 DOI: 10.18231/2394-2738.2017.0006

Association of Hormonal status with Anthropometric & Biochemical Parameters in women with Polycystic Ovarian Syndrome

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Abstract

Background: Polycystic ovarian syndrome (PCOS) is the metabolic endocrine disorder that affects 4–12% women of reproductive age and is a major cause of anovulatory infertility. Besides reproductive and obstetric complications, the consequences of PCOS extend beyond the reproductive axis and may lead to the substantial risk for the development of metabolic syndrome with the characteristic features of insulin resistance, central obesity, impaired glucose tolerance, dyslipidemia and hypertension.

Objectives: To evaluate the hormonal status and its association with the anthropometric measurements and biochemical parameters in females diagnosed with PCOS.

Materials & Methods: In this case-control study, women clinically diagnosed with PCOS (N=85) and age matched healthy control female subjects (N=85) in the age group (18 – 35) years were enrolled. Body mass index (BMI), waist: hip ratio (WHR), Fasting Blood Glucose, Lipid profile and Hormonal levels were estimated in both the groups and further compared using student t-test. Hormonal levels were also correlated with the anthropometric measurements & biochemical parameters and the results were analyzed using Pearson's correlation coefficients.

Results: We found that the levels of TSH, LH, FSH, LH/FSH ratio & prolactin were significantly raised in PCOS females as compared to healthy females ($P < 0.0001$). TSH showed significant positive correlation with anthropometric measurements (BMI, waist-to-hip ratio), biochemical parameters (TC, TG, LDL & TC/HDL ratio) and hormonal profile (LH, FSH, LH/FSH ratio & Prolactin) of PCOS women.

Discussion & Conclusion: We found that there is a derangement in hormonal & biochemical status of women suffering from PCOS that leads to an altered energy metabolism and endocrinological cascade of PCOS. Furthermore, our study showed high prevalence of hypothyroidism, dyslipidemia and increased levels of LH, FSH, PRL & a higher LH/FSH ratio in women with PCOS, which may further contribute towards the progress of metabolic disorders, irregular menstruation and infertility.

Keywords: Polycystic Ovarian Syndrome, Thyroid Stimulating Hormone, Body Mass Index, Hypothyroidism, Dyslipidemia, coronary artery disease.

Introduction

Polycystic ovarian syndrome is a condition characterized by menstrual irregularity, chronic anovulation, hirsutism and androgen excess. PCOS is the most common endocrine disorder of reproductive-aged women and affects approximately 4–12%. PCOS is a common endocrinopathy typified by oligo-ovulation or anovulation, signs of androgen excess, and multiple small ovarian cysts.[1]

The commonest criteria used for the diagnosis of PCOS these days is "Rotterdam revised Criteria" which includes any two of the following three features; 1) Oligo/anovulation 2) Clinical and/or biochemical evidence of Hyperandrogenemia and 3) Ultrasonographic findings of Polycystic ovaries; with exclusion of other known disorders of hyperandrogenemia.[2,3]

Stein-Leventhal syndrome is the clinical manifestation of PCOS typically associated with anovulation and infertility with classical triad of obesity, hirsutism & oligomenorrhea/ infertility. Besides reproductive and obstetric complications, the consequences of PCOS have extended beyond the reproductive axis and may lead to the substantial risk for the development of metabolic syndrome with the characteristic features of insulin resistance, central obesity, impaired glucose tolerance, dyslipidemia and hypertension.[3,4,5]

The aetiology of PCOS remains unknown however; both genetic and environmental factors contribute the PCOS pathogenesis. Approximately 50% of PCOS women are overweight or obese and 70% women with PCOS are found to have insulin resistance, early onset of type-2 diabetes mellitus, dyslipidemia, cardiovascular disease (CVD), premature arteriosclerosis, endometrial hyperplasia, thrombosis, obstructive sleep apnea and endothelial carcinoma.[6,7,8]

PCOS and obesity are common and complex disorders affected by genetic and environmental factors. Furthermore, biochemical and hormonal parameters are necessary to understand the pathogenesis of PCOS and hence, the study of association among hormonal profile, biochemical & anthropometric measurements might help to provide the significant information for the diagnosis and treatment of PCOS including regularization of menses and recovery from infertility.[8,9]

The aim of the present study is to evaluate hormonal status of women with Polycystic Ovarian Syndrome and to find out their correlation with anthropometric measurements and biochemical parameters.

