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Original Research Article

Thyroid function in women with polycystic ovary syndrome

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ABSTRACT

Background: This study aimed to assess the serum thyroid stimulating hormone (TSH) levels in women with polycystic ovary syndrome (PCOS), and its variation with obesity, insulin resistance and LH:FSH ratio.
Methods: This was a facility based cross sectional study conducted for a period of 18 months on a total of 165 females with PCOS diagnosed based on Rotterdam 2003 criteria. A thorough history and clinical and anthropometric examination was conducted for all females. USG abdomen and serum TSH levels and fT4 were also done and the findings were recorded on questionnaire.
Results: Subclinical hypothyroidism was documented in 17% females with PCOS. No statistically significant difference in mean values of LH:FSH ratio, insulin resistance, and obesity parameters were noted among euthyroid and subclinical hypothyroid females with PCOS ($p>0.05$). TSH levels in present study showed a statsitcally significant positive correlation with BMI.
Conclusions: The proportions of thyroid disorders are higher in females with PCOS and they both may present with various similar clinical features. BMI in females with PCOS has significant positive correlation with TSH levels. However, it is not clear whether thyroid dysfunction has significant effect on insulin resistance.

Keywords: Thyroid dysfunction, PCOS, Insulin resistance, Obesity, LH:FSH ratio

INTRODUCTION

Polycystic ovarian syndrome (PCOS) is one of the most common endocrine disorders affecting women of reproductive age group, and account for a majority of cases of hirsutism, menstrual disturbances and anovulatory infertility. Apart from these features associated with PCOS include insulin resistance, obesity, hypertension, nonalcoholic steatohepatitis (NASH) and, also metabolic syndrome.[1,2] Most widely accepted criteria for diagnosis of PCOS is Rotterdam criteria.[1]

The prevalence of PCOS has recently been shown up to 18% with current Rotterdam diagnostic criteria.[3] This increase in prevalence of PCOS has been attributed to increase in prevalence of obesity and metabolic syndrome in general population.[4]

Thyroid disorders are the commonest disease of endocrine system worldwide, and the reported prevalence of overt and subclinical hypothyroidism range from 3.5-4.2%, and 8.02-19.3% respectively.[5,6] Though the etiopathogenesis of thyroid disorders as well as PCOS is completely different, but they have certain common manifestations. Insufficient supply of thyroid hormones at the peripheral tissues have been associated with alteration in metabolic processes in the body.[7] At one end, thyroid dysfunctions are associated with increased ovarian volume and cystic changes and at other end it has been documented that thyroid dysfunction are more common among females with PCOS as compared to general population.[7-10]

Their coexistence may influence the clinical presentation of each other and hence also has a potential to affect the course of disease and management. The present study

was thus undertaken to assess the serum thyroid stimulating hormone (TSH) levels and Ft4 level in women with PCOS, and its variation with obesity, insulin resistance and LH:FSH ratio.

METHODS

The present cross-sectional study was conducted at obstetrics and gynecology department of tertiary care centre Bhopal for a period of 18 months i.e., from May 2018 to October 2019 on a total of 165 females with PCOS. The inclusion criteria were all the females diagnosed as PCOS based on Rotterdam 2003 criteria and belonging to age group of 15 to 45 years.[1]

Rotterdam 2003 criteria for diagnosis of PCOS

PCOS is diagnosed if at least 2 of 3 are present: Oligomenorrhoea/amenorrhoea (ovulatory dysfunction), clinical or biochemical signs of androgen excess, polycystic ovaries at ultrasound scan (at least one ovary >10 cc volume, and/or at least one ovary with >12 follicles of size 2-9 mm.

Women with other causes of anovulation and/or hyperandrogenism e.g., adrenal hyperplasia, adrenal hyperandrogenaemia, Cushing's disease, virilizing tumor, hysterectomized women, ovarian tumor, premature ovarian failure, hyperprolactinemia, women on medications that affect menstrual cycles such as hormonal preparations, lithium, domperidone etc. women not willing to participate were excluded from study.

