistance (OR 2.53, 95% CI: 1.53, 4.19, p < 0.001) and were at increased risk for cardiovascular events (OR: 2.17, 95% CI: 1.30, 3.63, p = 0.003).

The mean (SD) endometrial thickness was 6.99 (1.81) mm and ranged from 4 to 16.3 mm. A thickened endometrium was present in 108 (30.85%, 95% CI: 26.18%, 35.85%) women, an ovarian cyst was present in 10 (2.86%, 95% CI: 1.46%, 5.03%) and three (0.86%, 95% CI: 0.22%, 2.31%) women had fibroids.

DISCUSSION

Abdominal fat distribution and body mass indices were associated with insulin resistance and increased cardiovascular risk. The prevalence of android obesity (28.57%) in our study is nearly similar to the 22% reported by Dalton et al who took into consideration three parameters, namely, waist circumference, waist-hip circumference and body mass index.[11,12] An increased risk for adverse cardiovascular events is also consistent with existing knowledge. Using data pooled from 15 prospective studies that included 258 and 114 individuals, it was demonstrated that the risk of incident of cardiovascular disease increased in men and women with elevations in waist circumference or W/H ratio. A 1 cm increase in waist circumference was associated with a 2% increase in risk of future cardiovascular disease and a 0.01 increase in W/H ratio was associated with a 5% increase in risk.[13]

The clinical manifestations of PCOS included are menstrual irregularities, signs of androgen excess and obesity.[14] Polycystic ovaries can exist without clinical signs of this syndrome and the signs maybe expressed over a period of time. There are a number of interlinking factors that affect expression of PCOS. A gain in weight is associated with a worsening of symptoms. While weight loss will ameliorate the endocrine and metabolic

Table 1: Characteristics of 350 women with PCOS

Mean age (SD) in years	25.77 (4.72)
Married, n (%)	319 (91.14%)
Nulliparous, n (%)	298 (85.14%)
At least 1 previous abortion/miscarriage, n (%)	50 (14.29%)
Mean (SD) body mass index	27.32 (4.80)
History of infertility*, n (%)	261 (81.82%)
Oligoovulation, n (%)	347 (99.14%)
Smokers, n (%)	2 (0.57%)
Mean (SD) systolic blood pressure	111.71 (6.59)
Mean (SD) diastolic blood pressure	73.89 (5.07)
Waist-hip ratio > 0.85, n (%)	100 (28.57)
Clinical hyperandrogenism	216 (61.71%)

*Denominator includes only 319 women who are married

Table 2: Details of the biochemical analysis for 350 women with PCOS

Test	*Mean (SD)*
Fasting blood sugar mg/dl	89.33 (9.54)
Serum insulin	14.59 (7.47)
Total cholesterol	182.49 (38.69)
HDL cholesterol	40.16 (7.30)
LDL cholesterol	98.18 (21.42)

disturbances and symptomatology, increased rates of type 2 diabetes mellitus, dyslipidemia and endometrial cancer in PCOS that are not completely explained by obesity are seen.[15] Previous studies have reported that abdominal obesity is a powerful risk factor for heart disease and the waist circumference alone is a better predictor of heart disease risk among men and women.[16]

Hyperinsulinemia increases the risk of cardiovascular disease.[17] Hyperinsulinemia increases the risk of cardiovascular disease indirectly by its atherogenic activity and directly by its adverse effect on lipid profile.[17] Women with anovulation/ hyperandrogenism and hyperinsulinemia are at greater risk of developing NIDDM, approximately 30 years earlier than the general population.[17] Therefore control of blood sugar and lipid profile in these patients during the premenopausal years is very important. Robinson et al found that insulin insensitivity contributes significantly beyond body mass index to the low HDL cholesterol in women with PCOS.[18]

Polycystic ovary syndrome is a heterogeneous, familial condition characterized by ovarian dysfunction.[19] Anovulation is one of the three main criteria for diagnosis according to Rotterdam's criteria. While studying the prevalence of etiologies of infertility, Burney RO et al noted that 40 to 55% were due to female factors of which 30 to 40% were constituted by ovulatory dysfunction.[20] In the present study, 81.82% women presented with subfertility. Women with PCOS have a greater truncal abdominal fat distribution as demonstrated by higher waist-hip ratio that is independent of BMI. Women with PCOS have higher fasting glucose and insulin levels. This hyperinsulinemia leads to hyperandrogenemia, which in turn can cause suppression of ovulation leading to poor prognosis for fertility. In the study population, 28.57% women had android obesity which can have an influence on ovulation. Weight loss is important to improve the prospects of both spontaneous and drug–induced ovulation. In addition, overweight women with PCOS are at increased risk of obstetric complications including gestational diabetes mellitus and preeclampsia.

Although the presenting complaint was subfertility in these women, the android obesity which was picked up as part of our evaluation in fact served as a warning signal for the treating physicians to counsel about future risks of diabetes mellitus, hypertriglyceridemia and cardiovascular disease.

CONCLUSION

Long-term health hazards of PCOS have to be considered in women who present with subfertility as these may be prevented to some extent by early identification and interventions, such as changing the lifestyle of the individual.

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