



Correlation of Thyroid Disorders and Polycystic Ovarian Syndrome

Dr.K.Sravya, Dr.T.Sreenidhi Reddy,Ms,

Post graduate ,department of obstetrics and gynaecology, Narayana medical college and hospital, Nellore , andhra pradesh

Post graduate ,department of obstetrics and gynaecology, Narayana medical college and hospital, Nellore , andhra Pradesh

CORRESPONDING AUTHOR : *sita lakshmi.v.MD. professor and head of the department of obstetrics and gynaecology,Narayana medical college and hospital,Nellore*

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ABSTRACT: The present study aimed to know the prevalence of thyroid disorders in polycystic ovarian syndrome and to compare the clinical, metabolic, insulin resistance, hormonal, and lipid parameters between the hypothyroid and euthyroid PCOS women.

- This study included 150 PCOS women with all the inclusion and exclusion criteria. The subjects were divided into two groups depending on their thyroid status; group 1 included hypothyroid PCOS women, and group 2 included euthyroid PCOS women.
- This study found that the prevalence of hypothyroidism in PCOS women was 30%, whereas euthyroid PCOS was 70%.
- The current study found that demographic and anthropometric parameters in euthyroid PCOS and hypothyroid-PCOS patients were similar in age, height, and waist circumference. In contrast, the weight and BMI were statistically higher in the hypothyroid PCOS women compared to the euthyroid PCOS group.
- The current evidence did not support the hypothesis that menstrual cycle abnormalities might influence PCOS women. There was no significant difference in clinical manifestations of PCOS like hirsutism, acanthosis nigricans, infertility in both groups. While there were significantly higher values in Sr. prolactin, free testosterone, fasting insulin, and HOMA values in hypothyroid PCOS group but no difference was identified in FSH, FSH/LH and FBS values.
- The present study suggests that the coexistence of hypothyroidism in women with PCOS significantly increases the severity of IR and obesity, in patients with PCOS. IR in PCOS women is linked to and is associated with TSH and increased thyroid volume and nodularity,

so that the thyroid changes may aggravate IR in PCOS women. Therefore, the thyroid functions and volume in PCOS women are significantly associated with BMI, suggesting that obesity may link between IR and thyroid changes in these women.

- Statistically higher TC, TG, LDL concentrations were noted in the hypothyroid PCOS group compared to euthyroid PCOS women suggesting that hypothyroidism may worsen the lipid and carbohydrate metabolism in PCOS women. HDL-C is lower in hypothyroid PCOS than in euthyroid PCOS, but not statistically significant, attenuating the protective effect of HDL-C in the cardiovascular system of these patients.

I. INTRODUCTION

Polycystic ovarian syndrome (PCOS) is a heterogeneous, multisystem endocrinopathy in women of reproductive age characterized by menstrual and hormonal irregularities culminating in anovulation, hyperandrogenism, infertility, and insulin resistance (IR). The clinical manifestations of PCOS include oligomenorrhea/ amenorrhea, obesity, infertility, hirsutism, acne. Thyroid dysfunction is associated with alteration in a number of metabolic processes. More interestingly, hypothyroidism can initiate, maintain, and may even worsen PCOS.

The relationship between PCOS and hypothyroidism has been documented in previous

Thyroid hormones also act as insulin agonists in muscle and as antagonists in the liver, so a deficiency of thyroid hormones might also decrease glucose production and utilization. Thus, some authors have considered IR, which has been considered the principal factor in the pathogenesis of PCOS due to hypothyroidism⁵. Hypothyroidism



may lower sex hormone binding globulin (SHBG) and increase testosterone level but not invariably directed toward estradiol overproduction, resulting in polycystic ovaries, also known to affect gonadal function, puberty, and fertility⁶.

PCOS is also associated with metabolic and cardiovascular risk factors¹. These risk factors are linked to IR and compounded by the common occurrence of obesity (though IR is seen in non-obese/thin women with PCOS), irregular menstrual cycles, infertility, and increased pregnancy loss^{7,8,9}.

However, there is no proven hypothesis whether this is because of factors predisposing an individual to both of the disorders or a pathophysiological connection between the two disorders¹⁰.

Therefore, the purpose of this descriptive and exploratory review is to explore the relationship between thyroid disorders and polycystic ovarian syndrome.

studies stating ovarian enlargement and cystic transformation in thyroid disorders

II. AIMS AND OBJECTIVES

1. To study the prevalence of thyroid disorders in PCOS.
2. To compare demographic, anthropometric parameters, clinical presentation, insulin resistance parameters, PCOS hormonal profile, lipid profile parameters in hypothyroid and euthyroid PCOS women, which could throw light on the influence of hypothyroidism on PCOS women.

III. MATERIALS AND METHODS

The details of the current study methodology are described below:

Study source: The current study has been conducted in the Department of Obstetrics and Gynaecology in Narayana medical college and hospital, Chintareddypalem, Nellore

Study duration: the study was conducted for a period of 18 months from November 2019- March 2021.

Methodology:

This study was a hospital-based prospective study, includes 150 patients of PCOS in the reproductive age group (18-40 years) following the inclusion and exclusion criteria. Written and informed consent was taken from all the women in the study.

Data collection: They were subjected to a detailed history, personal and family, thorough general examination, clinical examination, laboratory investigations, and USG and divide them into two groups.

Group 1: PCOS women in the hypothyroid state.

Group 2: Euthyroid PCOS women.

Inclusion criteria: Includes all women with PCOS diagnosed using the Rotterdam criterion (2003) includes the presence of any 2 of the 3 features:

- a) Abnormal menstruation, including amenorrhea or oligomenorrhea, anovulation, and infertility.
- b) Hyperandrogenism either clinically or biochemical.
- c) Presence of polycystic ovaries (follicles 2-9 mm in diameter and ≥ 12 in number or ovarian volume ≥ 10 cm³) on USG.

Women with elevated TSH levels with normal FT3 and FT4 levels and without signs and symptoms of hypothyroidism were considered subclinical hypothyroid patients. Those with signs and symptoms of hypothyroidism, and increased TSH and decreased FT3 and FT4 levels were considered overt hypothyroidism. PCOS women with subclinical and overt hypothyroidism were grouped as hypothyroid PCOS women.

Exclusion criteria:

1. Women using any medication (e.g., OC pills, insulin-sensitizing drugs, statins, radioactive iodine, corticosteroids, GnRH agonist, and antagonist).
2. Women with diabetes mellitus, renal, hepatic, cardiac dysfunction.
3. Those with evidence of congenital adrenal hyperplasia, Cushing's syndrome, hyperprolactinemia, history of ovarian or adrenal neoplasia.
4. Pregnancy

History includes:

All the study subjects were assessed for various signs and symptoms of PCOS like obesity, abnormal excessive hair growth, acne, and acanthosis nigricans. Infertility history was taken in married women. A detailed menstrual history, marital status, parity were recorded in both groups. Family History of DM/ HTN/ Polycystic ovarian disease, history suggestive of obesity, irregular cycles, and infertility were inquired. History of PIH/ GDM/ RPL/ secondary infertility was taken.

Physical Examination:

Thorough physical examination includes measurement of height, weight, BMI
Body mass index was calculated = $\frac{\text{weight in kg}}{\text{Ht in m}^2}$

The waist measurement was done at the narrowest point between the highest point between the iliac



crest, and Hip measurement was taken at the maximum points of buttocks in cms.

Breasts examination was done to note if any evidence of galactorrhoea.

Examination of the thyroid gland.

Transabdominal ultrasound with evidence of pelvic viscera, diagnose polycystic ovarian disease using an L and T ultrasound scanner.

