Research Article

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ROLE OF STEROID HORMONES IN POLYCYSTIC OVARIAN SYNDROME (PCOS) IN SOUTH INDIAN WOMEN

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ABSTRACT

Polycystic ovary syndrome (PCOS), the common female endocrine disorder has multiple clinical manifestations with little known etiology. Genetics is said to be one of the factors contributing to this syndrome. It is generally the association of obesity with multiple ovarian cysts that leads to infertility, though differential insulin sensitivity, abnormal steroid hormone metabolism and adipocytokine secretion are also some of the causes. In the present study, we had compared Lipid profile and BMI levels as well as Steroid hormone Levels in obese & non obese PCOS patients. The body mass index in PCOS was higher with mean 25.36 and 23.19 in control subjects. The mean waist circumference was higher in control subjects with 86.76 and 77.97 in control women. Significant difference between PCOS and controls were observed in T3 and TSH levels. Mean T4 levels were more or less similar in PCOS and controls subjects with 8.68 and 8.57 respectively. Significant difference was observed in mean values of sex hormone binding globulin (SHBG), dehydroepiandrosterone sulphate (DHEAS), vitamin D, calcium, estradiol, follicle stimulating hormone (FSH) and luteinizing hormone (LH) levels. Poly cystic ovarian syndrome is a common heterogenous, disease characterized by multiple hormonal imbalances in reproductive age. It is generally the association of obesity with multiple ovarian cysts that leads to infertility. Moreover, it is also associated with differential insulin sensitivity, abnormal steroid hormone metabolism.

Keywords: Fasting blood sugar, BMI, lipid profile, steroid hormones in PCOS

INTRODUCTION

Polycystic ovary syndrome (PCOS) is the most prevalent metabolic disorder affecting women in their reproductive age. It is a complex and a multi-factorial disorder where the signs and symptoms vary among each patient. The reproductive function in women is greatly influenced by the body weight and metabolic status of the patient[1,2,3]. PCOS is also associated with insulin resistance, accumulation of abdominal fat and obesity which is positive in almost 50% of women with PCOS[4]. Insulin resistance in turn show an increased risk of impaired glucose tolerance, hyperinsulinemia and long term complications such as dyslipidemia, cardiovascular disease and endometrial cancer[5,6].

MATERIALS AND METHODS

This study dwells in evaluation and comparison of the biochemical and hormonal characteristics in women with PCOS and normal women.

Study design: case – control study. The study was approved by institutional ethics committee (011/022015IEC/SUdated12-02-2015).

Inclusion criteria

The study was conducted on 190 women, recruited from patients visiting a tertiary care hospital. 140 PCOS subjects were selected based on observation of oligomenorrhea / anovulation, clinical or biochemical evidence of hyperandrogenic and/or polycystic ovaries on ultrasonography and 50 normal, unaffected, age-matched fertile women with regular menstrual cycles (interval of 28-35 days) and with normal ovaries from the same geographical region were included in the study as controls.

Exclusion criteria

Women with galactorrhoea, hyperthyroidism, any systemic disease that affects their reproductive physiology, or any medication which interferes with the normal function of the hypothalamic-pituitary-gonadal axis.

Diagnosis of PCOS

PCOS was confirmed by ultrasound assessments by means of a transvaginal ultrasonography with a transvaginal probe of curved array 5.0 - 2.0 MHz (for ovary) with a frequency of 5.9MHz using diagnostic ultrasound system, Sonoscape Co., Ltd, China; with 12 or more follicles in each ovary, measuring 2-9 mm in diameter and/or increased ovarian volume (10 cm3). The test procedure and conformation of diagnosis was carried out by experienced gynaecologist.

Estimation of Body Mass Index (BMI)

BMI was calculated as weight in kilograms divided by the square of Height in meters and presented as kg/m2. BMI 18.0 –

22.9 kg/m2, 23.0 - 24.9 kg/m2, >25 kg/m2 were considered as normal, overweight and obesity respectively.

Biochemical and Hormonal analysis

Venous blood sample was collected from the subjects after overnight fasting for biochemical and hormonal assays on second or third day of their follicular phase. Fasting blood Glucose in the serum was estimated by glucose oxidase peroxidase method using the standard kit (Adevia 2400, Siemens)., lipid profile, calcium was carried out on Siemens-ADVIA Centaur Automated System and insulin, hormones T3, T4, TSH, FT3, SHBG, DHEAS, cortisol, testosterone is assayed by using chemiluminescent immunoassay technique (CLIA)., vitamin D, in the serum was estimated using the standard kit (ADVIA ®1200, Siemens)

Statistical analysis

The continuous variables were expressed as mean ± standard deviation. All statistical analysis was performed using the SPSS statistical software version 9.0. A p-value < 0.05 was considered to be statistically significant. The continuous variables were expressed as mean ± standard deviation. Qualitative and Quantitative variables were described by computation of frequency, mean, Standard Deviation (SD) and Chi square test of association.

