ANALYSIS OF CLINICAL, HORMONAL, AND METABOLIC ASSESSMENT IN RELATION TO BODY MASS INDEX OF POLYCYSTIC OVARY SYNDROME

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ABSTRACT

To determine the proportion of polycystic ovarian syndrome (PCOS) patients who have normal body mass index (BMI) and to compare the clinical, hormonal, and metabolic profile between lean and overweight patients of PCOS.

Materials and Methods: One hundred consecutive infertile women with PCOS were studied and divided into lean (BMI between 18.5 and 23) and overweight (BMI ≥ 23). Metabolic and hormonal profile (serum FSH, LH, testosterone, prolactin, TSH on days 2–3 of menstrual cycle; serum progesterone premenstrually; serum insulin—fasting and 2 hours postglucose, glucose tolerance test, and fasting serum lipid profile) was performed along with pelvic sonogropahy; and clinical features, viz. waist hip ratio, hirsutism, acne, acanthosis nigricans, and clitoromegaly were recorded.

Keywords: Metabolic syndrome, obesity, overweight, polycystic ovary syndrome

INTRODUCTION

The syndrome has strong association to infertility, hyperinsulinemia, insulin resistance (IR), impaired glucose tolerance, dyslipidemia, android fat distribution, and obesity. Approximately 60 % of women with PCOS are obese. IR is found in 40 % of normal weight women with PCOS and nearly all overweight women both with and without PCOS.[1]

Polycystic ovarian syndrome (PCOS) affects 15-20% women (1/5th) of reproductive age. It is symptoms with varied presentations such as hirsutism, acne, alopecia, anovulatory cycles, and obesity. According to ESHRE/ASRM/FOGSI consensus[2] workshop at Rotterdam in 2003, the diagnosis of PCOS is based on the presence of any two of three (1) chronic anovulation/Irregular cycle, (2) clinical/ biochemical parameters for hyperandrogenism, and (3) polycystic ovaries on ultrasonography. According to the AE PCOS (Androgen Excess and PCOS Society) criteria, PCOS should be defined by the presence of hyperandrogenism (clinical and/or biochemical), ovarian dysfunction (oligo- anovulation and/or polycystic ovaries), and the exclusion of related disorders. Overweight or obesity is not an essential criterion, although menstrual irregularities, obesity, and hypertension are considered as clinical indicators of PCOS. Recent studies have shown that insulin resistance is a key feature in the evolution of PCOS and predisposes to type 2 diabetes mellitus in the long run. Although a major proportion of PCOS patients are overweight or obese, some of them may be having normal or lower body mass index.

This study aimed to determine the proportion of PCOS subjects who are not overweight/obese and to compare the clinical, hormonal, and metabolic profile of lean [normal body mass index (BMI)] and overweight/obese PCOS women.

MATERIALS AND METHODS

One hundred consecutive women with age range 20- 38 years presenting with infertility over a 3-year period and diagnosed to have PCOS according to ESHRE/ASRM/ FOGSI criteria[1] were included in the study after obtaining an informed written consent. Patients with BMI <23 kg/ m² were included in the lean PCOS and those with BMI ≥23 kg/ m² were considered as overweight PCOS.[2]

A detailed history including menstrual pattern, personal, past, family, obstetric, and treatment history was recorded. A complete physical examination including general, systemic, breast, and pelvic examination was also performed, and subjects were screened for signs of hyperandrogenism such as hirsutism, acne, acanthosis nigricans, clitoromegaly, and alopecia. Hirsutism scoring was done according to Ferriman Gallwey score and women with a score >7 were considered hirsutism.[3] Height and weight were recorded by the standard methods. Waist circumference was measured at the level of the umbilicus without clothing and in standing position. Hip circumference was measured at the level of ischial tuberosity. Subjects with known thyroid disorder (including those with subclinical hypothyroidism), hypothalamic, pituitary or adrenal disease, neoplastic disease, hepatic/ renal/cardiovascular disorders, and tuberculosis were not included for the study.

A set of blood investigations was performed for each subject which comprised complete blood count with ESR (erythrocyte sedimentation rate), fasting lipid profile, hormonal profile (day 2 or 3 of menstruation) including LH/FSH ratio, total testosterone, prolactin, and TSH. Serum progesterone was measured on days 21–23 of menstrual cycle. Blood sugar values and serum insulin values were determined during a 75 g oral glucose tolerance test (GTT). Values of GTT were assessed according to ADA, 1997.[4] Presence of insulin resistance was defined by fasting or post-load insulin levels >25 and >41 µU/ml, respectively[5,6]. Lipid profile was estimated and criteria adopted were in consonance with NCEP-ATP III guidelines [7]. Deranged lipid profile was considered if any of the cholesterol, triglycerides, and HDL-cholesterol fractions were abnormal, the individual cutoffs taken were ≥200, ≥150, and <50 mg/ dL, respectively. Abnormal waist hip circumference was taken as ≥0.8.

