A study of hormonal and anthropometric parameters in polycystic ovarian syndrome.

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Introduction: Polycystic Ovarian Syndrome (PCOS) is an endocrinopathy with a complex metabolic disorder. PCOS is characterized by reproductive hormonal imbalances leading to the clinical presentation of hyperandrogenism and infertility. PCOS is also showing an increased prevalence of several other conditions such as obesity, dyslipidemia, hypertension, metabolic syndrome and type 2 diabetes mellitus (DM2) when compared with women without PCOS. The principal symptoms in patients with PCOS are irregular menstruation, acne, and excessive amounts of androgenic hormones. The Rotterdam PCOS consensus workshop has given specific criteria to establish PCOS diagnosis only after exclusion of other known disorders. Obesity is a common finding of women with PCOS, but it is not part of the diagnostic criteria. PCOS has metabolic characteristics that include prominent defects in insulin action and beta-cell function, defects that confer a substantially increased risk for obesity and type 2 diabetes mellitus. PCOS women have an increased level of luteinizing hormone (LH) and a decreased level of follicle-stimulating hormone (FSH), which leads to disorders in the regulation of the menstrual cycle. The values of LH and FSH are dependent on the day of the menstrual cycle in which the hormones are measured. Obesity also has an influence on these values. Objectives: The objective of this study was to compare the hormonal and anthropometric parameters in women with PCOS and healthy control group. Materials and Methods: This study was carried out in the Department of Pathology, Dr. D Y Patil Medical College and Research Centre, Pune, Maharashtra. Fifty female patients aged 16-40 years diagnosed with PCOS by known criteria were included in the study and compared with 50 healthy control group females. Conclusion: Elevated levels of thyroid-stimulating hormone, LH, FSH, and prolactin along with increased body mass index and waist-to-hip ratio were predictors of PCOS and the early metabolic abnormalities.

Introduction

Polycystic ovary syndrome (PCOS) is an endocrinopathy with a complex metabolic disorder. PCOS is characterized by reproductive hormonal imbalances leading to the clinical presentation of hyperandrogenism and infertility.[1] PCOS is also showing an increased prevalence of several other conditions such as obesity, dyslipidemia, hypertension, metabolic syndrome (MS), and type 2 diabetes mellitus (DM2) when compared with women without PCOS.[2] The principal symptoms in patients with PCOS are irregular menstruation, acne, and excessive amounts of androgenic hormones.[3],[4]

The Rotterdam PCOS consensus workshop concluded that two out of three criteria need to be present to establish PCOS diagnosis only after exclusion of other known disorders with similar clinical presentations, for example, thyroid dysfunction and hyperprolactinemia. The criteria are chronic anovulation, clinical and/or biochemical evidence of hyperandrogenism, and the presence of polycystic ovaries by ultrasound or by laparoscopic findings.[5] Obesity is a common finding of women with PCOS, but it is not part of the diagnostic criteria. PCOS has metabolic characteristics that include prominent defects in insulin action and beta-cell function, which confer a substantially increased risk for obesity and type 2 diabetes mellitus.[6] Few studies mention that there is an association between insulin resistance and PCOS, though insulin resistance is independent of obesity.[7],[8],[9]

PCOS women have an increased level of luteinizing hormone (LH) and a decreased level of follicle-stimulating hormone (FSH), which leads to disorders in the regulation of the menstrual cycle. The values of LH and FSH are dependent on the day of menstrual cycle in which the hormones are measured. Obesity also has an influence on these values.[10]

Since PCOS presents as a spectrum of diseases, the Rotterdam criteria divided the disease into four phenotypes as below:[5]

*Frank or classic polycystic ovary PCOS (chronic anovulation, hyperandrogenism, and polycystic ovaries) *Classic nonpolycystic

ovary PCOS (chronic anovulation, hyperandrogenism, and normal ovaries) *Nonclassic ovulatory PCOS (regular menstrual cycles, hyperandrogenism, and polycystic ovaries) *Nonclassic mild or normoandrogenic PCOS (chronic anovulation, normal androgens, and polycystic ovaries).

