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Original Research Article

Correlation of thyroid-stimulating hormone level with obesity in patients of polycystic ovary syndrome

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ABSTRACT

Background: Polycystic ovarian syndrome (PCOS), a heterogeneous endocrine disorder is most common in women of the reproductive age group. Thyroid disorders and PCOS are two of the most common endocrine disorders in women. Although the etiopathogenesis of hypothyroidism and PCOS is completely different, these two disorders have many common features. An increase in ovarian volume and cystic changes in ovaries have been reported in primary hypothyroidism. The aim of this study was to find the correlation of thyroid-stimulating hormone (TSH) level in obese and non-obese women, who were diagnosed to have PCOS.
Methods: The data of 161 women who visited the institution for diagnosis and management of PCOS were included in the study. Demographic data like age, height and weight of the women at the time of diagnosis of PCOS were collected and subjected to analysis.
Results: The results showed that 15% obese PCOS women had high TSH level and 7% non- obese PCOS had high TSH level.
Conclusions: The result of the study suggests that higher level of TSH seen in obese PCOS women than non -obese PCOS women.

Keywords: PCOS, Obesity, TSH

INTRODUCTION

Polycystic ovarian syndrome (PCOS), a heterogeneous endocrine disorder is most common in women of the reproductive age group which has psychological, social and economic sequel.[1] It is also known as Stein–Leventhal syndrome.[2] It is a heterogeneous disorder of multifactorial etiology and occurs due to disturbance in hormone levels in our body that happens during the reproductive phase. PCOS is the most common form of chronic anovulation associated with androgen excess, affecting about 5–10% of reproductive women.[3] It is one of the common gynaecological problems and the leading cause of female infertility and menstrual irregularity. PCOS is associated with increased cardiovascular and metabolic risk factors like obesity.[4] 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.[5] Additionally, hypothyroidism leads to increased weight gain by mucin deposits and salt and water retention.[6] It also affects the physical and mental health of women.

The morphology of the polycystic ovary is defined by the European Society for Human Reproduction and Embryology (ESHRE) and the American Society for

Reproductive Medicine (ASRM) that convened in Rotterdam, Netherland.[7] The ESHRE/ASRM concluded three major criteria should be found to diagnose PCOS.

If 2 out of these three criteria were verified, the female was diagnosed with PCOS. These criteria are: menstrual abnormalities like anovulation (or amenorrhea), oligomenorrhoea, or long cycle; hyperandrogenism - clinical or biochemical signs observed such as acne, hirsutism or high levels of testosterone; and the polycystic appearance of ovaries in ultrasound (US), containing multiple small follicles measuring from 2 to 9 mm.

Many studies support that thyroid disorders are more common in women with PCOS as compared to the normal population.[8] Whether this is due to some common factors predisposing an individual to both disorders, or due to a pathophysiological connection between the two disorders has not been established until now. The most obvious connection, perhaps, is the increased BMI and insulin resistance common to both conditions. Increase in BMI is an integral part of PCOS and is seen in a large majority (54-68%) of these cases.[9] The link between thyroid functions and obesity is again an interesting one, with unclear pathophysiological mechanisms; there is, however, enough evidence to say that TSH is higher in people with high BMI.[10] Obesity is associated with an altered milieu with increase in pro-inflammatory markers and increase in insulin resistance. This, through undefined mechanisms, leads to decreased deiodinase-2 activity at pituitary level resulting in relative T3 deficiency and increase in TSH levels.[10] Another pathway, based upon leptin, has been hypothesized to explain this observation. Increased leptin in obesity has been proposed to act directly on the hypothalamus resulting in increased TRH secretion.[11] Raised TSH levels, with any of these two pathways, act on adipocytes to increase their proliferation. In culture studies, TSH has been shown to increase proliferation of adipocytes as well as increase in production of pro-inflammatory markers from adipocytes, acting on TSH receptors present on adipocytes. The coexistence of hypothyroidism and PCOS has been related to complex pathophysiological changes caused by obesity and Insulin resistance observed in the PCOS, though not conclusively.[12] Hypothyroidism by virtue of raised thyrotropin releasing hormone (TRH) causes altered follicle stimulating hormone (FSH)/luteinizing hormone (LH) ratio and raised dehydroepiandrosterone (DHEA-S) levels. Also, excess thyroid stimulating hormone (TSH) causes stimulation of FSH receptor.it also decreases sex hormone binding globulin level, which converts the androstenedione into testosterone and aromatization to estradiol. Also, it reduces the metabolic clearance rates of androstenedione and estrone.[13]