Criteria used for diagnosing polycystic ovaries are

ADAMS Criteria: 8-10 peripherally oriented cysts or <10 mm surrounded by increased stromal mass and ovarian volume ≥ 10 cc which is replaced as ≥ 12 follicles between 2-8mm diameter with ovarian volume ≥ 10 cm³.

Ovaries were scanned in transverse and linear phases to obtain each ovary's length, width, and thickness. Ovarian volume = 0.523 x L x W x Thickness.

Other criteria to diagnose PCOS

The recommendations, according to Androgen Excess PCOS Society (AEPS) in 2006

1. increased androgen activity.

2. Oligoovulation / anovulation and/or polycystic ovaries.

According to the 1990 NIH Criteria (both 1 and 2).

- a. Chronic anovulation

b. Clinical and/or biochemical signs of hyperandrogenism excluding other etiologies.

Biochemical and Hormonal Profile: Depending on feasibility, enrolled patients were investigated for various hormonal and metabolic parameters, viz. serum levels of LH, FSH, LH: FSH ratio, testosterone, PRL, fasting insulin, and FBS after taking overnight fasting blood sample. Insulin resistance was evaluated according to the homeostasis model assessment (HOMA) using the following formula:

HOMA = (fasting insulin (IU/L) × fasting glucose (m mol/L))/22.5. (or)

Fasting insulin (IU/L) × fasting glucose (mg/dl)/405

Insulin resistance was diagnosed when HOMA was > 2.5.

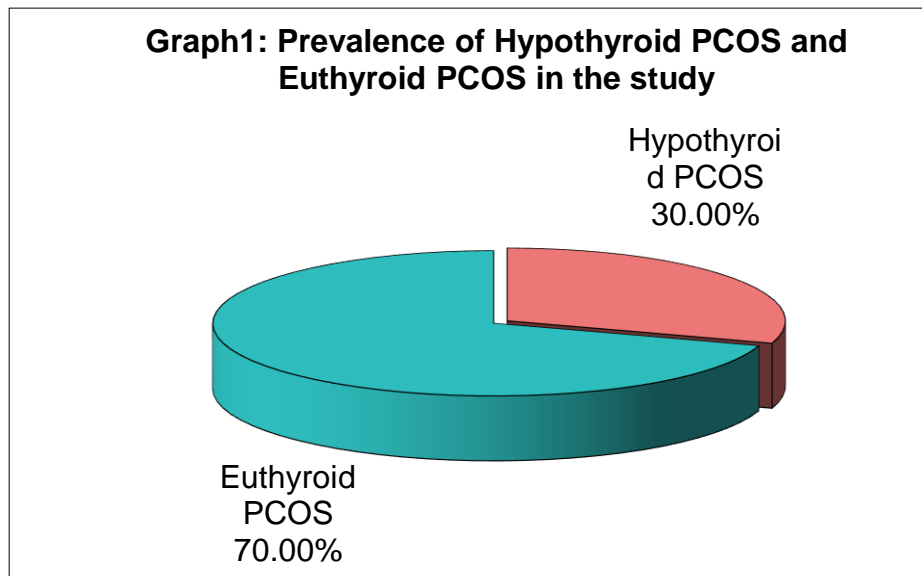
Statistical method for data analysis: Done by using SPSS 20.00 version. Chi-square test was used wherever applicable. An Independent T-test was taken to compare two groups.

IV. RESULTS AND OBSERVATION

Prevalence of hypothyroidism in PCOS women

Table 2:Prevalence of Hypothyroidism in PCOS women.

PCOS	Number	Percent
Hypothyroid PCOS	45	30.00
Euthyroid PCOS	105	70.00
Total	150	100.00



In the present study, the prevalence of hypothyroidism in PCOS women was 30%.

Demographic parameters

Includes comparison of the age, height, and weight of hypothyroid and euthyroid PCOS women.

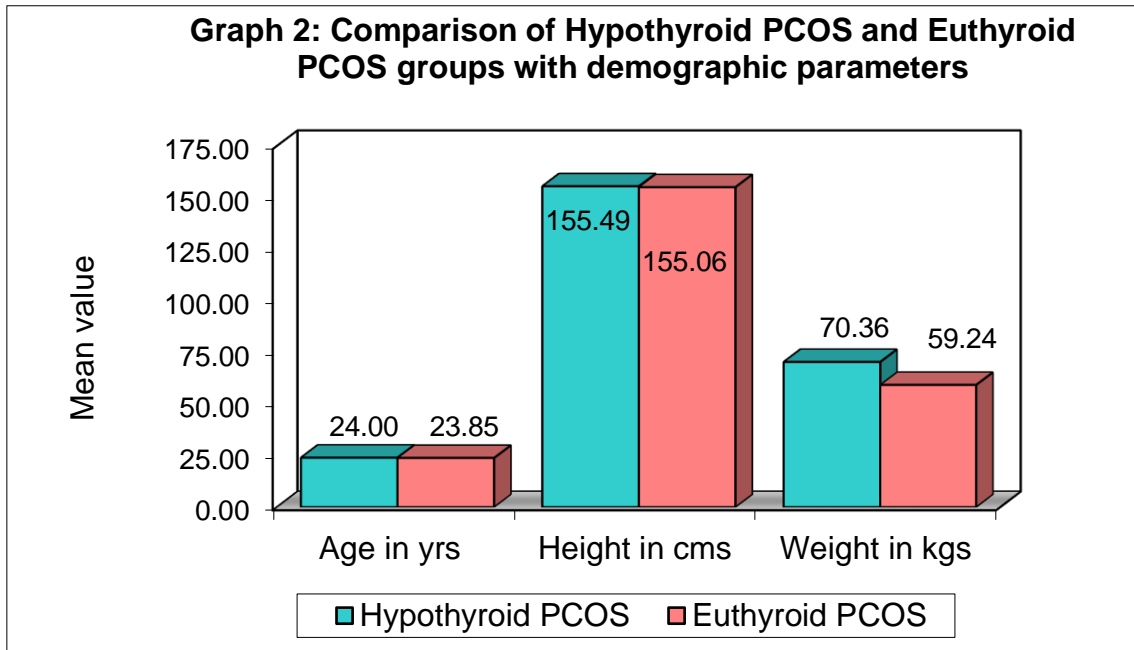
Table 3: Comparison of Hypothyroid PCOS and Euthyroid PCOS groups with demographic parameters by independent T-test.

Parameters	Hypothyroid PCOS			Euthyroid PCOS			t-value	p-value
	N	Mean	SD	N	Mean	SD		
Age in yrs	45	24.00	3.91	105	23.85	4.73	0.1900	0.8495
Height in cms	45	155.49	3.99	105	155.06	3.96	0.6101	0.5428
Weight in kgs	45	70.36	7.72	105	59.24	7.73	8.0775	0.0001*

*p<0.05

The age of both the groups were almost the same and so were statistically comparable (p=0.8495); similarly, the height of both the groups were equal statistically insignificant (p=0.5428),

whereas there was statistically significant difference of weight in hypothyroid PCOS women compared to euthyroid PCOS women (p= 0.0001).

