ORIGINAL RESEARCH PAPER

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THYROID DISORDER AMONG LEAN AND OBESE POLYCYSTIC OVARY SYNDROME PHENOTYPES

KEY WORDS:
hypothyroidism, polycystic ovary syndrome, obesity, prevalence

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ABSTRACT

Context: Polycystic ovary syndrome (PCOS) is the most common endocrine disorder among females in reproductive age and is associated with metabolic disorders, cardiovascular conditions and anovulatory infertility. Thyroid disorders share many overlapping features with PCOS, but their relation with PCOS is still controversial.

Aim: To evaluate the prevalence of thyroid disorders among the patients with PCOS, and its relative prevalence among the lean and obese phenotypes of PCOS.

Materials and methods: A prospective and observational study involving 89 females with PCOS as per the Rotterdam's/ESHRE criteria and 93 non-PCOS females as comparison group was carried out. All participants underwent history, clinical, anthropometry, ultrasonography and serum thyroid profile evaluation. A cut-off body mass index (BMI) of 23 kg/m^2 was used for classification of lean and obese phenotypes. Mann-Whitney U test and independent samples t-test were used to compare the non-normally distributed and normally distributed continuous variables, respectively. Pearson's chi-square (2) test was used for comparison of categorical variables.

Results: The PCOS group showed higher proportion of hypothyroidism (21.34%) than the comparison group (8.6%) (P = 0.015). Higher prevalence of hypothyroidism (33.33%; P = 0.009) and higher mean serum TSH values (3.8 mIU/L; P < 0.001) were seen in obese PCOS females in comparison to the lean PCOS phenotype (10.67% and 2.14 mIU/L, respectively).

Conclusion: There is higher prevalence of hypothyroidism in females with PCOS than the non-PCOS. Also, the obese PCOS have higher proportion of females with hypothyroidism than the lean PCOS subgroup.

INTRODUCTION

Polycystic Ovarian Syndrome (PCOS), the most common endocrine disorder amongst women in the reproductive age group,(Duncan, 2014) is characterized by hyperandrogenism, polycystic ovaries and ovulatory dysfunction. (Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group, 2004) Around 20% of normal women in the reproductive age group demonstrate polycystic ovaries,(Polson et al., 1988) and approximately 7-8 % have additional clinical and biochemical features of PCOS. (Franks, 1995) PCOS has shown association with various metabolic conditions like obesity, insulin resistance, hyperinsulinemia, type 2 diabetes mellitus, cardiovascular problems, and malignant tumours of breast and endometrium. It also has profound neurological and psychological effects on the quality of life.(Barthelmess & Naz, 2014) It is the most common aetiology of anovulatory infertility in women.(Franks, 1995) PCOS can be classified dichotomously into lean and obese clinical phenotypes based on body mass index (BMI).(Saxena et al., 2012;Toosy et al., 2018)

Thyroid dysfunction is one of the common endocrine disorders among women. The prevalence of subclinical hypothyroidism is around 10% in general population and 4-6% in reproductive age group females.(Singla et al., 2015) Though both hypothyroidism and PCOS have different etiopathogenesis, yet they share many overlapping features like an increase in volume of ovary, development of cystic changes,(Singla et al., 2015) irregularities of menstruation, infertility, hyperandrogenism and weight gain.(Ghosh et al., 1993; Krassas et al., 1999) Some studies have also demonstrated an increase in incidence of thyroid disorders amongst women with PCOS in comparison to the general population.(Benetti-Pinto et al., 2013; O. E. Janssen et al., 2004; Sinha et al., 2013b) The aim of this research was to investigate the prevalence of thyroid disorders among the patients with PCOS, and to study the relative prevalence of the same among the lean and obese phenotypes of PCOS.

MATERIALS AND METHODS

This prospective, observational study was conducted in the department of Obstetrics and Gynaecology at our institute. The study was approved by the institutional ethical committee. The study included all females presenting in the outpatient department from 1st March 2018 to 28th February 2019 who:

1. Fulfilled the 2003 Rotterdam/ ESHRE criteria for PCOS: 2 out of 3 of the following-
   a. Oligo- or anovulation
   b. Clinical and/or biochemical signs of hyperandrogenism
   c. Polycystic ovaries
2. Consented to be part of the study

Those females who did not fulfil the Rotterdam criteria, but had regular predictable ovulatory cycles were included in the comparison group.