After obtaining ethical clearance from institute's ethical committee, all the females fulfilling the inclusion and exclusion criteria were enrolled in study and written consent was obtained from them. A thorough history was taken including age, age at menarche, detailed menstrual history, excessive hair, acne, weight gain, history of PCOS in mother/sibling, drug intake (hormonal), family history of diabetes, etc and entered in questionnaire. Detailed history regarding menstrual pattern, acne, alopecia, hirsutism was noted. Height, waist circumference, hip circumference and weight of all the participants were obtained and they were classified as having obesity based on the following features-waist circumference greater than 80 cm, WHR greater than 0.8, BMI: overweight: 23 kg/m^2 or higher; obese 25 kg/m^2 or higher, (waist circumference; WHR:BMI).

Vitals such as pulse, blood pressure and respiratory rate was noted for all the patients. Secondary sexual characters were assessed for all females and androgen status was assessed for presence of hirsutism, acne, temporal recession of hair etc. Evidence of insulin resistance (acanthosis nigricans) if any was also looked for and findings were noted in questionnaire. Further USG was conducted for all the females to study PCO morphology and serum TSH levels and Ft4 were estimated. The normal range for TSH levels was 0.25-5 mIU/Ml whereas for fT4 9-19 pmol/L.

Statistical analysis

Data was compiled using Ms excel and analysed using SPSS software version 20. Data was grouped and expressed as frequency and percentage whereas numerical data was expressed as mean ± SD. ANOVA test was applied to assess the difference in mean values among females with different thyroid status.

RESULTS

The present study included a total of 165 females with PCOS diagnosed based on Rotterdam criteria.

Table 1: Distribution of study participants according to baseline variables.

Baseline variables		Frequency (n=165)	%
Age (years)	≤20	44	26.7
	21-30	113	68.5
	>30	8	4.8
Residence	Rural	40	24.2
	Urban	125	75.8
BMI (kg/m^2)	Underweight (<18.5)	17	10.3
	Normal (18.5-22.9)	73	44.2
	Overweight (23-24.9)	25	15.2
	Obese I (25-29.9)	48	29.1
	Obese II (30-34.9)	2	1.2
Waist circumference (cm)	≤80	63	38.2
	>80	102	61.8
Waist hip ratio	≤0.85	52	31.5
	>0.85	113	68.5

Mean age of females with PCOS was 23.21±4.57 years and majority of females belonged to 21 to 30 years of age (68.5%). About 75.8% females were resident of urban area whereas only 24.2% females were resident of rural area. About 30.3% females were obese in present study with BMI >25 kg/m^2. Waist circumference was >80 cm in 61.8% females whereas waist hip ratio >0.85 was observed in 68.5% females with PCOS.

In present study, USG was suggestive of polycystic morphology in 98.8% females with PCOS and one or more of the clinical features of hyperandrogenism were documented in 74.6% females i.e., acne in 68.4%, excess body hairs in 46.6% and alopecia in 9.7% females. However, acanthosis was documented in 26.7% and alopecia was observed in 9.7% females with PCOS.

Most common menstrual cycle abnormality in females with PCOS was oligomenorrhea observed in 60.6% females, followed by oligomenorrhea with hypomenorrhea observed in 14.5% females. However, menstrual cycles were regular in 6.7% females with polycystic ovarian syndrome.

Table 2: Distribution according to thyroid status.

Thyroid status	Frequency (n=165)	Percentage (%)
Subclinical hypothyroid	28	17
Euthyroid	137	83

Mean TSH levels in study was 2.69±1.50 µIU/ml, mean fT4 was 12.4±2.2 pmol/ L. Majority of females with PCOS were euthyroid (83%) whereas subclinical hypothyroidism was documented in 17% females. Though mean LH:FSH ratio, insulin resistance, waist hip ratio, waist circumference and BMI were higher in subclinical hypothyroid females with PCOS as compared to euthyroid females, in study documented no statistically significant difference in their mean values (p>0.05).

TSH levels in study showed a statsitcally significant positive correlation with BMI i.e. as BMI increased TSH levels increased (R^2=0.024, p=0.048). However no statistically significant correlation of TSH levels was observed with LH:FSH ratio, insulin resistance, waist hip ratio and waist circumference (p>0.05).