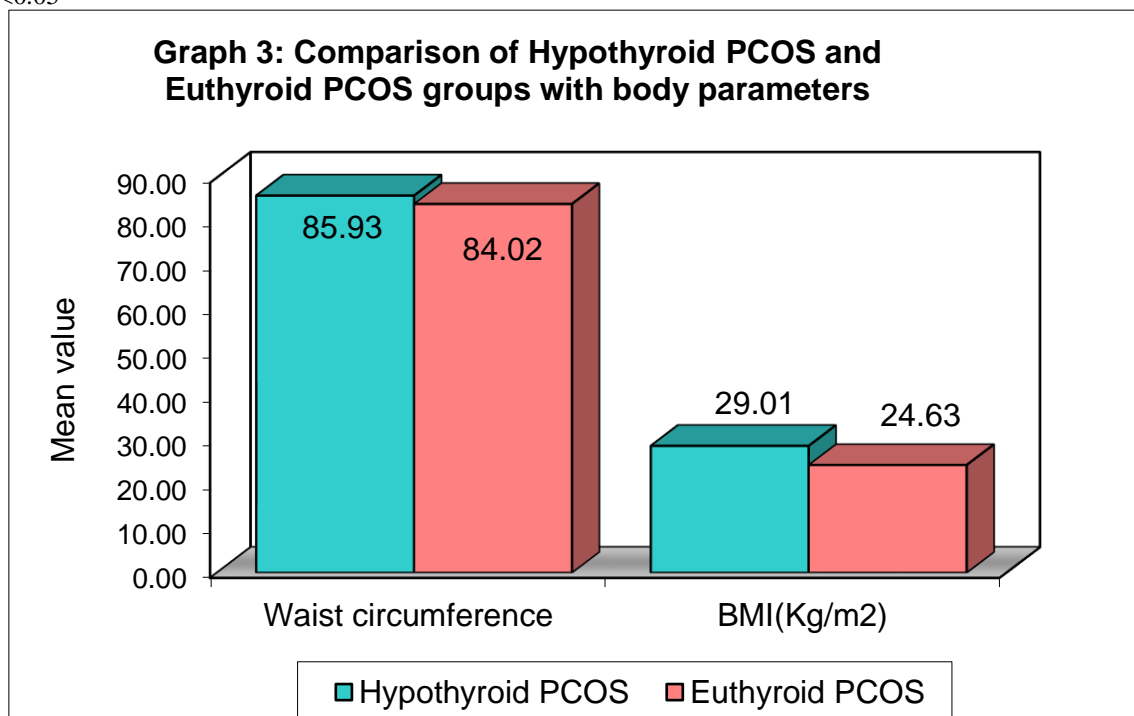


Anthropometric parameters:

Table 4: Comparison of Hypothyroid PCOS and Euthyroid PCOS groups with body parameters by independent T-test.

Parameters	Hypothyroid PCOS			Euthyroid PCOS			t-value	p-value
	N	Mean	SD	n	Mean	SD		
Waist circumference	45	85.93	5.16	105	84.02	5.82	1.9084	0.0583
BMI(Kg/m ²)	45	29.01	2.90	105	24.63	3.08	8.1284	0.0001*

*p<0.05





This study showed that the waist circumference has no difference between the two groups. BMI was higher in hypothyroid PCOS women than euthyroid PCOS women and has statistical significance (0.0001).

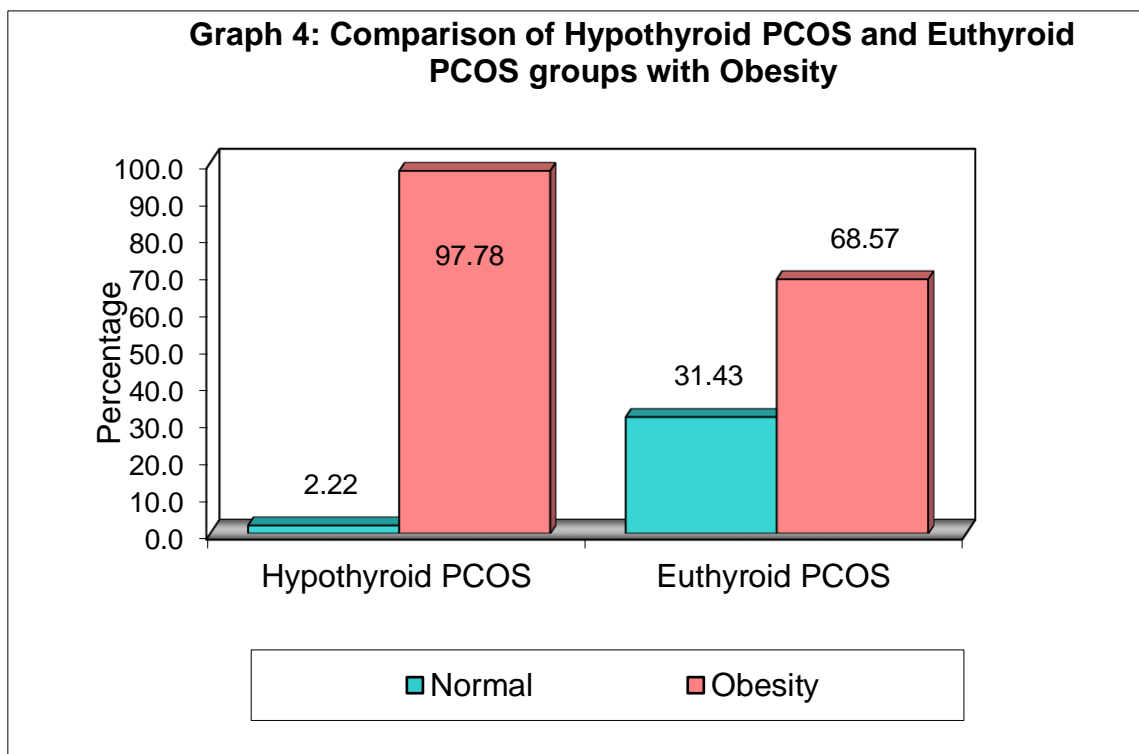
Obesity:

Table 5: Comparison of Hypothyroid PCOS and Euthyroid PCOS groups with obesity

Obesity	Hypothyroid PCOS	%	Euthyroid PCOS	%	Total	%	Chi-square	p-value
Normal	1	2.22	33	31.43	34	22.67	15.329	0.0001*
Obesity	44	97.78	72	68.57	116	77.33		
Total	45	100	105	100	150	100		

*p<0.05

Out of 150 PCOS women in the study, 77.33% were overweight/ obese, and only 22.67% were with normal BMI. Therefore, most hypothyroid PCOS women were obese/weight and has statistical significance (p= 0.0001).



Menstrual abnormalities:

In the current study, out of 150 subjects a total of 32% complained of amenorrhea, 42.67% present with oligomenorrhea, and 25.33% had no menstrual irregularities. Amenorrhea was seen in 28.57% in euthyroid individuals and 40% in the hypothyroid PCOS group, oligomenorrhea was