Those candidates who had a history or clinical evidence of other endocrinological disorders like diabetes mellitus, hyperprolactinemia, Cushing's disease, congenital adrenal hyperplasia (CAH), those with comorbidities involving the renal, hepatic or cardiac system and those on medications like oral contraceptive pills (OCPs), insulin sensitizing drugs, statins, levothyroxine, corticosteroids, GnRH agonists and antagonist were excluded from the study.

Oligo-ovulation was defined as menstrual cycles occurring at an interval of ≥ 35 days. Only the clinical signs and symptoms of hyperandrogenism i.e. hirsutism, acne and androgenic alopecia were considered. Hirsutism was defined using the modified Ferriman-Gallwey (mFG) score of ≥ 8. Polycystic ovaries were defined as the presence of ≥ 12 follicles in each ovary measuring 2-9 mm in diameter, and/or increased ovarian volume (> 10 mL). A BMI cut-off of 23 kg/m^2 based on the WHO recommendations for BMI in Asian population (Whiteley, 2003) was used to classify the patients into the 'lean' and 'obese' subgroups. For ease of calculation, the patients

belonging to the overweight category (23 - 27.4 kg/m^2) were also included in the 'obese' subgroup. Serum thyroid stimulating hormone (TSH), total T3, total T4 were measured using microplate-based ELISA and their normal values were defined as serum TSH: 0.4 - 5.5 mIU/L, total T3: 0.8 - 2.1 ng/mL, total T4: 5 - 13 µg/dL

All the statistical analyses were done using SPSS® version 23 (IBM Corporation, US). The continuous variables were assessed for normality using Shapiro-Wilk test and the means were depicted with standard deviation or range. We applied the Mann-Whitney U test and independent samples t-test to compare the non-normally distributed and normally distributed continuous variables, respectively. To compare the categorical variables, Pearson's chi-square (2) test was applied. Pearson correlation coefficients, the two-tailed method and 95% confidence intervals (95% CIs) were used to evaluate the correlation between the variables. The differences were considered statistically significant if the P-value was < 0.05.

RESULTS

During the study period, 182 subjects were enrolled in the study. 89 (48.9%) females who fulfilled the criteria for PCOS were placed in the PCOS study group, while the remaining 93 (51.1%) females formed the comparison group. The average age of the participants in the study was 22.6 years (range 16-37 years). Overall, thyroid dysfunction was seen in 27 subjects (14.83%) which was in the form of hypothyroidism. However, differentiation between subclinical and overt hypothyroidism was not carried out. The PCOS group demonstrated significantly higher proportion of patients with hypothyroidism in comparison to normal non-PCOS group (*P* = 0.015) [Table 1].

Table 1: Clinical characteristics of PCOS and Comparison group

	PCOS group (*n* = 89)	Comparison group (*n* = 93)	
Mean age (Range)	22.91 (16-35)	22.31 (16-37)	
Mean weight (kg)	54.77	49.92	*P* < 0.001
Mean BMI (kg/m^2)	23.63	21.34	*P* < 0.001
Thyroid dysfunction (%)	19 (21.34%)	8 (8.6%)	*P* = 0.015
Mean serum TSH	2.92 mIU/L	2.35 mIU/L	*P* = 0.027

In the entire study population, 52 females (28.57%) were found to have a BMI of more than 23 kg/m^2. The proportion of obese subjects (n = 42; 47.19%) among PCOS group was significantly higher than comparison group (n = 10; 10.75%) (P < 0.001). The mean weight and BMI in the PCOS group was also found to be significantly higher than the comparison group (P < 0.001).

Lean subjects had significantly lower prevalence (n = 6; 4.61%) of hypothyroidism when compared to obese females (n = 21; 40.38%) (P = 0.043). Obese subgroup among the PCOS study group had higher prevalence of hypothyroidism and higher mean serum TSH levels [Table 2]. An overview of thyroid profile among the study groups has been shown in figure 1.