Various studies have been conducted regarding hypothyroidism in PCOS patients. Most of the studies have shown a higher incidence of elevated serum TSH levels and higher prevalence of autoimmune thyroiditis in PCOS subjects.[14] But no study has revealed whether the obesity in PCOS patients is independent of hypothyroidism or not. This study has been conducted to evaluate the relationship of TSH level with obesity in PCOS patients attending a government medical college Kannauj.

METHODS

Present study was a hospital-based case-control study conducted in Government Medical College, Tirwa, Kannauj. All consecutive patients who attended our gynaecology outpatient department (OPD) from January to June 2022 in age group of 13–45 years, with complaints of hirsutism and/or oligomenorrhea or infertility. The study was explained to all such subjects in detail and consent was taken. In case of minor subjects, consent was obtained from parents/guardian. Demographic data like age, height and weight at the time of diagnosis of PCOS were asked from the patients. BMI was calculated and patients were classified according to the World Health Organization (WHO) criteria. The BMI is a simple and most commonly used measure to classify overweight and obesity in adults. BMI is defined as the weight in kilograms divided by the square of the height in meters (kg/m^2).

The Rotterdam classification was used for the diagnosis of PCOS. All other diagnosis, like congenital adrenal hyperplasia, virilising tumor, Cushing syndrome and prolactinoma was ruled out.[15] Clinical hyperandrogenism was defined as hypertrichosis (Ferriman–Gallwey score >7) and/or acne, and/or androgenic pattern of alopecia.[16] Biochemical hyperandrogenaemia was defined by elevated testosterone. A luteinizing hormone (LH)-to-follicle stimulating hormone (FSH) ratio above 2 was considered elevated. Transabdominal pelvic ultrasonography (USG) was performed to detect the presence of cystic ovaries. Detailed clinical history, elaborate clinical examination and laboratory investigations like Blood glucose (fasting and 2 h post 75 g glucose), serum LH, FSH, thyroid stimulating hormone (TSH), free thyroxine levels (free T3 and free T4), free testosterone measured.

Normal serum levels of different hormones and peptide were defined as: free T3- 1.2-2.8 nmol/l, free T4- 77-155 nmol/l, and TSH-0.3- 4 mIU/l. LH and FSH were measured on the 2nd day of menstruation.[17]

Inclusion criteria

Irregular menstruation for PCOS women: no menses in the past 6 months or menstrual cycle prolonged for more than 35 days; increased androgen levels and/or acne and/or alopecia (androgenic pattern) 11 or clinical hyperandrogenism; polycystic ovaries (follicles 2-9 mm in diameter and ≥12 in number or ovarian volume ≥10 cm^3) identified by transabdominal pelvic ultrasonography after excluding other diseases such as congenital adrenal hyperplasia and virilizing tumors; and women with age between 13-45 years were included.

Exclusion criteria

Patients use steroids, patients on contraceptive pills, pregnancy, neoplasia: thyroid or adrenal, and women with primary hypothyroidism were excluded.

RESULTS

After analysis of 161 PCOS patients, mean age of all the women included in the study was 25.94±4.90 year. 41.6% PCOS patients were below 25 years whereas 54% and 4.3% PCOS patients lied between 25 to 34 year and 35 to 45 years respectively. Frequency distribution of the women with PCOS according to the classification of socio-economic status shows that most of the PCOS women belongs to lower class whereas PCOS women of lower middle class were very less.