Table 3: Association of thyroid status with LH/FSH ratio, insulin resistance and obesity.

Variables	Euthyroid	Subclinical hypothyroid	T test	P value
LH:FSH ratio	3.61±8.34	4.61±5.6	0.61	0.54
Homa IR	1.55±1.23	2.1±1.92	1.94	0.05
WHR	0.88±0.59	0.91±0.07	0.27	0.79
WC	83.62±10.6	86.06±10.8	1.13	0.26
BMI	23.1±4.49	24.14±4.43	1.1	0.28

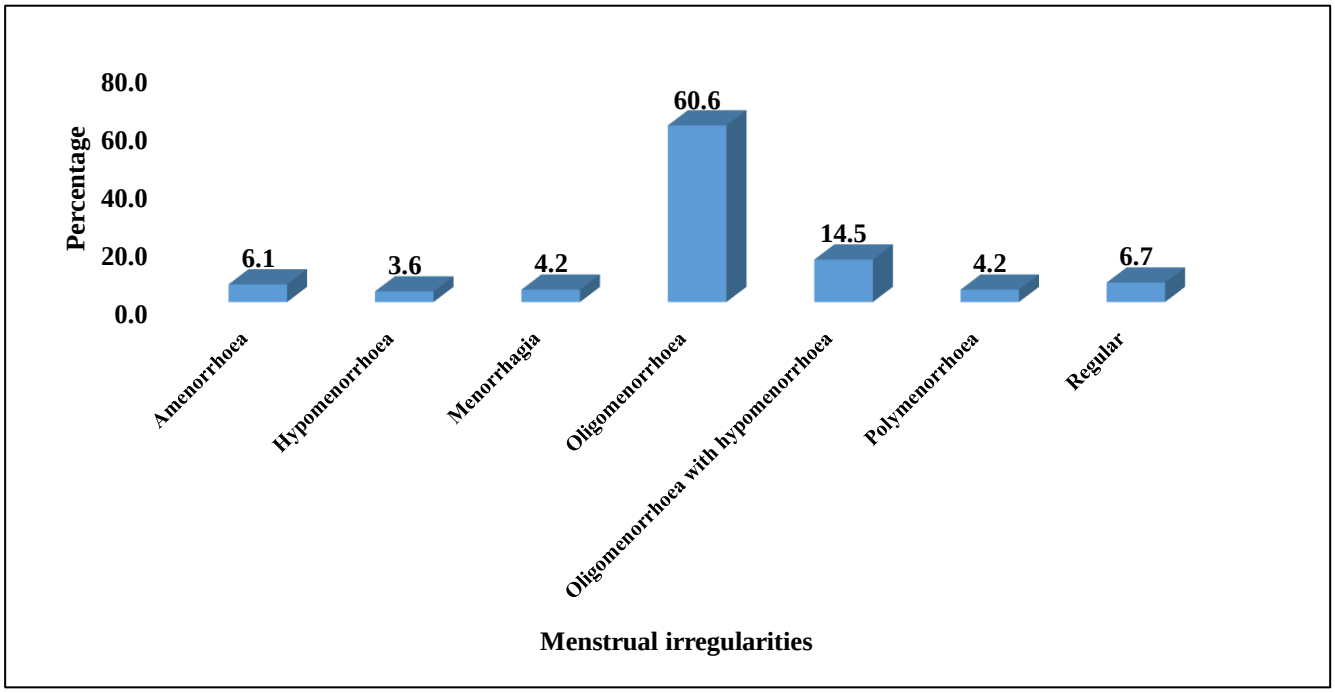

Figure 1: Distribution according to menstrual cycle characteristics.

Table 4: Correlation of TSH levels with LH/FSH ratio, insulin resistance and obesity.