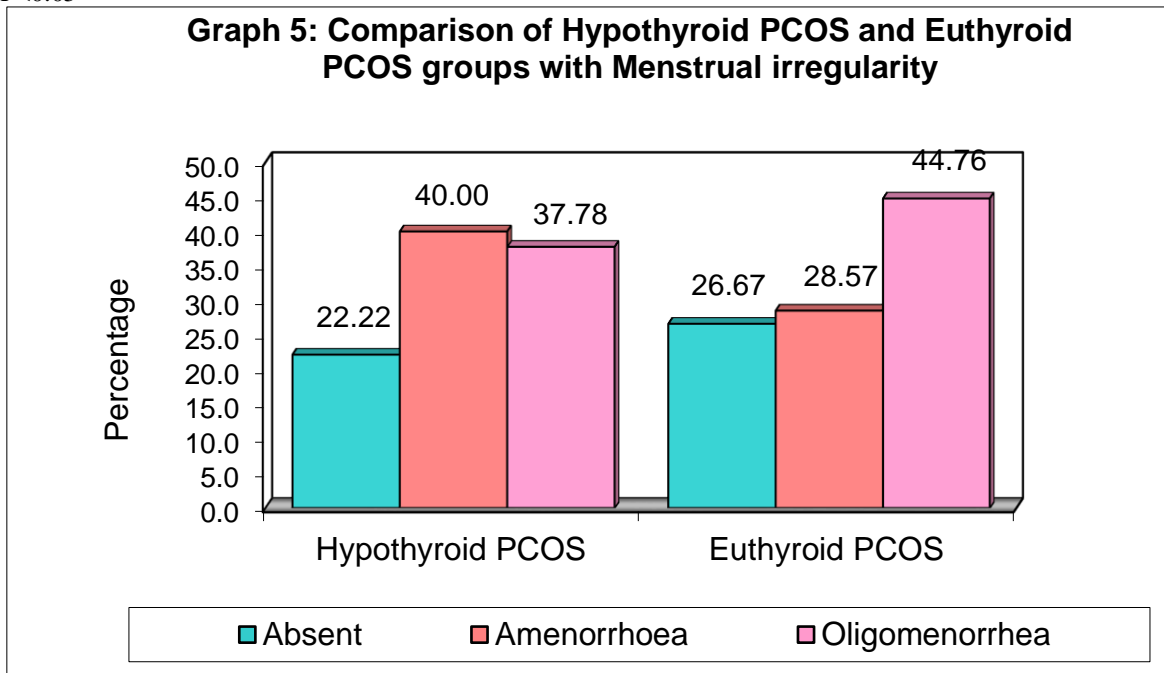
seen in 42.67% in euthyroid and 37.78% in the hypothyroid group. No menstrual irregularities were seen in 22.22% and 25.33% in the euthyroid and hypothyroid group of PCOS women, respectively. Therefore, menstrual irregularities had no statistical significance.



Table 6: Comparison of Hypothyroid PCOS and Euthyroid PCOS groups with menstrual irregularity.

Menstrual irregularity	Hypothyroid PCOS	%	Euthyroid PCOS	%	Total	%	Chi-square	p-value
Absent	10	22.22	28	26.67	38	25.33	1.891	0.338
Amenorrhoea	18	40.00	30	28.57	48	32.00		
Oligomenorrhoea	17	37.78	47	44.76	64	42.67		
Total	45	100	105	100	150	100		

*P<0.05



Hirsutism:

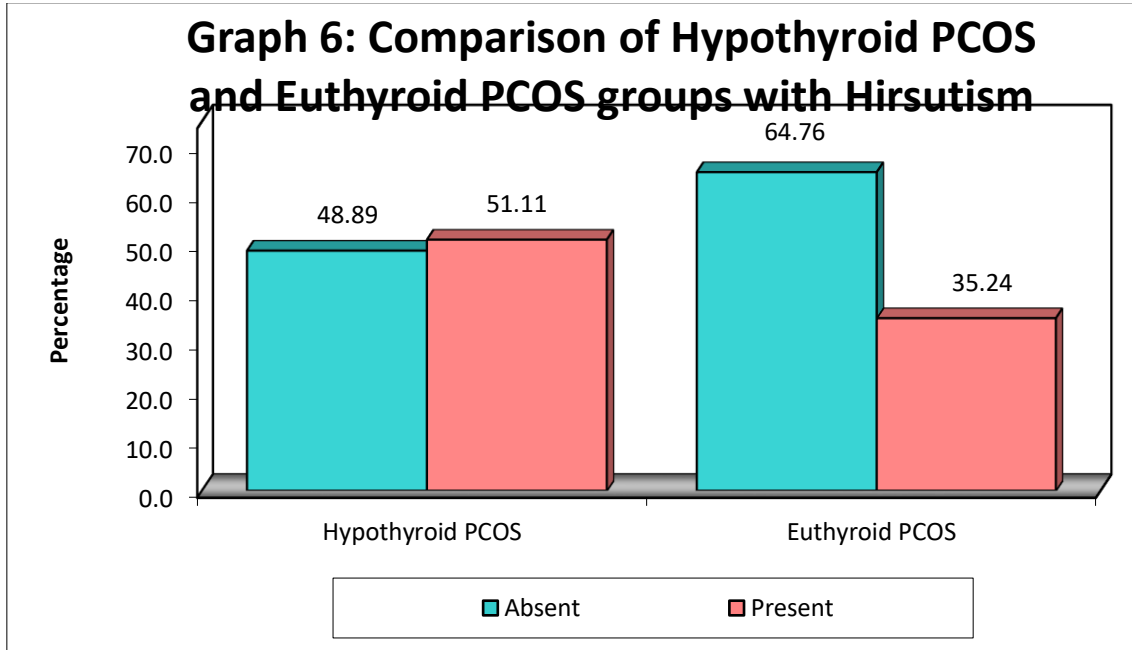
Table 7: Comparison of Hypothyroid PCOS and Euthyroid PCOS groups with hirsutism.

Hirsutism	Hypothyroid PCOS	%	Euthyroid PCOS	%	Total	Total %	Chi-square	p-value
Absent	22	48.88	68	64.76	90	60	3.3069	0.0689
Present	23	51.11	37	35.24	60	40		
Total	45	100	105	100	150	100		

*p<0.05



Hence, hirsutism was seen in 40% of PCOS women. Out of which 35.24% were in the euthyroid group, and 51.11% belonged to the hypothyroid group of PCOS women, there found no statistical difference ($p=0.0689$).



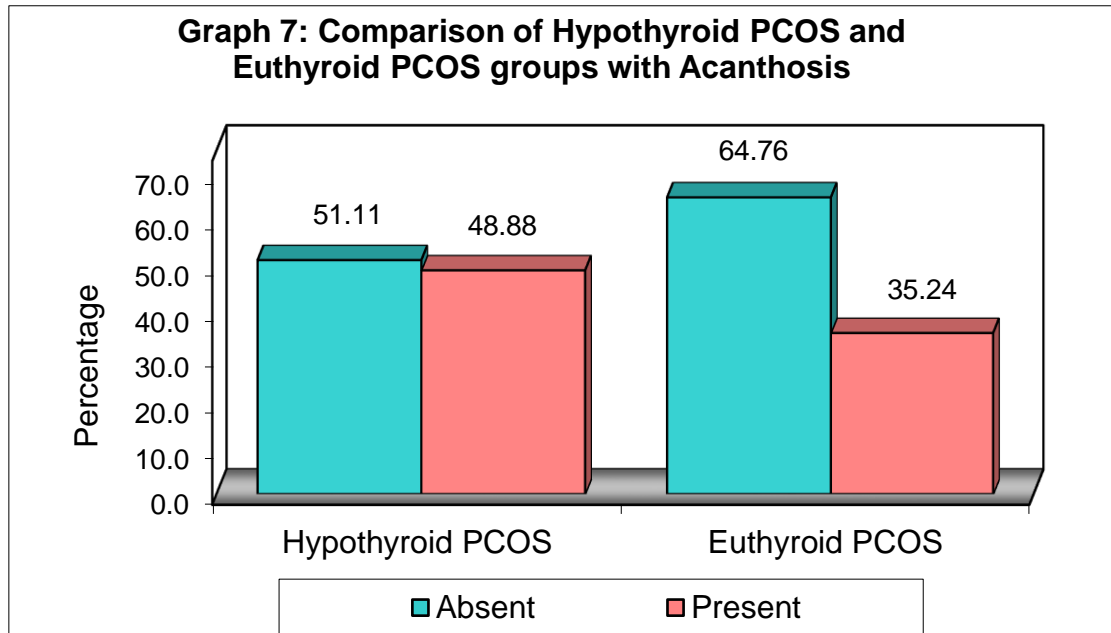
Acanthosis nigricans:

Table 8: Comparison of Hypothyroid PCOS and Euthyroid PCOS groups with Acanthosis nigricans

Acanthosis nigricans	Hypothyroid PCOS	%	Euthyroid PCOS	%	Total	Total %	Chi-square	p-value
Absent	23	51.11	68	64.76	91	60.66	2.4599	0.1167
Present	22	48.88	37	35.24	59	39.33		
Total	45	100	105	100	150	100		

* $p<0.05$

Acanthosis was identified in 39.33% of PCOS women out of 150 PCOS women. It was found in 35.24% in euthyroid PCOS women and 48.88% in hypothyroid PCOS women and the difference between these 2 groups was not statistically significant.