The defect in theca cells explains the hyperandrogenemia in patients with PCOS. Patients with PCOS secrete high levels of androgens due to an intrinsic activation of steroidogenesis even in the absence of trophic factors. This dysregulation also affects granulosa cells leading to the production of four times higher levels of anti-Mullerian hormone in PCOS compared to healthy controls.[11]

Materials and Methods

The case-control study was carried out in the Department of Pathology, Dr. D. Y. Patil Medical College, Hospital and Research Centre, Pune, Maharashtra. A consecutive sampling technique was used for the subjects who met the inclusion criteria; controls were matched accordingly.

Inclusion criteria

All the cases (subjects and controls) included in this study were aged between18 and 40 years and were attending obstetrics and gynecology outpatient clinic.

The females diagnosed with PCOS by known criteria, who had not been taking oral contraceptives for at least 3 months and were premenopausal (FSH <12 IU/L), were considered subjects.[5]

The control group consisted of women without PCOS attending obstetrics and gynecology outpatient clinic, for routine gynecological examination, who had regular menstrual cycles and no clinical or biochemical features of hyperandrogenism such as irregular menstruation and hirsutism.

Exclusion criteria

Patients aged below 18 years and more than 40 years were excluded from the study. Furthermore, patients suffering from diabetes mellitus, hypertension, thyroid disorders, renal diseases, cardiovascular diseases, and Cushing's syndrome; pregnant or lactating women; and patients on hormonal, hypoglycemic agents, and lipid-lowering medications within the previous 6 weeks were excluded from the study.

After the patient's consultation in the gynecology outpatient clinic, the consent for enrollment in the study was obtained. Detailed instructions were given to all the patients enrolled in the study before the collection of blood. During the outpatient clinic timings, i.e., 9:00 am to 12:00 pm, the anthropometric measurement of height, weight, hip-to-waist ratio, and body mass index (BMI) was taken by the doctor in the central clinical laboratory. After that, the patient's venous blood sample was collected by the phlebotomist in the central clinical laboratory on day 2 or 3 of the menstrual cycle during the early follicular phase after an overnight fast of 10-12 h. Fasting blood samples were withdrawn from the antecubital vein, at rest, in the supine position, and serum was separated from the blood by centrifuge. The measurement of thyroid-stimulating hormone (TSH), FSH, luteinizing hormone, and prolactin was done using electrochemiluminescence immunoassay (RocheHitachiCobase411).

All participants signed an informed consent form. The study was approved by the Institutional Ethical Committee.

Results

A total of 50 subjects diagnosed with PCOS and 50 controls were included in the study.

The mean age was found to be 25.52 [+ or -] 5.39 for subjects and 28.5 [+ or -] 6.01 years for controls. Majority of the participants, 86%, were between the ages of 18-30 years in subjects and 64% in controls. Waist-to-hip ratio was 0.95 [+ or -] 0.05 in subjects and 0.90 [+ or -] 0.03 in controls which was significant. The mean BMI was raised among the study subjects, 28.26 [+ or -] 6.3 compared to 24.6 [+ or -] 3.34 in the controls. The association of anthropometric parameters with PCOS is significant except for weight, which is raised in both population [Table 1].{Table 1}

The hormonal profile of TSH, LH, FSH, and prolactin is also raised. The association of hormonal profile with PCOS is significant. Unadjusted comparison of the levels of various reproductive hormones between subjects and controls is presented in [Table 2]. The mean TSH for study cases was found to be 3.58 [+ or -] 3.22 compared to 2.4 [+ or -] 1.22 in the controls. The mean FSH for cases was 6.0 IU/L [+ or -] 3.08, whereas that for the controls was 4.21 IU/L [+ or -] 0.91. In addition, the mean LH for subjects was 14.76 nmol/L [+ or -] 13.76 and for controls was 11.14 nmol/L [+ or -] 1.9. The mean prolactin level for the study subjects was 24.05 nmol/L [+ or -] 14.8, whereas that for controls was 12.28 [+ or -] 3.09 [Table 2].{Table 2}

Discussion

Polycystic ovarian syndrome (PCOS) is also referred Stein-Leventhal syndrome or hyperandrogenic anovulation. It is one of the most common endocrine system metabolic disorders that affect women in their reproductive age. This disease was described in 1935 by Stein and Leventhal, it represents a condition in which an estimated multiple small cysts develop on one or both ovaries.[12]

The manifestations of PCOS are obesity, dyslipidemia, hypertension, MS, and type 2 diabetes mellitus (DM2) in comparison with

women without PCOS. These features along with other alterations in the form of endothelial dysfunction and a chronic low-grade inflammatory state leading to a greater risk of developing cardiovascular disease and increased morbidity and mortality.[9]

