Original Article

Relationship of subclinical hypothyroidism and obesity in polycystic ovarian syndrome patients

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Abstract

Objectives: To determine the prevalence of obesity and its relationship with subclinical hypothyroidism in women with polycystic ovarian syndrome (PCOS). To compare the clinico-biochemical parameters of obese and lean PCOS patients. **Materials and Methods:** A total of 287 women with PCOS were included in this study after consent. The demographic, anthropometry, clinical, and hormonal (thyroid-stimulating hormone [TSH] and total testosterone) parameters were recorded along with pelvic ultrasonography (USG) for all PCOS subjects. They were divided into lean (body mass index [BMI] between 18.5 and 22.9) and overweight (BMI ≥23), and the number of subclinical hypothyroid patients were calculated in each group. The clinico-biochemical parameters of both groups were compared. **Results:** The majority (61%) of our patients were overweight. There was no significant difference in the prevalence of subclinical hypothyroidism between overweight and lean PCOS patients. The obese PCOS patients were older than lean PCOS patients, and they had higher serum testosterone with elevated systolic and diastolic blood pressure (BP). **Conclusion:** The majority of our patients were found to be overweight and there was no association between obesity and subclinical hypothyroidism among PCOS patients.

Keywords: Lean, overweight, polycystic ovarian syndrome, subclinical hypothyroidism

Introduction

Polycystic ovarian syndrome (PCOS) is the most common form of chronic anovulation associated with androgen excess, affecting about 5–10% of reproductive women.[1] It is a heterogeneous disorder of multifactorial etiology. PCOS is associated with increased cardiovascular and metabolic risk factors like obesity.[2] Obesity is a common finding in PCOS and aggravates many of its reproductive and metabolic features. On the other hand, thyroid disorders are more common in women than men and have unique consequences related to menstrual cyclicity and reproduction.[3] Additionally, hypothyroidism leads to increased weight gain by mucin deposits and salt and water retention.[4] Body composition and thyroid hormones appear to be closely related as the latter is known to be involved in the regulation of basal metabolism and thermogenesis, playing an important role in lipid and glucose metabolism.[5] Recently, different studies from various parts of the world regarding hypothyroidism in PCOS patients have tried to explore the PCOS–thyroid interface. Most of the results have shown a higher incidence of elevated serum thyroid-stimulating hormone (TSH) levels and higher prevalence of autoimmune thyroiditis in PCOS subjects.[6] But no study has revealed whether the obesity in PCOS patients is independent of hypothyroidism or not. This study has been contemplated to investigate the relationship of subclinical hypothyroidism

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with obesity in PCOS patients attending a tertiary care hospital in central India.

Methodology

This cross-sectional study was conducted in a tertiary care health institute in central India. All consecutive patients who attended our gynecology outpatient department (OPD) from February 2016 to October 2017 were included in this study after taking approval from the institute's ethics committee (25.02.2016). A total of 287 women, diagnosed with PCOS as per the revised 2003 Rotterdam criteria[7] were included after informed consent. The revised 2003 Rotterdam criteria are based on the presence of any two of the following factors:

1. Chronic anovulation
2. Clinical/biochemical parameters for hyperandrogenism
3. Polycystic ovaries on ultrasonography[7]

The objective of our study was to determine the prevalence of obesity and its relationship with hypothyroidism in women with PCOS and compare the clinico-biochemical parameters of obese and lean PCOS patients. Women having biochemical and clinical features of hyperandrogenism and/or polycystic ovary because of other disorders like hyperprolactinemia, overt hypothyroidism, congenital adrenal hyperplasia (CAH), adrenal tumor, Cushing's syndrome, acromegaly, or ovarian tumor were excluded from the study. A detailed history was taken and they were subjected to thorough clinical examination.