Ultrasonography (TVS) of the pelvis with transvaginal probe (7 MHz) was done on day 2/3 of menstrual cycle or withdrawal bleed to evaluate day 2 endometrial thickness. Polycystic ovaries were defined as an ovary with 20 or more follicles measuring 2–9 mm in diameter and/or increased ovarian volume more than 10 cm^3 along with stromal hyperplasia.

Data are presented as mean ± SD. The various clinical, metabolic, and hormonal characteristics were tabulated in the two groups and compared using unpaired, two-tailed Student's t-test. Significance was set at $P < 0.05$. All statistical analyses were performed by using MS Office 2007 Excel.

The study group had 58 subjects with BMI ≥23, i.e., 58% were overweight or obese PCOS with infertility, the rest had normal weight. In fact, 28% were obese with a BMI ≥27. The clinical features in both the groups are shown in Table-1. Average age was 28.4 ± 4.2 years in the lean PCOS group (n = 42) and 29 ± 5.2 years in the overweight PCOS group (n = 58). Presence of hirsutism, hirsutism score, irregular menstrual cycles, endometrial thickness of >4 mm, and acanthosis nigricans were comparable in both the groups. The hormonal profile was similar in both the groups, with serum LH/FSH ratio and testosterone levels higher and serum progesterone levels lower denoting anovulation in both the groups. The average systolic as well as diastolic blood pressures were significantly higher in the overweight or obese subjects Table-1.

<u>T</u><u>ABLE</u><u>-1</u>

<u>C</u><u>LINICAL AND HORMONAL PROFILE IN THE LEAN AND OVERWEIGHT POLYCYSTIC OVARIAN SYNDROME SUBJECTS</u>

Mean age (year)	28.4 ± 4.2	29 ± 5.2
Systolic Blood pressures (mmHg)*	116 ± 14.6	121.8 ± 9.99
Diastolic Blood Pressure(mmHg)**	74 ± 9.99	81.7 ± 8.3
Hirtustism	32 (80.9%)	52 (89.7%)
Hirtustism score	14.8 ± 4.1	15.4 ± 2.3
Irregular cycles	39 (92.8%)	56 (96.6%)
Acne	4 (9.5)	9 (15.5)
Polycystic ovaries with stromal hyperplasia on TVS	42 (100%)	58 (100%)
Endometrial thickness >4mm	4 (9.5%)	9 (15.5%)
Acanthosis nigricans	4 (9.5%)	7 (12.06%)
Clitoromegaly	1 (2.3%)	2 (3.4%)
Serum LH(mIU/mL)	16.6 ± 0.68	16.8 ± 10.42
Serum LH/FSH ratio	2.6 ± 1.1	2.5 ± 0.83
Serum Testosterone (ng/dl)	1.6 ± 1.1	1.8 ± 1.2
Serum Progesterone (ng/dl)	2.3 ± 2.1	2.1 ± 1.1
Serum FSH (mIU/mL)	4.2 ± 1.8	4.4 ± 1.5
Serum Prolactine (ng/dl)	13.6 ± 8.2	11.9 ± 4.6
Serum TSH (mU/ml)	2.4 ± 1.8	2.3 ± 1.6

Unpaired t-test *P=0.02; ** P<0.0001; rest of the parameters are not significant (P>0.05)

Metabolic parameters in both the groups are shown in Table-2. The BMI and waist-to-hip ratio were significantly higher in the overweight group denoting the prevalence of android obesity. Number of patients with impaired GTT and higher postprandial insulin were more in the overweight PCOS group. Family history of diabetes, deranged lipid profile, 2-hour postprandial insulin, and insulin resistance were significantly more in overweight patients. However, fasting and the postprandial glucose levels were comparable. Insulin resistance was present in a large number of the study subjects irrespective of whether they were lean or obese. 83.3% of lean subjects and 93.1% of overweight subjects had insulin resistance Table-2.

TABLE-2

ANTHROPOMETRIC AND METABOLIC PARAMETERS IN THE TWO GROUPS

Parameters	Lean PCOS(N=42)	Over weight PCOS (N=58)
BMI *	22.3 ± 4.1	28.1 ± 5.8
Waist-to-hip ratio*	0.83 ± 0.04	1.04 ± 0.06
Family history of diabetes	4 (9.5%)	14 (24.1%)
Deranged lipid profile*	6 (14.2%)	18 (31.03%)
Fasting plasma glucose (mg/dl)	76.3 ± 15.8	78.3 ± 13.7
2-hour postprandial glucose (mg/dl)	89.3 ± 16.5	85.3 ± 10.6
Impaired glucose tolerance test (GTT)*	2 (4.7%)	6 (10.3%)
Fasting insulin (mIU/ml)	11.6 ± 8.3	19.2 ± 3.4
2-hour postprandial insulin (mIU/ml)**	52.6 ± 18.4	95.6 ± 16.2
Insulin resistance*	35 (83.3%)	54 (93.1%)