Frequency distribution of the women with PCOS according to the classification of BMI showed that 47.2% women had normal BMI and 49.7% were overweight, 3.1% were obese.

Table 1: Distribution of subjects according to bio-social characteristics.

Variables	No.	%
Age (years)		
15-24	67	41.6
25-34	87	54.0
35-44	7	4.3
Mean±SD	25.94±4.90	
Social status		
Lower	53	32.9
Lower middle	15	9.3
Upper lower	42	26.1
Upper middle	33	20.5
Upper	18	11.2
BMI		
18-24.9 (healthy)	76	47.2
25-29.9 (overweight)	80	49.7
30-34.9 (obesity)	5	3.1
Obesity		
Obesity/overweight	85	52.8
Normal	76	47.2

The elevated TSH was observed in 43 (26.7%) cases, free T3 was found in low level among 54 (33.5%) cases and high in 5 (3.1%) cases. Free T4 was found in low level among 65 (40.4%) cases and high in 1 (0.6%) case.

This correlation and regression analysis showing relationship of BMI with thyroid hormone levels revealed that significant negative correlation exists between BMI and free T3 level (r=-0.277, p<0.001), while the correlation of individual BMI values was not significantly correlated with TSH level (r=0.133, p=0.093) and free T4 (r=-0.009, p=0.909).

Table 2: Distribution of subjects according to thyroid hormone levels.

Variables	No.	%
TSH		
Normal	118	73.3
Elevated	43	26.7
Free T3		
Normal	102	63.4
Low	54	33.5
High	5	3.1
Free T4		
Normal	95	59.0
Low	65	40.4
High	1	0.6

Table 3: Correlation and regression analysis showing relationship of BMI with thyroid hormone levels.

Variables	BMI (kg/m^2)		Regression equation
	R value	P value	
TSH	0.133	0.093	TSH=1.86+0.084 (BMI)
Free T3 (pmol/l)	-0.277	<0.001	T3=8.13-0.195 (BMI)
Free T4 (ng/dl)	-0.009	0.909	T4=1.06-0.002 (BMI)

Further the regression equation showing relationship of TSH with BMI is given by:

$$TSH = 1.86 + 0.084\ (BMI)$$

The regression equation showing relationship of free T3 with BMI is given by,

$$T3 = 8.13 - 0.195\ (BMI)$$

The regression equation showing relationship of free T4 with BMI is given by,

$$T4 = 1.06 - 0.002\ (BMI)$$

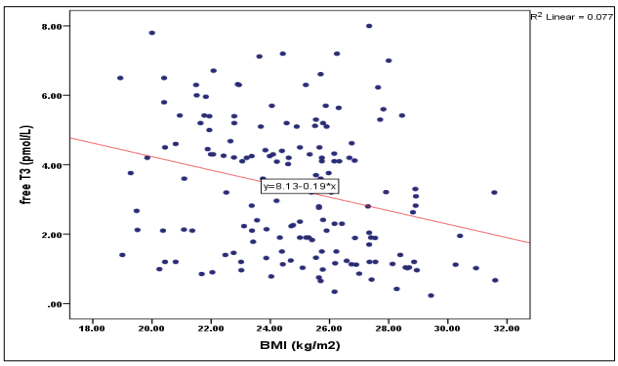

Figure 1: This regression analysis showing negative correlation between BMI with free T3 hormone level.

When BMI of PCOS patients comprises with TSH level, it was found that the proportion of elevated TSH was significantly higher in overweight (p=0.027) and obese PCOS cases (p<0.001). The odds for risk of elevated TSH among overweight was 2.33 (95% CI: 1.09 – 4.98) and among obese the odds for risk were 19.38 (95% CI: 2.00 – 187.86).

The odds for risk of elevated TSH among overweight/obese combined was 2.64 (95% CI: 1.26 – 5.57) which was significant statistically (p=0.009).