Infertility:

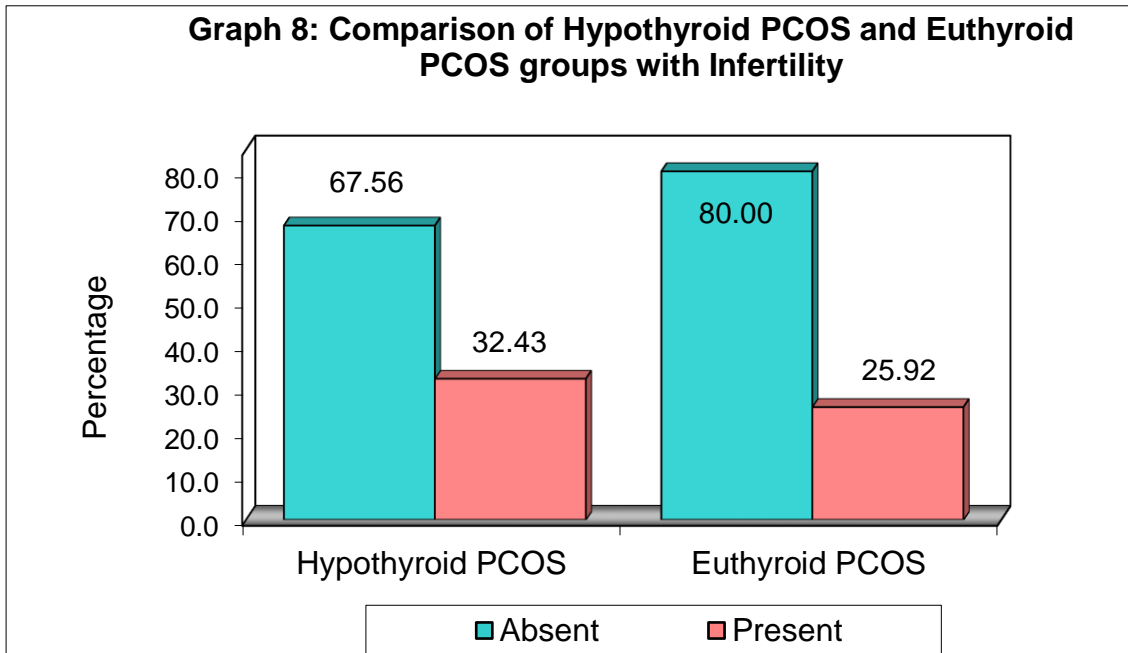
In the current study, out of 150 PCOS women, 118 were married PCOS women. There were 37 married women in the hypothyroid PCOS group and 81 married ones's euthyroid PCOS group.

Table 9: Comparison of Hypothyroid PCOS and Euthyroid PCOS groups with infertility.

Infer- tility	Hypothyroid PCOS (37)	%	Euthyroid PCOS (81)	%	Total	total%	Chi- square	p-value
Abse- nt	25	67.56	60	74.07	85	72.03	0.5337	0.465
Pres- ent	12	32.43	21	25.92	33	27.96		
Total	37	100	81	100.0	118	100		

*P<0.05

Therefore, infertility in hypothyroid PCOS women was not statistically significant compared to euthyroid PCOS women.

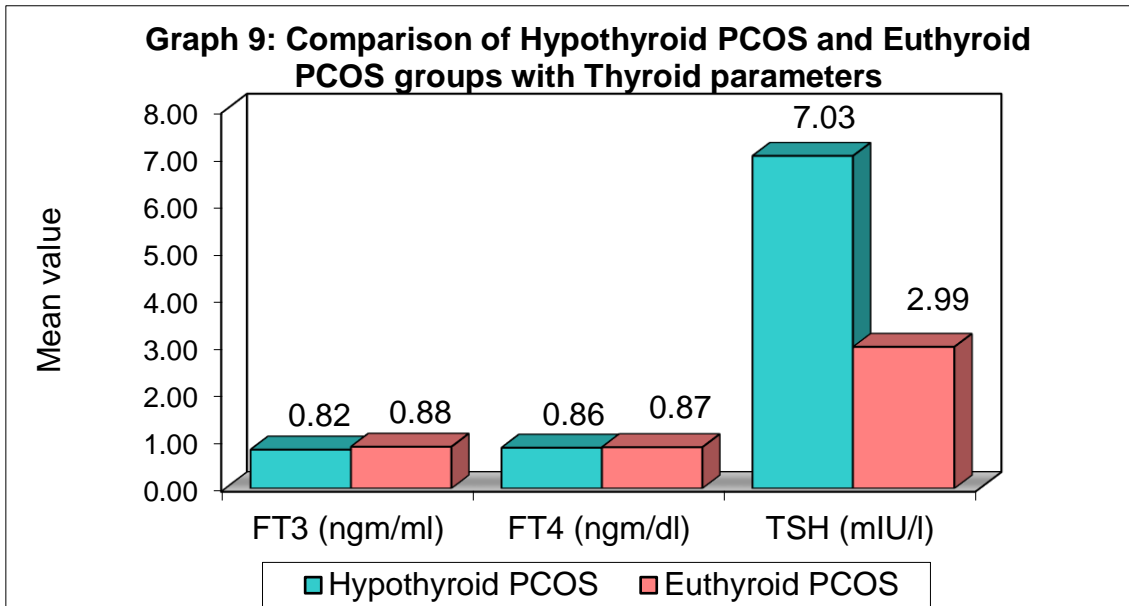


Thyroid profile:

Table 10: Comparison of Hypothyroid PCOS and Euthyroid PCOS groups with thyroid parameters by independent T-test.

Thyroid parameters	Hypothyroid PCOS			Euthyroid PCOS			t-value	p-value
	n	Mean	SD	n	Mean	SD		
FT3 (0.6-1.8ngm/ml)	45	0.82	0.25	105	0.88	0.17	-1.8201	0.0708
FT4 (0.61-1.12 ngm/dl)	45	0.86	0.15	105	0.87	0.15	-0.3340	0.7389
TSH (0.34- 5.6mIU/l)	45	7.03	1.48	105	2.99	0.87	20.881	0.0001*

*p<0.05



Both the subclinical hypothyroid women and overt hypothyroid women were included under the hypothyroid PCOS group of women. The average TSH level in the euthyroid group and the hypothyroid group showed a significant increase in the hypothyroid group ($p=0.0001$). But, FT3 and FT4 levels were similar in the two groups of PCOS women, and both of them were in the normal range.

