ORIGINAL ARTICLE

Elevated Luteinizing Hormone, Testosterone and Free Triiodothyronine with Increase in Body Mass Index in Polycystic Ovary Syndrome

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Abstract

Background: Polycystic ovary syndrome (PCOS) is the most common endocrine disorder among women in the reproductive age group. The association of testosterone, luteinizing hormone (LH), follicle stimulating hormone (FSH) and thyroid hormones in obese PCOS women are not clear. Hence, the present study was performed to assess the serum levels of gonadotrophins, testosterone and thyroid hormones in obese and nonobese PCOS women.

Materials and methods: Sixty-three patients (41 obese and 22 nonobese) with PCOS were recruited for the study. Serum levels of testosterone, LH, FSH, thyroid stimulating hormone (TSH), free thyroxine (free T4) and free triiodothyronine (free T_3) levels were measured.

Results: Serum LH ($p = 0.040$), testosterone ($p = 0.010$) and free triiodothyronine ($p = 0.006$) levels were significantly elevated in obese PCOS women as compared to non-obese PCOS women. Both LH ($r = 0.478$, $p = 0.002$) and free T3 ($r = 0.379$, $p = 0.036$) were correlating positively with body mass index (BMI) in obese PCOS subjects. Testosterone was positively associated with duration of infertility in obese PCOS women ($R^2 = 0.187$, $\beta = 0.433$, $p = 0.005$)

Conclusion: We conclude that LH, testosterone and free T3 levels are increased with increase in BMI among women with PCOS.

Keywords: Gonadotropins, Luteinizing hormone, Obesity, Polycystic ovary syndrome, Testosterone, Thyroxine.

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Introduction

Polycystic ovary syndrome (PCOS) is the most common disorder of endocrine etiology affecting women of reproductive age group. PCOS is characterized by irregular menstruation, hyperandrogenism, and ovaries containing several small cysts or follicles filled with fluid on ultrasound examination.[1] Even though the exact mechanism underlying the pathology of PCOS is not well established, several studies have linked the etiology of PCOS to hyperandrogenism and altered thyroid and sex hormone levels.[2] Infertility is the most common complication associated with PCOS followed by obesity which leads to long-term complications such as type 2 diabetes mellitus and cardiovascular diseases.[3,4] Whether obesity is the cause or aftereffect of PCOS still remains unclear.[5,6]

Gonadotropins like LH and FSH are the hormones secreted by the anterior pituitary gland which controls ovulation and maintains the regularity of the menstrual cycle in women. Although the levels of LH and FSH in most of the PCOS women are within the normal reference range, their LH level is usually a few times higher than their FSH levels. This results in an altered LH to FSH ratio, which can disrupt normal ovulation leading to the irregular menstrual cycle and other manifestations of PCOS.[7,8] A recent study by Woo et al. has revealed that LH to FSH ratio >1 could be used to identify PCOS subjects who develop dominant follicle on treatment with letrozole.[9]

Several pieces of evidence suggest that hyperandrogenism plays an important role in the pathogenesis of PCOS.[10] Hyperandrogenism is considered to be responsible for polycystic ovary morphology and ovulatory dysfunction in women with PCOS.[11,12] High testosterone levels are reported to be associated with reduced placental and fetal growth.[13] Also, elevated testosterone is known to increase the risk of developing PCOS in women.[10]

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The prevalence of thyroid abnormalities is increasing in PCOS, with few studies reporting hypothyroidism or subclinical hypothyroidism and others reporting elevated TSH, T_3, and T_4 in subjects with PCOS.[14-16] A recent study has demonstrated that there is a positive correlation between thyroid hormones and various symptoms of metabolic syndrome in obese women with PCOS.[17]

Obesity, which is commonly seen associated with PCOS, is considered to be one of the factors responsible for poor response to infertility treatment.[18] Since there are limited data available in the literature about an alteration in testosterone, LH/FSH ratio and thyroid hormones in obese PCOS women, the present study was designed to evaluate the levels of these hormones in obese and nonobese PCOS subjects.

Materials and methods

The present study was a cross-sectional study conducted in the Department of Biochemistry, JIPMER, Puducherry in collaboration with the Department of Obstetrics and Gynecology. The study was approved by the Institute Ethics Committee, Intramural grant, JIPMER. Written informed consent was obtained from all study participants before enrollment in the study.