In this study, we measured the level of anthropometric parameters and reproductive hormones of women diagnosed with PCOS according to the Rotterdam criteria along with the control. In our studied population, controls were slightly older than the subjects but from the same region. In addition, both study subjects and controls had a higher BMI of nearly 25 kg/m2, which reflects that overweight is a common finding in the general population and PCOS. Furthermore, study cases had higher BMI compared to controls, with a mean BMI of 28.6 kg/m2. Although weight is statistically not significant in our study, BMI has been suggested to influence the levels of reproductive hormones in PCOS.[10],[13] Few studies show that raised BMI was associated with lower LH levels,[14],[15] but other studies described that BMI had no influence on LH.[16],[17] On the other hand, age and increased BMI (obesity) are powerful magnifying factors of several aspects of PCOS, which will reflect in clinical presentation and metabolic manifestations.[18],[19] In our study, the central obesity which is reflecting in the increased waist-to-hip ratio was significantly higher in women with PCOS as well as in the general population. The higher BMI and the central obesity increase the incidence of PCOS with associated complications involving infertility. These results also support previous studies, where increased waist and hip circumferences increase the incidence of PCOS.[20]

Obese girls with PCOS are at increased risk of developing insulin resistance and MS. Studies explain that patients with PCOS have higher visceral and subcutaneous body fat distribution because of increased androgen production rates and it is followed by central obesity and masculinized body fat distribution. The amount of visceral fat and degree of insulin resistance play a significant role in expressing the metabolic features of PCOS and obesity. However, it is debatable whether obesity leads to PCOS or whether PCOS leads to obesity.[21],[22],[23]

Insulin resistance, hyperinsulinemia, and an increase in androgen production are all linked together in PCOS patients. The patients with PCOS demonstrate an increased secretion of androgens and adrenocortical precursor steroids basally and in response to ACTH stimulation which include pregnenolone, 17-hydroxypregnenolone, dehydroepiandrosterone (DHEA), androstenedione, 11-deoxycortisol, and possibly cortisol.[24]

There is an abnormal LH/FSH ratio which is the main reason for the continuation of anovulatory state in PCOS subjects. Increased LH and decreased or normal FSH are due to gonadotropin-releasing hormone (GnRH) pulsatile secretion or high estrogen environment. This intense androgenization due to excess androgen production is observed in PCOS. Hyperandrogenemia induces the increase in testosterone, androstenedione, DHEA, DHEA-S, 17-hydroxyprogesterone, and estrone (E1) when excess androgen is converted to E1 by peripheral fat. A similar picture is also shared by hypothyroidism where increased TSH is associated with hyperglycemia, raised levels of sex hormone-binding globulin, and dyslipidemia.[25]

The variation of hormonal levels in the reproductive age group is mainly affected by the menstrual cycle. LH appears to be more elevated in lean PCOS patients compared to obese PCOS.[26] Our study also shows similar findings of an average increase of LH and FSH, but the ratio of LH:FSH is increased in subjects compared to the controls. The TSH levels are also at a higher normal level in our study, though the known patients with thyroid disorders were excluded from the study. A likely reason for this observation may be an increased prevalence of subclinical hypothyroidism in women with PCOS, as reported by few previous studies.[27] The prolactin levels are increased in the study subjects compared to the controls. A previous study showed that PCOS is associated with relatively high estrogen levels and hyperandrogenemia, which could stimulate prolactin secretion.[28]

The study limitations include the small sample size, and the nonassay of the other hormonal variations in PCOS patients such as insulin, GnRH, and gonadotrophins. Future studies with a larger sample size which would include other hormonal assays of insulin, GnRH, and gonadotrophins are required for a better understanding of PCOS.

Conclusion

Elevated levels of TSH, LH, FSH, and prolactin along with the increased BMI and waist-to-hip ratio were predictors of PCOS and the early metabolic abnormalities. However, future studies with larger sample sizes and other hormonal parameters are needed for better understanding of PCOS.

Implication

The use of these simple and cost-effective anthropometric and hormonal parameters may help in the detection of early metabolic changes in women with PCOS. This study will also help to educate patients about dietary habits, exercise, and precautions to lower the risk of PCOS.

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Conflicts of interest

There are no conflicts of interest.

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