When BMI of PCOS patients compared with T3 level into normal, low and high, it was found that the proportion of low T3 was significantly higher in overweight (p=0.01) and obese (p=0.006) cases. The odds for risk of low T3 among overweight was 2.42 (95% CI: 1.19 – 4.89) and among obese the odds for risk were 13.18 (95% CI: 1.38 – 125.96).

The odds for risk of low T3 among overweight/obese combined was 2.65 (95% CI: 1.32 – 5.31) which was significant statistically (p=0.005).

When BMI of PCOS patients compared with T4 level into normal, low and high, no significant association of T4 level was found with overweight and obesity (p>0.05) either by low T4 level or high T4 level.

Table 4: Association and risk estimation of obesity with TSH.

Groups	TSH				Risk estimation			
	Normal		Elevated					
	No.	%	No.	%	OR	95% CI	Chi square	P value
BMI								
18-24.9 (healthy)	63	82.9	13	17.1	Ref.	-	-	-
25-29.9 (overweight)	54	67.5	26	32.5	2.33	1.09-4.98	4.93	0.027
30-34.9 (obesity)	1	20.0	4	80.0	19.38	2.00-187.86	11.19	<0.001
Obesity								
Obesity/overweight	55	64.7	30	35.3	2.64	1.26-5.57	6.78	0.009
Normal	63	82.9	13	17.1	Ref.	-	-	-

Table 5: Association and risk estimation of obesity with T3.

Groups	FreeT3_cat						Risk estimation				
	Normal		Low		High						
	No.	%	No.	%	No.	%	Comparison	OR	95% CI	Chi square	P value
BMI											
18-24.9 (healthy)	56	73.7	17	22.4	3	3.9	Ref.	-	-	-	-
25-29.9 (overweight)	45	56.3	33	41.3	2	2.5	T3 normal to low	2.42	1.19-4.89	6.16	0.013
							T3 normal to high	0.83	0.13-5.18	0.04	0.841
30-34.9 (obesity)	1	20.0	4	80.0	0	0.0	T3 normal to low	13.18	1.38-125.96	7.65	0.006
							T3 normal to high	NA	NA	0.05	0.817
Obesity											
Obesity/ overweight	46	54.1	37	43.5	2	2.4	T3 normal to low	2.65	1.32-5.31	7.78	0.005
							T3 normal to high	0.81	0.13-5.07	0.05	0.812
Normal	56	73.7	17	22.4	3	3.9	Ref.	-	-	-	-

Table 5: Association and risk estimation of obesity with T4.

Groups	FreeT4_cat						Risk estimation				
	Normal		Low		High						
	No.	%	No.	%	No.	%	Comparison	OR	95% CI	Chi square	P value
BMI											
18-24.9 (healthy)	48	63.2	28	36.8	0	0.0	Ref.	-	-	-	-

Continued.

Groups	FreeT4_cat						Risk estimation				
	Normal		Low		High						
	No.	%	No.	%	No.	%	Comparison	OR	95% CI	Chi square	P value
25-29.9 (overweight)	44	55.0	35	43.8	1	1.3	T4 normal to low	1.36	0.72-2.60	0.89	0.344
							T4 normal to high	0.83	0.13-5.18	0.04	0.841
30-34.9 (obesity)	3	60.0	2	40.0	0	0.0	T4 normal to low	1.14	0.18-7.26	0.02	0.887
							T4 normal to high	NA	NA	NA	NA
Obesity											
Obesity/ overweight	47	55.3	37	43.5	1	1.2	T4 normal to low	1.35	0.72-2.55	0.86	0.354
							T4 normal to high	NA	NA	1.01	0.315
Normal	48	63.2	28	36.8	0	0.0	Ref.	-	-	-	-

DISCUSSION

The mean age of this study is 25.94±4.90 year, and the range is within the reproductive age. PCOS women when grouped as overweight or obese and normal according to BMI, it was found that group including overweight and obese together had higher numbers of PCOS women than normal. The majority of women with PCOS (38-88%) are either overweight or obese.[18] Data from the Northern Finland Birth Cohort (NFBC) 1966 show a significant association between body mass index (BMI) and features of PCOS at all ages.[19] Furthermore, modest weight-loss (around 5%) often results in clinically meaningful improvements in the reproductive, hyperandrogenic, and metabolic features of PCOS.[20]