Materials & Methods

Study Population: This case-control study enrolled 85 women with PCOS. All women in the age group (18 – 35) years attending outpatient in the department of Obstetrics & Gynecology at SGT Medical College, Hospital & Research Institute, Gurgaon, Haryana, India, with the primary complaints of menstrual irregularities (amenorrhea or oligomenorrhea) and/or hirsutism with or without infertility were evaluated in detail for polycystic ovarian syndrome. PCOS confirmation was done by ultrasonography in the follicular phase as per the Rotterdam revised criteria.[3] All those with a confirmatory diagnosis of PCOS were included in the study after exclusion of known cases of diabetes mellitus, hypertension, hyperprolactinemia, Cushing's syndrome, history of smoking and/or alcohol intake, androgenic/anabolic drug use or abuse, thyroid dysfunction. The size of the ovaries, volume, morphology and the number & size of the follicles were noted. Polycystic ovarian morphology was defined as bulky bilateral ovaries with 12 or more peripherally arranged follicles (String of Pearls) measuring 2-9 mm in diameter and/or increased ovarian volume > 10 cm^3 along with echogenic stroma. Eighty five (85) healthy women were studied during the same period. They did not show hirsutism, acne or male-type baldness, family history of PCOS or signs of hyperandrogenism. All of them had regular menstrual cycles ranging from 28 to 35 days; none of them fulfilled any of the Rotterdam revised criteria.

All the participants were asked to provide detailed history that included menstrual irregularity, hirsutism, alopecia, infertility, voice change, weight gain, presence of clinical acne and detailed obstetric history was noted. Hirsutism was quantified with the modified Ferriman–Gallway score.[10]

Anthropometric measurements: Standard anthropometric data that included height, weight, waist circumference (WC), hip circumference (HC), was measured and noted for each subjects. Body Mass Index (BMI) was calculated using the equation(body weight in kilograms divided by body height in meters squared)(kg/m^2).[11] The waist-to-hip ratio (WHR) wasmeasuredusing dressmakers tape, taking care that it was applied horizontally.Waist circumference (middle circumference between the iliac crest and the lateral coastal margin)and hip circumference (maximum circumference around the buttocks posteriorly and indicated anteriorly by the symphysis pubis).

Laboratory Analyses

Biochemical Parameters: After 12 hours overnight fasting, about 5 ml of venous blood samples were collected in plain tubes (for estimations of lipid profile & hormonal profile) and in tube containing sodium fluoride and Oxalate (for plasma Glucose estimation). Serum was separated and preserved at -20ºC for subsequent analyses. Estimations of fasting plasma Glucose, serum total cholesterol (TC), triglycerides (TG) and High-density lipoprotein (HDL) concentrations were assayed by using commercial kits available for standard photometric methods in fully automatedERBA XL (EM-200) Biochemistry analyzer.Low-density lipoprotein (LDL)was calculated by using Fredrickson Friedewald's formula.[12]

Hormonal Assays: serum luteinizing hormone (LH), follicle stimulating hormone (FSH), prolactin (PRL) and thyroid stimulating hormone (TSH) were assayed by Chemi Luminescent Immunoassay (CLIA) method using Siemen's Advia Centaur CP kit. Laboratory controls were used to check the accuracy and precision of the analyzer, reagents and assay results.

The study was approved by the Institutional Research Ethics Committee and informed written consent was obtained from all the participants.

Statistical Analysis: Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 24.0, for Windows (SPSS, Inc., Chicago). The normality of distribution of all the variables was checked by using Kolmogorov–Smirnov test. The quantitative data were expressed as mean ± standard deviation (SD). Unpaired Student's t–test was used to compare the values (PCOS *vs* Controls) and Pearson's correlation coefficient was used to elucidate the relationship between the variables. $P<0.05$ was considered statistically significant.

Results

The women diagnosed with PCOS (N=85) and the healthy women controls (N=85) were in the age group (18–35) years. The mean age of PCOS women was (23.87±4.45) years and for controls was (22.47±2.31) years.We have evaluated both PCOS and the control subjects for fasting blood sugar, serum lipid profile, thyroid stimulating hormone, LH, FSH, LH/FSH ratio and prolactin levels. Comparisons were made between both the groups and the results of anthropometric, biochemical and hormonal profile findings are shown in the Table 1 and 2 respectively.