Consecutive PCOS patients attending JIPMER Obstetric and Gynecology OPD clinic fulfilling the inclusion and exclusion criteria were recruited in the study. Twenty-two nonobese (body mass index (BMI) <25 kg/m^2) and forty-one obese (BMI >25 kg/m^2) patients diagnosed with PCOS were included in the study. The patients with diabetes mellitus, hypertension, thyroid disorders, hyperprolactinemia, Cushing's disease, hepatic or renal failure, malignancy, and ischemic heart disease were excluded from the study. Patients who are taking medications such as antilipidemic drugs, oral contraceptive pills, anti-androgen agent, antihypertensives were also excluded.

Weight and height were measured without their shoes. BMI was calculated using the formula weight in kilograms divided by square of the height in centimeters. Five mL of blood was collected in the plain tube without any anticoagulants. Serum was separated and stored at –80°C till further analysis of hormones. Serum levels of FSH, LH, testosterone, thyroid stimulating hormone, free thyroxine (T3 and T4) were measured with specific chemiluminescence assays using an ADVIA Centaur® immunoassay system (Siemens Healthineers, Germany).

Statistical Analysis

Statistical analyses were performed using SPSS version 20. Results were shown as mean ± standard deviation. The comparison of biochemical parameters between the study groups (obese and nonobese PCOS) was carried out using an independent student't' test. The correlation between body mass index and hormonal parameters were analyzed by Pearson's correlation. Linear regression analysis was used to assess the association between the duration of infertility and testosterone in obese PCOS women. A *p* value of <0.05 was considered statistically significant.

Results

The baseline characters and hormone levels in obese and nonobese PCOS are shown in Table 1. LH, testosterone and free T_3 levels were significantly elevated in obese PCOS group than in nonobese PCOS subjects. There was no statistically significant difference in FSH, TSH, free T4, age and duration of infertility between two groups.

Table 2 shows the correlation between BMI and hormone levels in obese PCOS women. Both LH (r = 0.478, p = 0.002) and free T_3 (r = 0.379, p = 0.036) were positively correlated with body mass index in obese PCOS subjects. There was no significant correlation between BMI and other hormone levels.

Univariate linear regression analysis showed testosterone levels as significant association with duration of infertility in obese PCOS group (R^2 = 0.187, β = 0.433, p = 0.005) (Graph 1).

Discussion

Obesity is reported to affect the ovulatory function and several studies have suggested that the BMI of an individual can affect the hormonal balance of the hypothalamic-pituitary-gonadal axis.[19,20] The association of the LH/FSH ratio with obesity is unclear. Previous studies have demonstrated that most of the PCOS women with a normal level of LH/FSH ratio were usually obese, whereas Moran et al. and Beydoun et al. did not find any association between LH/FSH ratio and BMI in PCOS women.[21-23] In the present study, we found a higher concentration of the luteinizing hormone in obese PCOS women as compared to nonobese PCOS women. There was no such difference in the levels of FSH or LH/FSH ratio between both groups. LH was positively correlating with BMI in obese PCOS women. Previous studies have reported that obesity suppresses gonadotropin secretion and elevated LH can be attributed to hyperandrogenism seen in PCOS.[24]

In the present study, serum levels of LH were significantly higher in obese PCOS women compared to PCOS women with BMI less than 25. Even though FSH was increased in obese PCOS women it was not significant. Hence we did not observe any significant difference in the LH/FSH ratio between the two groups. If the study is extended to more samples, the difference may become significant. Since this is a short term student project, we could

Table 1: Age, duration of infertility, clinical characteristics and hormonal parameters in obese and nonobese PCOS subjects

Parameters	*PCOS subjects with BMI < 25 (n = 22) Mean ± SD*	*PCOS subjects with BMI > 25 (n = 41) Mean ± SD*	*p value (Independent sample t test)*
Age (years)	25.27 ± 2.64	25.10 ± 2.69	0.805
Waist circumference (cm)	82 ± 13	107 ± 15	0.001
Hip circumference (cm)	101 ± 12	110 ± 14	0.01
Waist-hip ratio	0.82 ± 0.12	0.98 ± 0.16	0.001
Duration of infertility (years)	2.6 ± 0.59	2.75 ± 0.86	0.495
LH (mIU/mL) 1.7–15 mIU/mL	14.10 ± 4.88	16.83 ± 4.95	0.040
FSH (mIU/mL) 1.4-9.9 mIU/mL	5.36 ± 1.68	6.05 ± 1.78	0.143
LH/FSH	2.79 ± 1.16	2.97 ± 1.10	0.545
Testosterone (ng/dL) 15 to 70 ng/dL.	39.51 ± 15.12	53.07 ± 21.10	0.010
TSH (μIU/mL) 0.35–5.5 μIU/mL	2.33 ± 0.92	2.43 ± 0.99	0.679
Free T3 (pg/mL) 2.1–4.4 pg/mL	2.60 ± 0.71	3.04 ± 0.48	0.006
Free T4 (ng/dL) 0.8–2.7 ng/dL	1.54 ± 0.43	1.40 ± 0.32	0.150