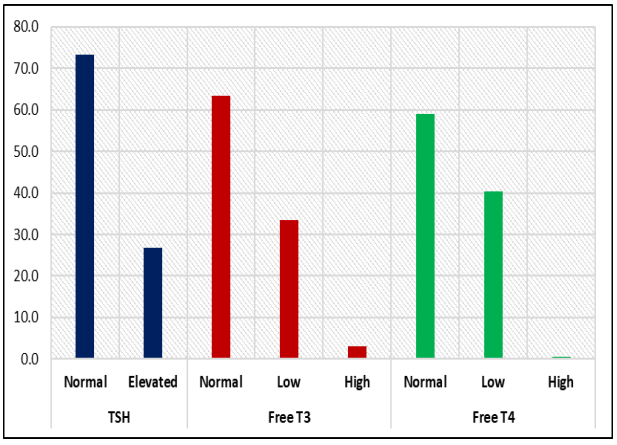

Figure 2: Distribution of subjects according to thyroid hormone levels showing that most of the PCOS women had normal TSH level. 54 PCOS women had low free T3 hormone level whereas 5 PCOS women had high free T3 hormone level. Free T4 was found in low level among 65 (40.4%) cases and high in 1 (0.6%) case.

52.8% patient of our study were either obese or overweight, which is also similar to other studies. Mean age is 26±4.2 and a BMI 29±4.4 with 32% of PCOS patients are obese in study of Deepa et al.[21] Prevalence of obesity is approximately 57% among 318 PCOS patients as observed by Najem et al, 54% overweight in study of Gomathi et al.[22]

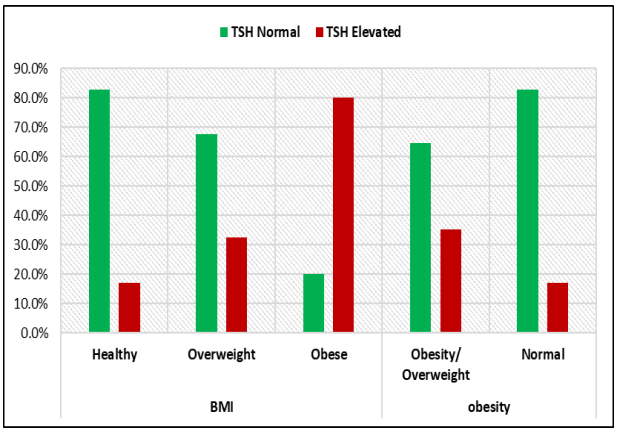

Figure 3: Relationship between TSH level and BMI. TSH level is elevated in overweight and obese PCOS patients than the PCOS patients with normal BMI. So, we can say overweight and obese PCOS patients are at high risk of being development of subclinical hypothyroidism.

The elevated TSH was observed in 43 (26.7%) cases. A few studies have previously analyzed subclinical hypothyroidism in PCOS subjects. In a study done by Enzevaei et al in Iran, they have observed 25.5% of subjects having subclinical hypothyroidism, while, in a study conducted by Sinha et al in Indian population, 22.5% subjects with PCOS were detected to be having subclinical hypothyroidism.[23,24] Furthermore, Ding et al demonstrated that the PCOS risk increased as a result of clinical

hypothyroidism and depressive symptoms such as anxiety.[25] Also, they claimed that subclinical hypothyroidism during pregnancy could lead to multiple adverse maternal and neonatal outcomes, including premature rupture of membranes and neonatal death.

CONCLUSION

In conclusion, the prevalence of thyroid dysfunctions, especially hypothyroidism, is increased in women with PCOS patients. There is a positive association between obesity and hypothyroidism in PCOS patients.

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