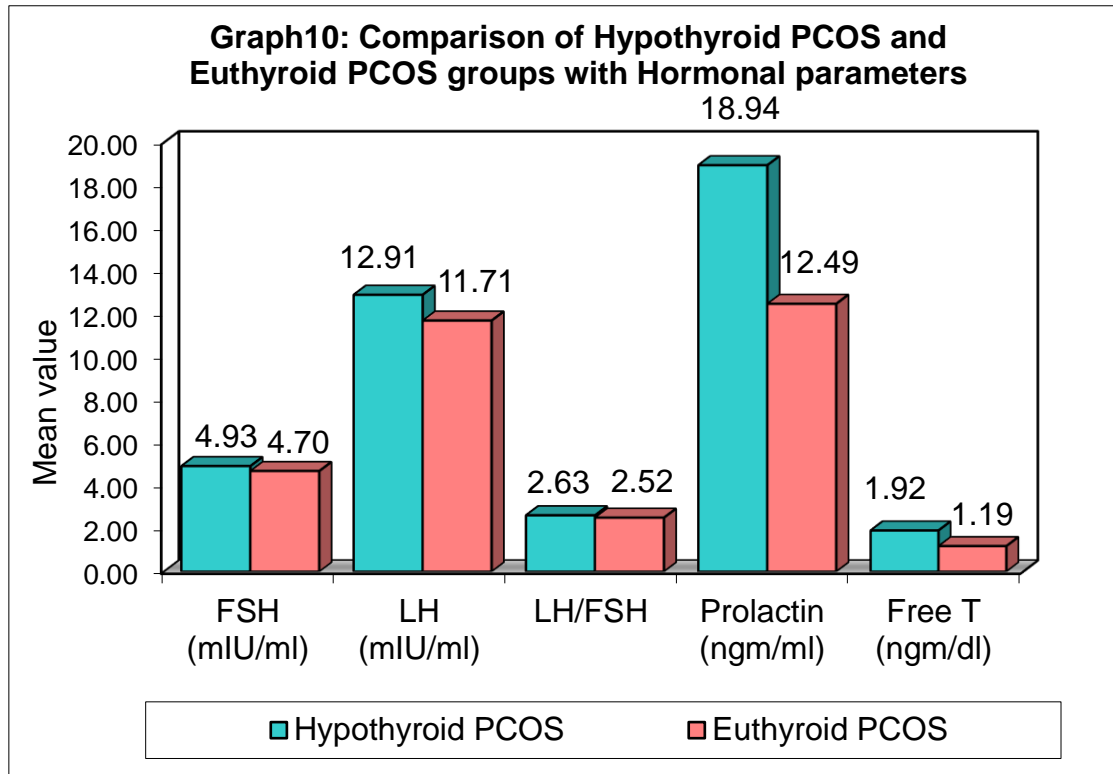
Hormonal parameters

In the current study, FSH, LH: FSH ratio parameters were almost the same in both groups. While a statistically significant difference was noted for LH ($p=0.0007$), sr. prolactin (0.0001) and free testosterone levels ($p= 0.0001$).

Table 11: Comparison of Hypothyroid PCOS and Euthyroid PCOS groups with Hormonal parameters by independent T-test

Hormonal parameters with normal values	Hypothyroid PCOS			Euthyroid PCOS			t-value	p-value
	n	Mean	SD	n	Mean	SD		
FSH (mIU/ml) (3.85- 8.78)	45	4.93	0.71	105	4.70	0.77	1.7276	0.0861
LH (mIU/ml) (2.12- 10.89)	45	12.91	2.64	105	11.71	1.55	3.4775	0.0007*
LH/FSH (<2:1)	45	2.63	0.50	105	2.52	0.34	1.5464	0.1241
Prolactin (ngm/ml) (3-27ngm/ml)	45	18.94	6.86	105	12.49	4.20	7.0463	0.0001*
Free T (ngm/dl) (0.3- 0.89)	45	1.92	0.19	105	1.19	0.37	12.5638	0.0001*

* $p<0.05$



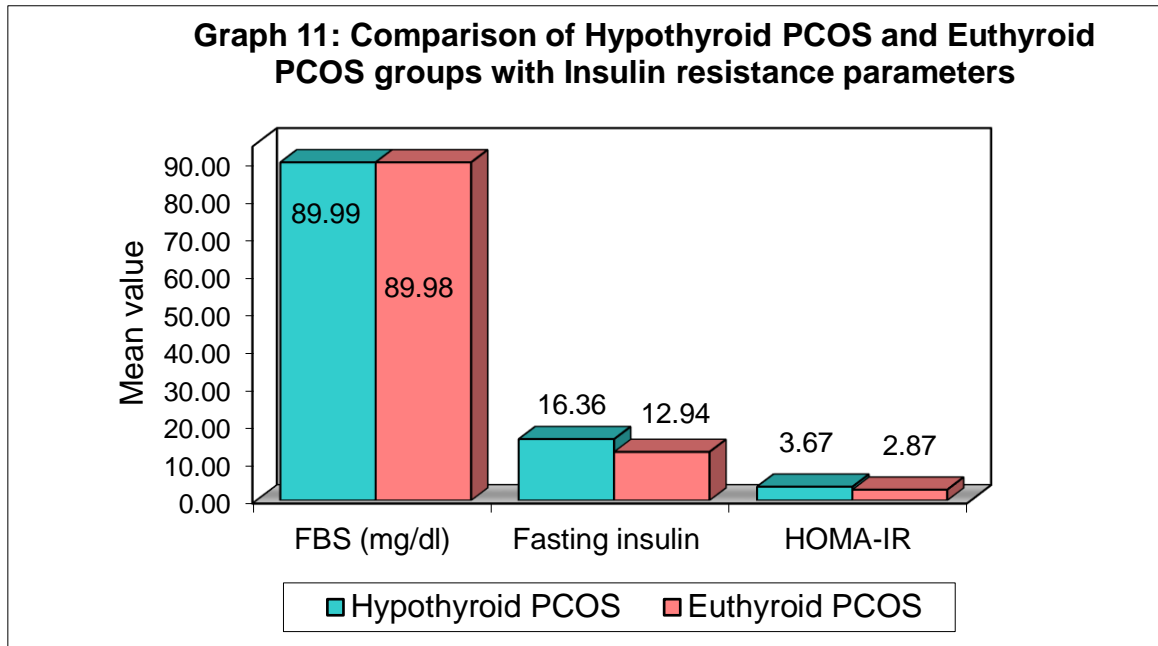
Insulin resistance:

Fasting insulin and HOMA-IR values are the essential parameters in identifying insulin resistance.

Table 12: Comparison of Hypothyroid PCOS and Euthyroid PCOS groups with Insulin resistance parameters by independent T-test.

Insulin resistance parameters	Hypothyroid PCOS			Euthyroid PCOS			t-value	p-value
	n	Mean	SD	n	Mean	SD		
FBS (<110mg/dl)	45	89.99	9.81	105	89.98	12.48	0.0047	0.9962
Fasting insulin (µIU/ml) (<20)	45	16.36	3.66	105	12.94	2.24	7.0029	0.0001*
HOMA-IR (<2.5)	45	3.67	0.91	105	2.87	0.67	6.0099	0.0001*

*p<0.05



Fasting insulin and HOMA values were higher in hypothyroid group compared to euthyroid group and the difference was statistically significant. It was noted that hypothyroid PCOS women have insulin resistance than euthyroid PCOS.

Lipid parameters:

Table 13: Comparison of Hypothyroid PCOS and Euthyroid PCOS groups with Lipid profile parameters by independent T-test.