Table 1: Comparison of Anthropometric measurements among PCOS subjects and Controls

Parameters	PCOS cases (Mean ± SD)	Controls (Mean ± SD)	*P*-values
Age	23.87±4.45	22.47±2.31	0.011
Height	1.59±0.064	1.57±0.05	0.009
Weight	63.87±10.16	49.50±6.3	< 0.0001
BMI	25.03±3.56	20.12±2.58	< 0.0001
WC	32.98±3.5	30.41±2.76	< 0.0001

HC	38.24±4.42	39.13±2.66	0.112
WHR	0.85±0.052	0.77±0.47	< 0.0001

Table 2: Serum concentration of lipid profiles and hormone levels in PCOS and control subjects

Parameters and their normal ranges	PCOS cases (Mean ± SD)	Controls (Mean ± SD)	*P*-values
FBS (70 – 110 mg/dl)	92.05±8.17	88.90±7.39	0.009
TC (< 200 mg/dl)	170.62±28.82	143.26±17.40	< 0.0001
TG (40 – 160 mg/dl)	128.40±50.63	91.68±23.79	< 0.0001
HDL (45 – 65 mg/dl)	44.79±8.74	42.98±3.90	0.084
LDL (< 130 mg/dl)	115.43±27.56	84.61±12.77	< 0.0001
TC/HDL ratio (< 3.5)	3.93±0.95	3.35±0.49	< 0.0001
TSH(0.35–5.50 mg/dl)	3.34±3.09	1.56±0.85	< 0.0001
LH (1.9 – 12.5 mg/dl)	7.82±6.11	3.41±0.70	< 0.0001
FSH (2.5 – 10.2 mg/dl)	5.31±2.03	4.23±0.66	< 0.0001
LH/FSH ratio (< 1.2)	1.61±1.26	0.80±0.13	< 0.0001
PRL (1.2 – 19.5 mg/dl)	13.25±8.56	7.40±1.14	< 0.0001

FBS=Fasting blood glucose.

The mean BMI, WC, WHR of women with PCOS were significantly higher (P<0.0001) than the controls. The mean FBS of women with PCOS was significantly higher (P<0.009) than the controls. The mean TC, TG, LDL and TC/HDL ratio of women with PCOS were significantly higher (P<0.0001) than the controls. On the other hand, HDL showed no significant statistical difference (P=0.084) between the groups. The mean TSH, LH, FSH, LH/FSH ratio & Prolactin were significantly higher (P<0.0001) than the controls. 41.17% (N=35) women with PCOS were found to have a BMI >25 and were overweight and 5.88% (N=5) with BMI >30, were obese. 28.23% (N=24) of the women had a WC above the normal range of < 88cm. 20% (N=17) women were diagnosed with Hirsutism. 9.41% (N=8) women were found to have acne.

Table 3: Pearson's Correlation of hormonal levels with biochemical and anthropometric parameters

	TSH	LH	FSH	LH/FSH	PRL	BMI	WHR	FBS	TC	TG	LDL	TC/HDL
TSH	1	0.369**	0.283**	0.240**	0.236**	0.249**	0.343**	0.125	0.168*	0.319**	0.224**	0.194*
LH		1	0.310**	0.870**	0.119	0.117	0.309**	0.077	0.211**	0.024	0.112	0.091
FSH			1	-0.104	0.015	0.249**	0.318**	0.085	0.282**	0.278**	0.322**	0.233**
LH/FSH				1	0.158*	0.094	0.266**	0.017	0.134	-0.033	0.071	0.050
PRL					1	0.229**	0.340**	0.056	0.060	0.084	0.172*	-0.023
BMI						1	0.541**	-0.006	0.475**	0.414**	0.592**	0.425**
WHR							1	0.000	0.360**	0.396**	0.404**	0.253**
FBS								1	0.068	0.063	0.093	0.100
TC									1	0.376**	0.741**	0.723**
TG										1	0.526**	0.429**
LDL											1	0.645**
TC/HDL												1

**Correlation is significant at the 0.01 level (2-tailed);
* Correlation is significant at the 0.05 level (2-tailed).

As seen in the Table 3, TSH showed significant positive correlations with BMI (r= 0.24), WHR (r= 0.34), TC (r= 0.16), TG (r= 0.31), LDL (r= 0.22) & TC/HDL ratio (r= 0.19) in women with PCOS. LH showed significant positive correlation with WHR (r=0.30), TC (r=0.21) in women with PCOS. FSH showed significant positive correlation with BMI (r=0.24), WHR (r=0.31), TC (r=0.28), TG (r=0.27), LDL (r=0.32), TC/HDL ratio (r=0.23) in women with PCOS. Prolactin showed significant positive correlation with BMI (r=0.22), WHR (r=0.34), LDL (r=0.17) in women with PCOS. LH/FSH ratio showed significant positive correlation with WHR (r=0.26) and PRL (r=0.15) in women with PCOS. No significant statistical correlations were found among LH/FSH ratio, BMI and biochemical parameters in women with PCOS.