Variables	R	R^2	Adjusted R^2	SE	ANOVA	P value
LH:FSH ratio	0.110	0.012	0.006	1.620	1.997	0.160
Homa IR	0.081	0.007	-0.002	1.660	0.759	0.386
WHR	0.142	0.020	0.014	1.616	3.295	0.071
WC	0.139	0.019	0.013	1.614	3.222	0.075
BMI	0.154	0.024	0.018	1.610	3.952	0.048

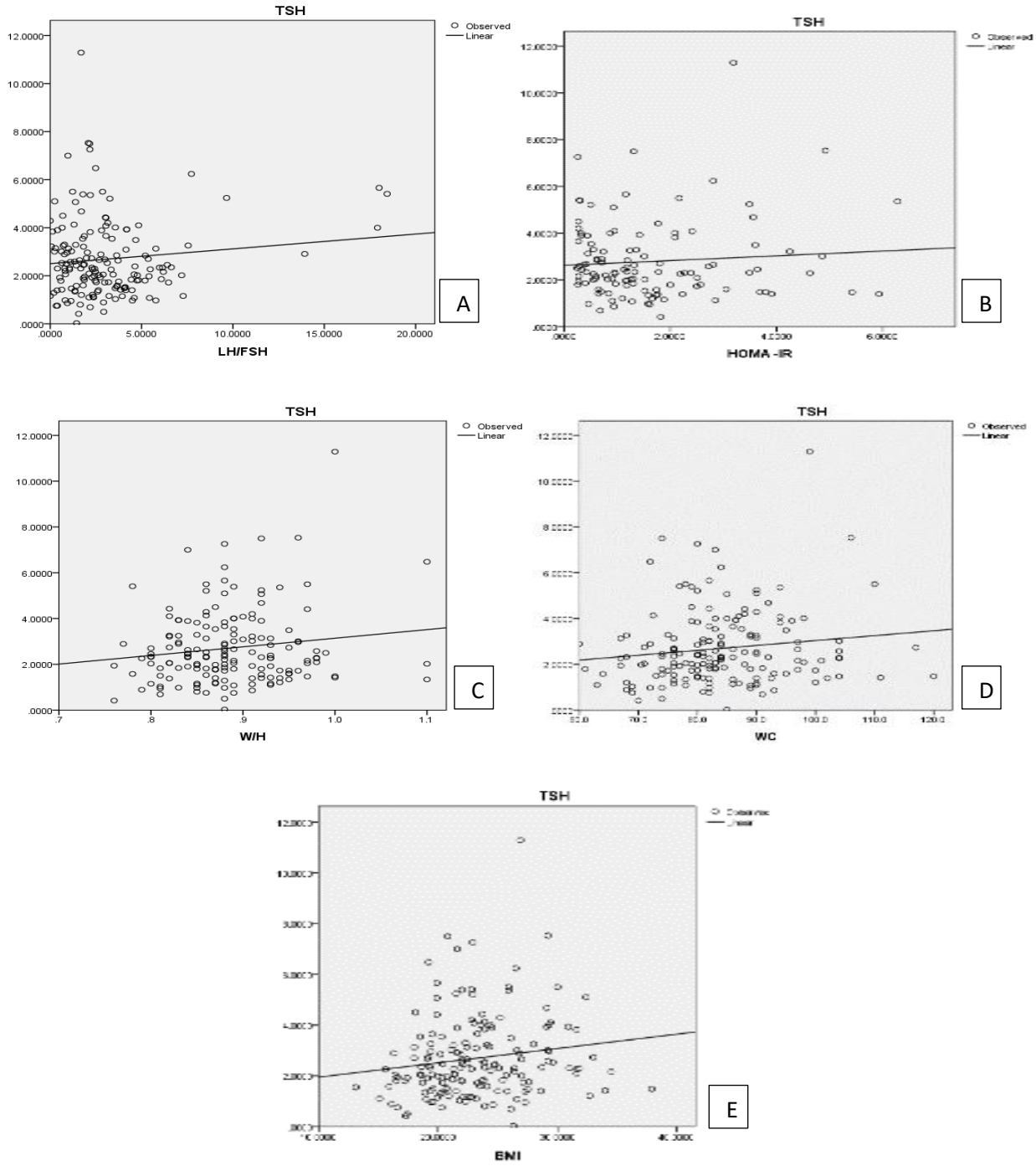

Figure 2: Correlation of correlation of TSH levels with LH/FSH ratio (A), insulin resistance (B), waist hip ratio (C), waist circumference (D) and BMI (E).