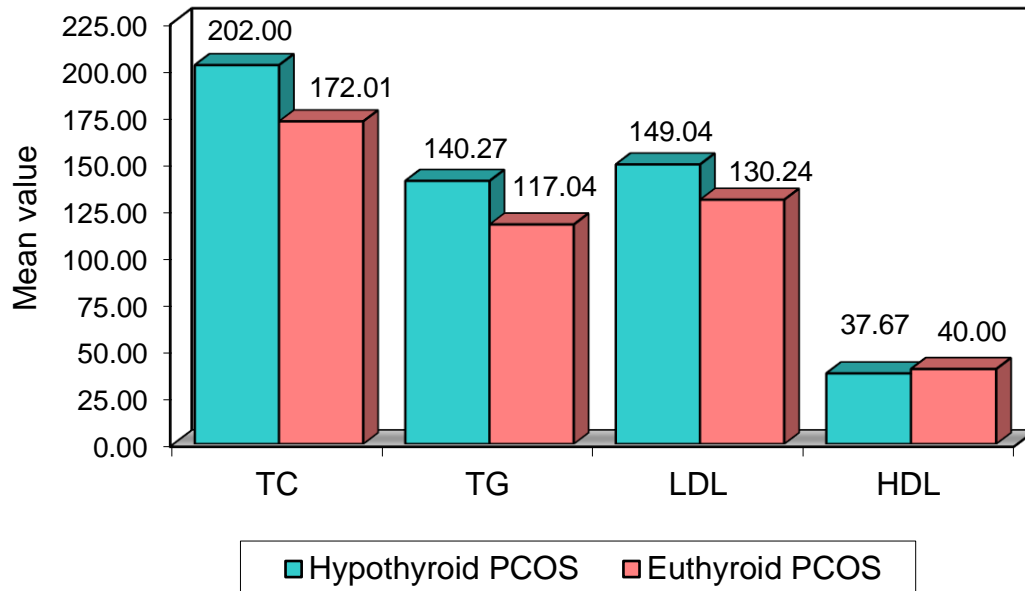
Lipid profile parameters	Hypothyroid PCOS			Euthyroid PCOS			t-value	p-value
	N	Mean	SD	N	Mean	SD		
TC (<190mg/dl)	45	202.00	12.60	105	172.01	14.20	12.2482	0.0001*
TG (<150mg/dl)	45	140.27	11.48	105	117.04	11.87	11.0901	0.0001*
LDL(<130mg/dl)	45	149.04	7.53	105	130.24	9.79	11.5022	0.0001*
HDL (>60mg/dl)	45	37.67	2.82	105	40.00	3.04	0.64117	0.5563

*p<0.05

In the present study hypothyroid PCOS women had high TC, TG, LDL values and the difference was statistically (p=0.0001). In contrast, HDL value was less in group 1 compared to group 2 but did not have statistical significance (P=0.5563). Therefore, hypothyroid PCOS women have dyslipidemia compared to euthyroid PCOS women.



Graph 12: Comparison of Hypothyroid PCOS and Euthyroid PCOS groups with Lipid profile parameters



V. DISCUSSION

PCOS is the most common endocrinological disorders affecting women in the reproductive age group. Some of the PCOS women had hypothyroid features, which affects pathophysiology, and so on PCOS.

The current study included 150 PCOS women with all the inclusion and exclusion criteria. All the subjects were divided into two groups depending on their thyroid status.

Group 1 included hypothyroid PCOS women.

Group 2 included euthyroid PCOS women.

In the current study, the hypothyroid group of PCOS women included both subclinical and overt cases.

Prevalence of hypothyroid PCOS women:

In the current study, out of 150 PCOS women, 45 women (30%) were in group 1 and 105 women (70%) were included in group 2. Comparing this with a study done by Enzevaei et al. in Iran, they observed 25.5% of subjects having SCH. In contrast to an Indian study by Sinha et al., 22.5% of PCOS subjects were detected to have subclinical hypothyroidism. Another study conducted on young women with PCOS found the prevalence of subclinical hypothyroidism to be 11.3%. Murk Fatima et al. found the prevalence of

SCH to be 34%, which was statistically significant n higher than those found in other study groups. But, De Medeiros et al. stated that only 6% of women had SCH among PCOS groups.

Demographic parameters:

In the current study, there was no significant difference between ages of euthyroid PCOS and hypothyroid PCOS similar to other studies done by, Enzewai et al., Ramanand SJ et al., Murk Fatima et al., De Medeiros et al.

Anthropometric measurements:

In the current study, the height and waist circumference of hypothyroid PCOS women were higher than euthyroid PCOS women but had no statistical significance. However, had a statistical significance in terms of weight and BMI. Muller et al. found statistical significance in BMI. Trakakis et al. found that patients with SCH and PCOS did not differ from PCOS patients with normal thyroid function in BMI, waist/hip circumference, and HOMA-IR. Benetti-Pinto et al. also supported these findings.

In the study by Enzevaei et al., all PCOS cases were similar in age, weight, height, and BMI⁶⁰. Bedaiwy et al., a few other studies showed a significant difference between euthyroid and SCH in weight, BMI, HOMA-IR, and insulin.



De Medeiros et al. stated no significant difference between the two groups in terms of waist circumference, waist-hip ratio, BMI.

Clinical parameters:

Obesity/overweight:

Stein and Leventhal had recognized obesity as a characteristic feature of PCOS. Hypothyroidism is also commonly associated with obesity. Even slightly elevated serum TSH levels are associated with an increase in obesity.

In Ramanand SJ et al. study, most patients in both groups were overweight/ obese. Though the difference between the numbers of overweight/obese women in both groups was statistically insignificant, the BMI of hypothyroid PCOS women was significantly more than the euthyroid PCOS group. Hence, the presence of hypothyroidism could exaggerate the severity of obesity in PCOS women and render them to its adverse consequences. Furthermore, the number of PCOS women complaining of weight gain was significantly higher in hypothyroid than the PCOS women's euthyroid group.

Duntas et al. mentioned leptin, an adipocyte hormone, acts as a significant factor linking obesity and thyroid autoimmunity⁴⁶. When TSH binds to the receptor on adipocytes, it stimulates the release of interleukin-6 and then mediates proliferation, differentiation, and secretion of leptin by preadipocytes adipocytes. The growing evidence also shows an association between altered thyroid function and obesity, which causes a lasting state of low-grade inflammation. At the same time, Nayak et al. found no association between obesity and subclinical hypothyroidism among PCOS patients.

Menstrual irregularities:

In the current study, 33.3% had amenorrhea, 42.4% had oligomenorrhea, and 24.2% did not have any menstrual symptoms in group 1, whereas 29.059 % of women had amenorrhea, 43.58% had oligomenorrhea, and 27.35% did not have any menstrual irregularities in the group 2, this difference found no statistical significance.

These results were similar to the other related studies by Dittrich et al., Ganie et al., Muller et al., Lavanya et al., and Azziz et al.

Hirsutism:

Hirsutism is one of the main characteristic features of PCOS. In the Ramanand SJ et al. study, the percentage of women complaining of abnormal excessive hair growth and showing hirsutism in

euthyroid PCOS and hypothyroid PCOS groups were comparable.

Futterweit W et al. stated that patients with diffuse alopecia, even in the absence of hirsutism, oligomenorrhea, or amenorrhea, might have hyperandrogenism. The most common endocrine disorder in those with diffuse alopecia was a polycystic ovarian disease⁸⁰. Diffuse hair loss is sometimes the presenting symptom of hypothyroidism. It is well-known that the thyroid hormone is essential for the development and maintenance of the hair follicle. Sterry W et al. reported that trichograms from the parietal and occipital areas showed increased dysplastic and broken hair suggesting that alopecia in thyroid disease was not by changes within the hair cycle by impaired hair quality. Nevertheless, limitation of this study was the only the consideration of women presented with hirsutism and did not considered those with baldness.