RESULTS

The anthropometric and biochemical profile of the studied cases and controls are compared and presented in Table 1. The mean age among PCOS and control subjects were 25.33 and 22.18 respectively. The body mass index was classified as lean (<18.5), normal (18.5-24.9), overweight (25-29.9) and obese (≥30). The distribution of these categories in PCOS and control subjects are depicted in Figure 1. The body mass index in PCOS was higher with mean 25.36 and 23.19 in control subjects. The mean waist circumference was higher in control subjects with 86.76 and 77.97 in control women. Thyroid profiles were also

tested between PCOS and control subjects. Significant difference between PCOS and controls were observed in T3 and TSH levels. Mean T4 levels were more or less similar in PCOS and controls subjects with 8.68 and 8.57 respectively. The mean fasting blood sugar levels were 92.01 in PCOS and 90.63 in control subjects.

The lipid profile in both PCOS and control subjects were tested and the mean values are presented in Table 2. Significant difference between PCOS and control subjects were observed in total cholesterol and low density lipoprotein (LDL) levels. Hormonal profile was analysed from serum of PCOS and control subjects. The mean values are presented in Table 3. Significant difference was observed in mean values of sex hormone binding globulin (SHBG), dehydroepiandrosterone sulphate (DHEAS), vitamin D, calcium, estradiol, follicle stimulating hormone (FSH) and luteinizing hormone (LH) levels.

DISCUSSION

The diverse manifestation in PCOS starts at an early age so it is vital to diagnose at early stages to reduce the burden of the syndrome. In the present study, the obesity reported in PCOS subjects were 11%. A prevalence of 45% PCOS women reported to be underweight and 5% of them were lean. The mean body mass index observed in PCOS subjects were higher compared to the control subjects. A study involving 7 urban cities in India with age group of 20-35 showed the prevalence of obesity to be 30%[7]. In a systemic review and meta-analysis it was shown that women with PCOS had a greater risk of overweight, obesity, and central obesity[8]. Lack of exercise and low physical activity may play a significant role in the rise in prevalence of PCOS[9].The rate of obesity in the PCOS population ranges from 38% to 87%[10]. We found an increase in the waist circumference observed in the normal control women compared to PCOS subjects in our taken population.

Table 1: The anthropometric and biochemical profile of the studied cases and controls

Variables	Control mean (SD) (n=50)	PCOS mean (SD) (n=140)	P value
Age	22.18±4.35	25.33±4.82	**<0.001****
Body mass index	23.19±4.87	25.36±4.00	**0.003****
Waist circumference	86.76±15.39	77.97±21.63	**0.009****
T3	5.93±23.23	125.52±26.57	**<0.001****
T4	8.57±1.36	8.68±1.68	0.697
TSH	1.61±1.16	2.95±1.64	**<0.001****
FBS	90.63±18.16	92.01±11.40	0.534
HbA1C	10.44±27.53	5.32±0.61	**0.03***

T3-Triiodothyronine, T4-thyroxine, TSH-thyroid stimulating hormone, FBS-fasting blood sugar, HbA1C- Hemoglobin A1c, SD-standard deviation.

Table 2: Lipid profile of the studied cases and controls

Variables	Control mean (SD) (n=50)	PCOS mean (SD) (n=140)	P value
Total cholesterol	176.62±48.66	159.11±26.95	**0.002****
TGL	118.84±61.53	117.34±33.86	0.831
HDL	44.45±10.72	42.27±9.70	0.181
LDL	105.92±38.97	94.66±26.74	**0.026***
TC/HDL	4.43±2.37	3.94±1.05	0.052

TGL-triglycerides, HDL-high density lipoprotein, LDL-low density lipoprotein, TC-total cholesterol.

Table 3: The serum hormonal profile of the studied cases and controls

Hormone	Control mean (SD) (n=50)	PCOS mean (SD) (n=140)	P-value
Leptin	5.35±1.33	11.41±14.59	0.004
SHBG	53.37±21.39	36.88±19.08	**<0.001**[**]
DHEAS	105.74±63.64	156.08±86.36	**<0.001**[**]
AMH	10.00±4.24	26.98±66.90	0.721
VIT D	17.41±6.82	12.52±6.95	**<0.001**[**]
Calcium	9.15±0.62	9.37±0.29	**0.001**[**]
Cortisol	11.63±4.07	11.97±7.12	0.748
Testosterone	46.31±17.97	51.07±20.12	0.145
Estradiol	98.17±28.08	182.31±108.75	**<0.001**[**]
FSH	5.62±1.88	9.46±6.08	**<0.001**[**]
LH	7.81±2.35	14.62±18.59	**0.012**[*]
Prolactin	10.87±4.14	9.97±5.37	0.286