LH, luteinizing hormone, FSH, follicle stimulating hormone, TSH, Thyroid stimulating hormone, T3–Triiodothyronine, T4, thyroxine

Table 2: Correlation of body mass index with hormonal parameters in obese PCOS subjects (n = 41)

Parameters	*r*	*p*
Luteinizing hormone	0.478	0.002
Follicle stimulating hormone	0.271	0.087
LH FSH ratio	0.164	0.306
Thyroid stimulating hormone	–0.071	0.657
Free triiodothyronine	0.379	0.036
Free thyroxine	0.090	0.571

not increase the sample size due to ethical issues and financial constraints.

High testosterone levels are linked with both obesity and PCOS.[10,25] Earlier studies have demonstrated an increase in testosterone levels with an increase in BMI in PCOS subjects. La Zovic et al. have reported an association between BMI and androgen levels, whereas Yasmin et al. did not find any significant correlation between BMI and serum testosterone in women with PCOS.[26,27] In agreement with these studies, we observed elevated testosterone levels in obese PCOS women as compared to nonobese PCOS but did not found any association of testosterone with BMI. Also, we found a positive association of testosterone with a duration of infertility in obese PCOS women suggesting that hyperandrogenemia may be associated with the complications of PCOS.

Several investigators have estimated thyroid hormones in PCOS, but results are inconsistent. Trummer et al. and Yin et al. have demonstrated elevated TSH levels, whereas Mohammed et al. have reported elevated free T3 in PCOS women.[16,28,29] To the best of our knowledge, there are no studies in the literature about thyroid hormone levels in PCOS women with an increase in BMI. In the present study, we have reported elevated free T3 levels in obese PCOS as compared to nonobese PCOS patients, but TSH and free T4 levels were not significant between both the groups. Free T3 was positively correlating with BMI in obese PCOS women. Elevated free T3 levels in obese PCOS could be due to increase in leptin levels, which may increase the activity of deiodinase enzyme leading to increase in the conversion of T4 to T3 resulting in increased concentration of Free T3 in obese patients.[30,31]

This study also has a few limitations such as a smaller sample size. Further studies with a larger sample size can help to validate the results obtained in this study. Also, other steroid hormones and metabolites of testosterone were not estimated due to financial constraints.

Conclusion

These results show that obesity differently affects the serum LH, testosterone, and free T3 levels and play a significantly different role in the etiopathogenesis of PCOS patients leading to change in prognosis as well as manifestations of disease severity and long-term complications such as type 2 DM and cardiovascular disorders associated with PCOS.

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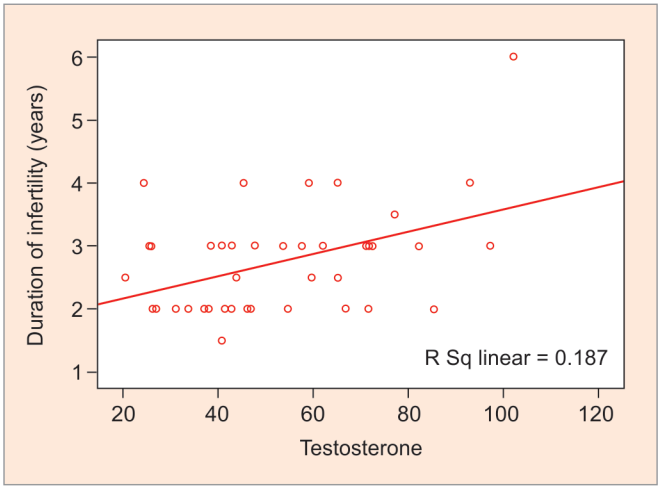

Graph 1: Linear regression analysis of testosterone with duration of infertility in obese PCOS women (R2 = 0.187, β = 0.433, *p* = 0.005)

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