Table 2: Difference in mean serum TSH between obese and lean PCOS

	Obese PCOS subgroup (n = 42)	Lean PCOS subgroup (n = 47)	
Thyroid dysfunction (%)	14 (33.33%)	5 (10.67%)	*P* = 0.009
Mean serum TSH	3.8 mIU/L	2.14 mIU/L	*P* < 0.001

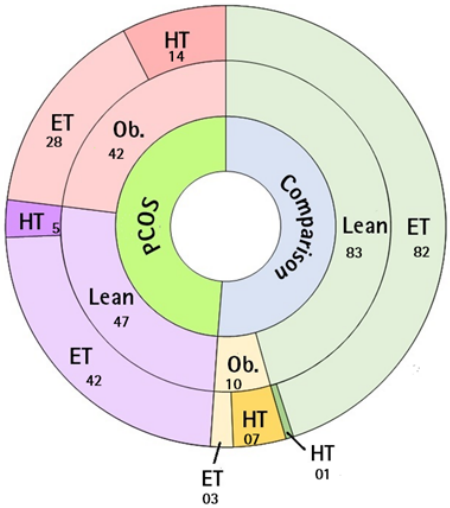

Figure 1: Graph showing distribution of thyroid disorders in PCOS and Comparison group (Ob.= Obese; ET = Euthyroid; HT = Hypothyroid)

DISCUSSION

In our study, the proportion of PCOS patients with BMI > 23 kg/m^2 was 47.19% (*n* = 42). This is lower in comparison to other studies. (Barcellos et al., 2007; Majumdar & Singh, 2009; Najem et al., 2008) Even with the cut-off BMI of 25 kg/m^2 for differentiation between lean and obese PCOS, the proportion of obese PCOS ranged from 54.9% to 81.13% in these studies. The mean BMI among the PCOS females in the current study was 23.63 kg/m^2, which is comparable to another study performed in the Indian subcontinent by Sinha et al. (Sinha et al., 2013b) However, in other studies carried out in Libya (Najem et al., 2008) and Brazil, (Barcellos et al., 2007) the mean BMI among PCOS females ranged from 29-34 kg/m^2. We could attribute this to two potential reasons: First, a significant number of the patients with PCOS in our study belonged to the adolescent age group which is evident by the mean age of 22.91 years. The other studies we found had enrolled PCOS patients with higher age. Secondly, most of our PCOS patients had come from a low socioeconomic background. However, further evaluation into such a correlation is required.

We found significantly higher serum TSH levels among PCOS population in comparison to the non-PCOS control group. Similar observations were found in other studies (Abdelsalam & Ibrahim, 2015; O. Janssen et al., 2004; Sinha et al., 2013a). In contrast, another research while studying the prevalence of autoimmune thyroiditis among Iranian women with PCOS did not demonstrate any difference in the TSH levels among the PCOS and non-PCOS subpopulations (Kachuei et al., 2012). In the past, it had been tried to speculate the pathophysiology behind the hypothyroid-associated PCOS (Yen, 1980). It was postulated that hypothyroidism would induce an overactivation of the 16 -hydroxylation reaction leading to overproduction of estriol. This would then contribute to development of PCOS by altering the feedback regulation of gonadotropin.

Very few studies have evaluated the correlation between BMI and thyroid function among PCOS patients. In the current study, obese PCOS group had significantly higher serum TSH than lean PCOS group. However, Benetti-Pinto et al in his study of 168 PCOS females did not find statistically significant difference in BMI between euthyroid (TSH < 4.5 mIU/L) and subclinical hypothyroid (serum TSH = 4.5 – 10 mIU/L) groups. (Benetti-Pinto et al., 2013) Our findings can be indirectly contributed to the established link between obesity and thyroid function. Obesity is associated with increase in circulatory levels of proinflammatory substances and insulin resistance, which in turn leads to decreased

deiodinase-2 activity at pituitary level resulting in relative T3 deficiency and increase in serum TSH levels.(Singla et al., 2015)

CONCLUSION

We conclude that there is a higher prevalence of hypothyroidism and obesity among females with PCOS. Also, that PCOS females with obesity may have higher prevalence of thyroid dysfunction. However, whether the thyroid disorder is a causative factor for PCOS or PCOS somehow leads to hypothyroidism is still unclear.

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