Unpaired *t*-test. *P<0.05; **P<0.001; rest are not significant

DISCUSSION

Women with PCOS are generally overweight or obese; however, 42% in the present study had a normal BMI. This study outlines the fact that patients with PCOS, irrespective of their weight, demonstrate clinical manifestations such as irregular cycles, acne, hirsutism; hormonal abnormalities such as higher LH, LH/FSH, and testosterone levels. Metabolic disturbances, viz. impaired GTT, abnormal lipid profile, higher fasting/2-hour insulin levels, and higher insulin resistance, are also witnessed in the PCOS patients, but were markedly higher in PCOS with elevated BMI. Similar findings have been observed in previous studies.[5,6,8]

This study indicates that irrespective of weight, PCOS patients (lean as well as overweight or obese), are inherently insulin resistant with compensatory hyperinsulinemia and this plays a central role in the pathogenesis of PCOS.[9-11] Hyperinsulinemia probably acts at the level of hypothalamic–pituitary axis and stimulates LH secretion which leads to anovulation with irregular cycles. In the liver, it decreases production of sex hormone-binding protein and IGF-1-binding protein which results in an increase in free androgen in the blood and an increase in free IGF-1 in the ovary. Within the ovary, it promotes formation of androstenedione and testosterone which is seen clinically as hirsutism and acne.

Insulin resistance and hyperinsulinemia are presently considered risk factors in the development of atherosclerosis raising serum triglycerides and lowering the level of high-density lipoprotein cholesterol, and this may play an etiological role in the development of hypertension[12,13]. Hyperinsulinemia increases the risk of cardiovascular diseases. Thus, the metabolic disorders associated with PCOS along with their long-term sequelae have to be closely evaluated in both lean and obese PCOS patients [13]. From above study we may

presumes that hyperinsulinemia may be genetically predispose among those two groups along with their BMI[13].

Presence of obesity makes these patients susceptible to deranged lipid profile, impaired GTT and a greater degree of insulin resistance. Recently, obesity has been reported to be a significant predictor for development of metabolic syndrome within the PCOS subjects[14]. Two-hour postprandial insulin levels and insulin resistance and acanthosis nigricans (marker of insulin resistance) were much higher in the overweight group as compared to the lean PCOS patients in this study. Family history of diabetes was also more common in overweight as compared to lean, and this may indicate a genetic predisposition. Glucose tolerance test is considered better than simply the fasting and postprandial values in the evaluation of PCOS patients.[6]

To conclude, insulin resistance is inherent to PCOS, irrespective of whether the subject is lean or obese. Metabolic abnormalities are more frequently observed when obesity is associated in PCOS. It is suggested that all PCOS subjects should be considered at risk of atherosclerosis and its manifestations in view of the insulin resistant state; periodic monitoring of blood pressure, lipids, and an annual OGTT especially for obese PCOS patients should be performed.

RESULTS

42% of the PCOS subjects had normal BMI. Average age, hirsutism (80.9% vs. 89.7%), irregular cycles (92.8% vs. 96.6%), acne (9.5% vs. 15.5%), clitoromegaly (2.3% vs. 3.4%), endometrial thickness ≥4 mm (9.5% vs. 15.5%), and hormonal profile were similar in the lean and overweight PCOS groups. Family history of diabetes (9.5% vs. 24.1%), abnormal glucose tolerance test (GTT) (4.7% vs. 10.3%), deranged lipid profile (14.2% vs. 31%), and 2-hour postprandial insulin levels were higher in the overweight PCOS ($P < 0.05$). Insulin resistance was observed in 83.3% of lean PCOS but was still lower than 93.1% seen in overweight PCOS ($P < 0.05$).

CONCLUSION

42% of the PCOS had normal BMI, but clinical and hormonal profile was similar to PCOS patients with elevated BMI (overweight/obese). However, insulin resistance is observed in 83.3% of lean PCOS. Family history of diabetes, impaired GTT, deranged lipid profile, and insulin resistance were more prevalent in overweight PCOS.

Abbreviations:

ESHRE: *European Society of Human Reproduction and Embryology*

ASRM: American Society for Reproductive Medicine

FOGSI: *Federation of Obstetric and Gynecological Societies of India*

AE-PCOS: Androgen Excess and PCOS Society

PCOS: Polycystic Ovarian Syndrome

LH/FSH: Luteinizing Hormone/ Follicular stimulation Hormone

TSH: Thyroid stimulating Hormone

OGTT: oral Glucose tolerance test

BMI: Body Mass Index

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