DISCUSSION

Both PCOS as well as thyroid dysfunction has certain common clinical manifestations. Apart from their important role in regulating metabolism, thyroid hormones also play important role in reproductive health. Thyroid receptors as well as TSH receptors are expressed in uterus and ovaries in females.[11] PCOS is the most common disorder in females of reproductive age group.[1] In present study, maximum females with PCOS belonged to 21 to 30 years of age (68.5%) with mean age of 23.21±4.57 years. Similar findings were reported by Goyal et al in which maximum females belonged to 21-30 years of age and the mean age of females with PCOS was 26.76±6.7 years.[12] Lamberg and Abufaza et al

documented that PCOS mainly affects women in age range of 18-35 years.[13,14]

The presence of obesity amongst females with PCOS is one of the classical features, though its presence is variable. It has been observed that higher BMI is associated with greater insulin resistance and hyperandrogenism. Thus, hirsutism and alopecia are one of the common features amongst obese anovulatory females.[15] In present study, normal BMI was observed in 44.3% females whereas 30.3% females were obese whereas Waist circumference and waist hip ratio were raised in 61.8 and 68.5% females respectively with PCOS. Goyal et al also documented that females with PCOS had significantly higher body mass index (BMI) as compared to controls.[12]

Thyroid dysfunctions i.e., subclinical hypothyroidism was documented in 17% females. Mean TSH levels among study participants was 2.69±1.5 µIU/ml and mean fT4 was 12.4±2.2 pmol/L. These findings were supported by Benetti-Pinto et al in which prevalence of subclinical hypothyroidism in females with PCOS was estimated to be 11.3% (mean TSH level of 6.1±1.2 mIU/L).[16] Enzevaei et al documented 25.5% prevalence of subclinical hypothyroidism in their study.[17]

The present study also aimed to assess the variation in LH:FSH ratio, insulin resistance, waist hip ratio, waist circumference and BMI with thyroid dysfunction. The mean values of above-mentioned variables were higher in females with thyroid dysfunction as compared to euthyroid females, but test of significance (ANOVA) observed no statistically significant difference ($p>0.05$).

It has been postulated that hypothyroidism is associated with increased TSH and TRH levels. Increased TRH in cases with primary hypothyroidism leads to increased secretion of prolactin and TSH. This increased level of prolactin further inhibit ovulation and thereby contribute to polycystic ovarian morphology and thus can affect LH:FSH ratio. Also raised level of TSH has spill-over effect on FSH receptor and thus further contribute altered LH:FSH ratio. Increased TSH also contributes due to its spill-over effect on FSH receptors.[18] However no significant correlation of thyroid dysfunction was documented with LH:FSH ratio in present study, this could be explained by small sample size or presence of higher number of cases with subclinical hypothyroidism.

However, we documented a statistically significant positive correlation between TSH levels and BMI ($R^2=0.024$, $p=0.048$). Obesity is an integral part of PCOS and has been also associated with hypothyroidism. The etiopathogenesis of obesity in hypothyroidism has been attributed to activation of adipocytes in the adipose tissue which alter the milieu and increase the levels of pro-inflammatory markers and further contribute to insulin resistance.[19] Another possible pathogenesis linking obesity and hypothyroidism has been postulated by leptin pathway. The levels of leptin are increased in obese individuals which directly act on hypothalamus and increase TRH secretion.[20] Muscogiuri et al in their study documented that both adiposity and insulin resistance were significantly associated with raised TSH.[19]

The cause-and-effect relationship may not be visible accurately in such a small sample of sub-groups. A larger sample size would further help to provide a more validated data. A majority of women in the present study were urban and so the generalizability of the results is limited for rural women. Also, serum T3, and anti TPO antibody levels could not be assessed which could have yielded better results.

CONCLUSION

The proportions of thyroid disorders are higher in females with PCOS and they both may present with various similar clinical features. BMI in females with PCOS has significant positive correlation with TSH levels. However, it is not clear whether thyroid dysfunction has significant effect on insulin resistance.

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