Discussion

Stein and Leventhal first reported polycystic ovarian syndrome in modern medical literature. PCOS is a common, heterogeneous and multi-aetiological

endocrine disorder associated with derangement of metabolic and endocrinological status. Besides reproductive and obstetric complications, the consequences of PCOS extend beyond the reproductive axis and may lead to the substantial risk for the development of metabolic syndrome with the characteristic features of insulin resistance, central obesity, impaired glucose tolerance, dyslipidemia & hypertension.[3-5] In the present study, we have attempted to explore the alterations in biochemical and hormonal parameters in PCOS women.

Obesity is a common and complex disorders affected by genetic and environmental factors. It may be regarded as an underlying risk factor for atherosclerosis, coronary artery disease because it raises the substantial risk through the other associated risk factors that include atherogenic dyslipidemia.[13] The marker for body fat content is the body mass index. In our study, 47.05% of the women with PCOS were found to be either overweight or obese according to their BMI and 28.23% of women had a waist circumference above the normal range of <88 cm. These observations show dyslipidemia and android type of obesity in PCOS subjects, which supports the previous studies.[13,14,15] The prevalence of metabolic syndrome increases with increasing BMI and WHR.Waist-to-hip ratio is known to be a measure of central obesity and hence measurement of waist circumference can be more advantageous to correlate excess abdominal fat with the presence of metabolic risk factors than the total body fat.[13] Elevated body mass index, waist circumference, waist-to-hip ratio, FBS, total cholesterol, TG, LDL-c levels and low level of HDL-c are associated with the risk for the development of metabolic syndrome.[2] Our study showed deranged lipid profile in PCOS women with the findings of elevated TC, TG and LDL-c levels and low HDL-c levels supporting the existing knowledge of Sarbhai et al.,[5] Kumar et al.[9] and Naidu et al.[13] which indicated that dyslipidemia is prevalent in women with PCOS. The present study showed significantly raised WHR in PCOS women and is similar to the findings of Thathapudi Sujatha et al.[16] but contradictory to the findings of Rasool Suzan Omer.[15]

Hypothyroidism is a clinical condition in which there is deficient thyroid hormone production by the thyroid gland. In our study, mean serum TSH level was significantly higher ($P < 0.0001$) than the control subject. This study strongly supports existing knowledge of Kumar et al.,[9] Eldar-Geva et al.,[17] Yasmin et al.[18] and Anwary et al.[19] but contradictory to the result (normal TSH level) found by K Gomathi et al. [14] In our study TSH showed significant positive correlation with anthropometric measurements (BMI, waist-to-hip ratio), biochemical parameters (TC, TG, LDL & TC: HDL ratio) and hormonal profile (LH, FSH, LH:FSH ratio & Prolactin) of PCOS women which strongly supports existing knowledge of Kumar et al.[9] and Bastemir et al.[20] but is contradictory to the evidence reported by Enzevaei A et al.[21] However, raised LH and an elevated LH:FSH ratio,did not correlate well with BMI and other biochemical parameters which supported results from previous studies.[5,22]

Hypothyroidism is associated with increased risk of hyperlipidemia, type-2 diabetes mellitus and coronary artery disease. Identification of hypothyroidism and biochemical derangement would help us to treat and prevent future complications in PCOS women.

Conclusions

The current study revealed that there is a derangement in hormonal & biochemical status of women suffering from PCOS which leads to an altered energy metabolism and endocrinological cascade of PCOS. TSH showed significant positive correlation with anthropometric measurements (BMI, waist-to-hip ratio), biochemical parameters (TC, TG, LDL & TC/HDL ratio) and hormonal profile (LH, FSH, LH/FSH ratio & Prolactin) of PCOS women. Furthermore, our study showed high prevalence of hypothyroidism, dyslipidemia with android type of obesity and & increased levels of gonadotropin hormones which plays an important role in clinical, hormonal and metabolic alterations in women with Polycystic Ovarian Syndrome. Hence, the evaluation of biochemical, metabolic and endocrine parameters are of paramount importance in early diagnosis of PCOS and its monitoring.

Acknowledgment

We would like to thank the entire staff of Obstetrics & Gynecology department and technicians of central Biochemistry Laboratory of SGT Hospital, Gurgaon, India for their constant support & help. Special thanks to Dr. Pooja, Dr. Anubhuti, Mr. Praveen Bhatt and all the sample donors for their valuable contribution to this study.

Conflicts of Interest

The authors have no conflicts of interest to declare.

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