Benetti pinto et al. found no significant difference between the two groups. Qun Yu et al. found no significant difference between euthyroid and hypothyroid PCOS⁶².

Acanthosis nigricans:

Acanthosis nigricans in PCOS may attribute to insulin resistance. Hypothyroidism is also one of the endocrine diseases associated with acanthosis nigricans, which is unlikely to affect the hypothyroid state directly but may instead be an indirect action mediated through obesity subsequent insulin resistance. Insulin resistance and hyperinsulinemia seem to be commonly associated with acanthosis nigricans seen in many endocrine diseases.

Infertility:

Infertility is found in most PCOS women, but now there was no difference in the number of women having infertility between the two groups.

The current study correlated with the previous studies done by Benetti- pinto, Dittrich et al., Michalakakis et al., which also should no difference between the two groups.

Comparison of thyroid profile:

In the current study, there was no significant difference between euthyroid PCOS and hypothyroid PCOS women in terms of FT3 and FT4 levels, while there was a statistically high significant difference in the TSH level.

De Medeiros et al. also found no significant difference between the two groups in FT4.

Hormonal parameters

Comparison of LH, FSH, LH/FSH ratio:

Murk Fatima et al., showed no statistically significant differences for LH, FSH, and



testosterone levels in the two groups of PCOS women.

In a study by Ramanand et al., mean values of LH, FSH, and LH/FSH ratio were found in-significantly less in hypothyroid PCOS women. The Qun Yu et al. study found no significant difference in LH, FSH, LH / FSH ratio.

Enzevaei et al., in their study aimed to evaluate the relationship between hormones and SCH, and found no significant difference between estradiol, progesterone, LH, FSH, and the LH/FSH ratio in the two groups.

A study by Sinha et al., which compared PCOS subjects and controls, found significant differences in LH, FSH, LH/ FSH.

In the current study, there was no significant difference between hypothyroid and euthyroid PCOS in terms of LH, FSH, LH/FSH.

Comparison of prolactin and free testosterone:

In a study by Ramanand et al., serum prolactin and testosterone's mean values were more significant in the hypothyroid PCOS group, though not significant.

In Murk Fatima et al. study, there were no significant differences between LH, FSH, and testosterone levels in the two groups of PCOS women. Along with this, there was no correlation found between TSH and LH, FSH, and testosterone.

In a study by Sinha et al., there was a significant difference in free testosterone than the controls. Enzevaei et al. reported that free testosterone was significantly different in the SCH and euthyroid PCOS groups. De Medeiros's, in their study, stated no significant difference in free testosterone.

Significance of insulin resistance:

As there is no universal best cut-off for the HOMA-IR model, the present study adopted the most commonly used cut-off of >2.5

A study by Enzevaei et al. reported contradictory findings, stating that SCH in PCOS does not significantly impact IR ($p = 0.74$). Still, they considered HOMA-IR >3.2 cut off for insulin resistance. In a study of the Indian population, Ganie et al. reported no significant difference in IR between the SCH and euthyroid PCOS subjects.

Celik et al. reported that in Turkey, there was no significant difference in both the groups in IR after removing the confounding impact of BMI. Interestingly all these studies showed higher HOMA-IR in SCH PCOS subjects than euthyroid PCOS, and also, the cut-off for IR varied amongst these studies. However, Mueller et al., in their study, reported an association between raised TSH levels and IR independent of BMI. Hosseinpanah et

al. reported that IR was 27.2%, difference was not significant⁸².

El-Hafez HA et al. reported a significant correlation between TSH and IR levels in PCOS subjects. Mehboob B et al., Ganie et al., and Laway et al. did not find an association of TSH with HOMA-IR. A few other studies showed a positive correlation between TSH and fasting insulin and HOMA IR, as seen in other studies. Bedaiwy et al. also mentioned that TSH had a positive association with HOMA-IR. There is no correlation of TSH with FBS compared to the Bedaiwy et al. study, which showed an association between TSH and FBS⁷¹.

In his study, de Medeiros et al. showed normal FBS levels in the SCH group.

In the current study, Fasting insulin and HOMA were higher in group 1 compared to group 2 and the difference was statistically significant.

Metabolic parameters:

The current study found that TC, TG, and LDL were statistically higher in hypothyroid PCOS group compared to euthyroid PCOS group, similar to a study by Qun Yu et al., and HDL was lower in hypothyroid PCOS than compared to euthyroid PCOS but the difference was not significant.

Al Sayed et al., Tuzcu et al. reported significantly higher TC and LDL in SCH subjects than controls still, it did not limit the population to PCOS subjects. Contradictory to findings, Enzevaei et al. found no significant difference in lipid profiles in SCH and euthyroid PCOS group⁶⁰. Laway et al.⁸⁵ study also failed to differentiate lipid profiles in SCH and euthyroid PCOS subjects significantly; whereas, in the study done by Ganie et al.⁶⁷, the TG in the SCH group had statistically higher levels than the control group, but in the study undertaken by Tuzca et al.⁸⁷, increase in LDL without any changes in TG and HDL in the SCH were observed in comparison with the control group^{75,76}. Brenta et al. found no difference in lipid levels in PCOS+SCH patients compared to the control group⁸⁸. Benetti et al. in their study, LDL was found significantly higher in the cohort with subclinical hypothyroidism⁴.

A study by Muderris et al., taken 26 hypothyroid women and 20 people as controls, found that 10 out of 26 hypothyroid women had significantly higher ovarian volumes than control group, even the subgroup without appearing polycystic ovaries had significantly higher ovarian volumes. This study's most remarkable findings were the normalization of ovarian volume in all the patients, with or without polycystic ovaries, after the replacement of thyroxine.



In another study by Sinha et al., a comparison of 80 PCOS females with 80 controls found a significantly higher prevalence of goiter and subclinical hypothyroidism in PCOS patients than controls³.

Another recent Indian study found a high prevalence of thyroid disorders among PCOS- 33% of overall PCOS had thyroid dysfunction, 11% had a goiter, and 18% had subclinical hypothyroidism. However, in this study, one of the main limitations is the lack of controls³.

Muscogiuri et al. studied 60 euthyroid to find a correlation of TSH to either adipose tissue or insulin resistance. On univariate analysis, both adiposity and IR significantly associated with raised TSH, but after multivariate regression, visceral adipose tissue volume was the only predictor of TSH.

Limitations of the study:

1. The current study has not grouped subclinical and overt hypothyroid PCOS women separately; instead, both were grouped under the hypothyroid PCOS group.
2. The current study did not include a control group.
3. The pitfall of this study is not taking the autoimmune thyroid status, SHBG levels, 17 (OH) progesterone values of PCOS women into consideration.
4. This study is a single centered study with a small number of subjects; therefore, multi-centered research should be recommended with a larger sample size to prove the significance of thyroid dysfunction in patients with PCOS, especially fertility.

VI. CONCLUSION

This study concludes that there is higher prevalence of hypothyroidism in women with PCOS, and there is a significant effect of hypothyroidism on PCOS women.

In view of the above findings, PCOS is not just oligomenorrhea, amenorrhea, or infertility; hence, it is must to know the risk factors for PCOS and its associated complications so as to intervene with a preventive approach, which may restore normal menstrual function, ovulation, fertility, and prevent its long term complications.

Physicians should also consider screening for thyroid function tests at the diagnosis of PCOS, even in the absence of symptoms for thyroid dysfunction.

As the clinical implications of differences found in patients with euthyroid PCOS and hypothyroid-PCOS are still unclear, there is a

strong need for further studies in this field, which might help us shed more light on this particular group of women to determine whether they need closer follow-up.

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