Clinical and anthropometric data, such as age, height, weight, body mass index (BMI), waist circumference (WC), and blood pressure (BP), were recorded. Height and weight were measured with subjects wearing light clothing but without shoes, using stadiometers and calibrated digital weighing scales, respectively. The BMI was calculated by dividing the weight in kilograms by the height in meters squared. As per the World Health Organization (WHO), the BMI range for Asians normal, overweight, and obesity is defined as a BMI of 18.5 to 22.9 kg/m2, 23.0 to 26.9 kg/m2, and ≥27 kg/m2, respectively.[8] WC was measured at the midpoint between the lower costal margin and the iliac crest at the end of normal expiration using an inch tape as per National Institute of Health (NIH) guidelines.[9] BP was measured in the sitting position after resting for 10 min, twice with 5-min intervals, using a mercury sphygmomanometer, and the average value in mmHg was used. The presence of hirsutism was noted using the modified Ferriman–Gallwey (mFG) scoring system.[10] Hirsutism is the presence of terminal (coarse) hair in females in a male-like pattern, which affects around 5–10% of women.[11] A visual method of scoring hair growth in women was first reported by Ferriman and Gallwey in 1961.[12] Each of the body areas depicted is scored from 0 (absence of terminal hairs) to 4 (extensive terminal hair growth), and the scores in each area are summed for a total hair growth score. However, in the mFG score, the number of body sites is reduced to nine after excluding forearm and lower leg. Generally, hair growth scores of 8 or greater represent hirsutism, mild hirsutism is equal to a score of 8 to 16, moderate is 17 to 24, and finally a score of more than 24 indicates a severe type of hirsutism.[13] The serum TSH and total serum testosterone levels of all these patients were assessed. TSH was measured by sandwich assay in direct chemiluminescent assay (CLIA) technology. Our laboratory cutoff value for the diagnosis of euthyroid is 0.35–4.2 mIU/L as per recommendations by the American Thyroid Association (ATA).[14] Hence, those having a serum TSH value of more than 10 mIU/L were considered as overt hypothyroid and those having a TSH level below 0.35 mIU/L were considered as hyperthyroid.[14] All patients with a serum TSH level between >4.2 mIU/L to 10 mIU/L are considered subclinical hypothyroid. The patients were classified as euthyroid, overt hypothyroid, subclinical hypothyroid, or hyperthyroid according to the reference values. Patients having overt hypothyroidism and hyperthyroidism were excluded from the study. None of the patients were known to be hypothyroidism before evaluation. Serum total testosterone was measured by competitive immunoassay by direct CLIA technology. Our laboratory cutoff of a normal serum testosterone level in females is 14 to 76 ng/dl. Hence, those having a serum total testosterone value more than 76 ng/ml were considered as hyperandrogenemia.

Statistical analysis

Statistical analysis was done using the Statistical Package for the Social Sciences (SPSS) software version 17. All continuous data were summarized as mean and standard deviation (SD). The categorical data were expressed as frequency (percentages), which were compared using the Chi-square test. To compare the subjects of different groups, student's *t*-test was used. $P < 0.05$ was considered significant.

Results

Our patients were classified into two groups, namely, lean PCOS (BMI between 18.5 and 22.9) and overweight PCOS (BMI ≥23). We had 112 (39%) lean PCOS patients and 175 (61%) overweight PCOS patients. Out of the total 112 lean PCOS patients, 21 (19%) were found to be subclinical hypothyroid and 91 were found to be euthyroid, while in the overweight group of 175 subjects, 37 (21%) were subclinical hypothyroid and 138 were euthyroid. Among the lean PCOS group, 88 subjects had an mFG score <8 and 24 had an mFG score ≥8. Similarly, among the overweight PCOS group of 175 subjects, 118 of them had no features of hirsutism, whereas 57 had hirsutism.

The clinical and biochemical findings of these two groups were compared [Table 1]. The overweight PCOS patients were older than the lean PCOS counterparts ($P < 0.001$ for mean age). The total testosterone, BMI, systolic BP, and diastolic BP of overweight PCOS patients were significantly higher than the lean PCOS patients. There was no significant difference in the WC, mFG score, and TSH level between the two groups.