SHBG-sex hormone binding globulin, DHEAS-dehydroepiandrosterone sulfate, AMH- anti-mullerian hormone, VIT D-vitamin D, FSH-follicle stimulating hormone, LH-luteinizing hormone.
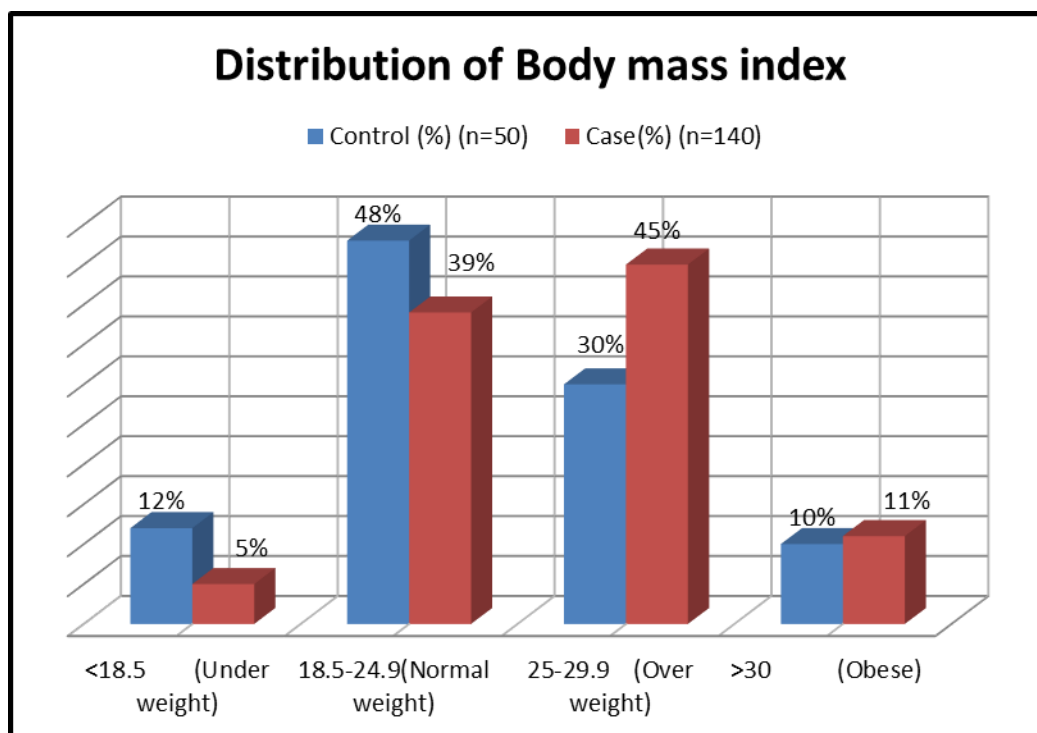

Figure 1: Distribution of body mass index in PCOS and control subjects

PCOS women were also reported to have thyroid abnormalities. Hypothyroidism and PCOS are often accompanied by increased serum free testosterone, luteinizing hormone (LH) and high cholesterol. Alteration in thyroid function, particularly hypothyroidism, can cause ovulatory dysfunction and lead to impaired female fertility. Although the pathophysiology of PCOS is unclear a variety of biochemical abnormalities have been thought to be associated with this syndrome. The mean fasting blood sugar levels were higher in the PCOS group. We also found that the PCOS subjects reflected a decrease in the total cholesterol, TGL and LDL levels compared to the controls. This shows that women of the taken population showed a better lipid profile than the control subjects. Nevertheless, the high density lipoprotein level which normally has to be higher to maintain a proper action was found to be decreased in the PCOS subjects. Cardiovascular risk factors are increased in patients with PCOS when compared with weight-matched controls[11,12]. Reports have shown high-density lipoprotein cholesterol levels are lower and triglyceride levels and very-low- density lipoprotein cholesterol is higher in PCOS women[13].

An increase in testosterone production by theca cells of women with PCOS exposed to insulin compared with testosterone production from the theca cells of normal women and by suppressing hepatic production of sex hormone binding globulin (SHBG), a rise in testosterone levels by the insulin was observed[14]. At the level of the granulosa cell, insulin intensifies the response of granulosa cells to LH. Hence, these cells undergo abnormal differentiation and premature arrest of follicular growth, and thus anovulation. Assessing the hormonal presentation in PCOS and control subjects we found that a significant difference in the mean values of sex hormone binding globulin (SHBG), dehydroepiandrosterone sulphate (DHEAS), vitamin D, calcium, estradiol, follicle stimulating hormone (FSH) and luteinizing hormone (LH) levels. Another important feature of PCOS is altered gonadotropin dynamics.

Several studies have shown higher LH pulse and amplitude in women with PCOS[15,16]. Although an increase in LH level drives the ovarian theca cells to produce more androgens, insufficient follicle-stimulating hormone (FSH) may be the more immediate cause of anovulation. In most women with PCOS, LH levels are elevated or the LH/FSH ratio is high; however, the mean LH pulse amplitude is attenuated in obese women with PCOS[17].

CONCLUSION

Poly cystic ovarian syndrome is a common heterogenous, multifactorial and complex disease characterized by multiple hormonal imbalances, dominated by manifestations of hyperandrogenism affecting around 7-10% of women in reproductive age. It is generally the association of obesity with multiple ovarian cysts that leads to infertility. Moreover, it is also associated with differential insulin sensitivity, abnormal steroid hormone me tabolism.Increased obesity and abdominal adiposity further aggravate the clinical, hormonal and metabolic parameters in PCOS and, if treated, can reverse most of these abnormalities to a clinically significant degree.

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