A Chi-square test was performed to find the relationship between obesity and subclinical hypothyroidism (TSH >4.2 to 10 mIU/L)

in the two groups [Table 2]. No significant association was found between BMI and TSH ($P = 0.622$).

Discussion

Although it is believed that PCOS patients are usually obese and probably obesity is the cause of clinical manifestations of PCOS, in our study we found that 39% of our patients were lean and 61% of them were overweight. Hence, our study result shows that PCOS and its clinical manifestations are seen across overweight and normal BMI patients. This means all the PCOS patients, irrespective of their BMI, have irregular cycles, features of hyperandrogenism, and a raised serum testosterone level. A study from India by Saxena *et al.* also shows the prevalence of lean PCOS as 42%.[15] It has been found that insulin resistance, which plays the central role in the development of PCOS and genetic susceptibility, is responsible for developing PCOS.[16-19] In the present study, the obese PCOS patients have significantly higher BP and higher total serum testosterone level when compared with their lean counterparts. Obese patients are susceptible to deranged lipid profile and increased insulin resistance.[15] Hence, this insulin resistance in PCOS patients, which leads to atherosclerosis of the vessels because of raised triglycerides and decreased level of high-density lipoproteins (HDLs), contributes to hypertension.[20-22] Similarly, hyperinsulinemia leads to reduced sex hormone-binding globulin (SHBG) in obese PCOS patients resulting in higher levels of free testosterone in their blood in comparison with their lean PCOS counterparts.[23,24] Hence, although insulin resistance is a common finding in PCOS that is independent of obesity, PCOS-associated defects in insulin sensitivity and secretion are further exacerbated by obesity.

Table 1: Comparison of clinical and hormonal parameters between lean and overweight PCOS subjects

Clinical Features	Lean PCOS (*n*=112)	Overweight PCOS (*n*=175)	*P*
Mean Age (years)	21.39±4.23	23.13±6.10	<0.001**
Systolic BP (mmHg)	111.43±7.74	114.18±8.97	0.003*
Diastolic BP (mmHg)	71.75±6.22	73.77±7.02	0.004*
WC (cm)	77.46±17.03	92.58±14.10	0.883
BMI (kg/m^2)	20.18±1.87	27.93±5.26	<0.001**
TSH (mIU/L)	2.72±1.56	3.10±1.94	0.079
mFG scoring	5.05±4.54	3.91±4.25	0.168
Testosterone (ng/dL)	63.48±23.25 (*n*=77)	65.11±33.18 (*n*=113)	0.005*

*P<0.05 significant, **P<0.001 highly significant. PCOS=Polycystic ovarian syndrome, BP=Blood pressure, WC=Waist circumference, BMI=Body mass index, TSH=Thyroid stimulating hormone, mFG=Modified Ferriman–Gallwey

Table 2: Association of obesity with subclinical hypothyroidism among PCOS subjects

Groups	Hypothyroid	Euthyroid	Total	*P*
Lean PCOS	21	91	112	0.622 (ns)
Overweight PCOS	37	138	175	
Total	58	229	287	

PCOS=Polycystic ovarian syndrome, ns=Non-significant

Although the association of hypothyroidism and obesity is not fully teased out, researchers have shown that TSH is higher in people with a high BMI.[4] The raised TSH levels are associated with the rapid production of fat cells either by inflammatory mediators or via another hormone called leptin, thereby leading to obesity.[4] But, in our study, we did not find any significant difference in the TSH status when we compared lean and obese PCOS patients. Hence, this study indicates that BMI in PCOS patients is not affected by thyroid status of the body.

The limitations of our study are that we have not calculated the sample size for our study.

Conclusion

We have seen that the majority of the PCOS patients are overweight and there is no relationship between obesity and hypothyroidism in PCOS patients. The presence of insulin resistance poses risk of future cardiovascular and metabolic disorders among all PCOS patients, but the presence of obesity in PCOS patients makes them more susceptible to such kinds of risks in the future. Hence, such patients should be counseled and advised for intensive lifestyle modifications.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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