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THE PREVALENCE OF THYROID DYSFUNCTION IN PCOS WOMEN IN COMPARISON WITH A CONTROL GROUP

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ABSTRACT

Background: One of the common disorders that affect females of reproductive age is the Poly-Cystic Ovarian Syndrome (PCOS). Thyroid dysfunction is also more prevalent in this age group. This study aimed to evaluate the prevalence of thyroid dysfunction in women with PCOS in comparison with control and to investigate the association between hypothyroidism and PCOS in women of ovulatory age. **Patients and Methods:** Eighty female subjects of fertility age were selected and divided into two equal groups. The first 40 subjects are healthy females as a control group. The second 40 group are patients with PCOS. The PCOS women were diagnosed by Rotterdam criteria and performed thyroid tests, sex hormones and lipid profile tests. **Results:** The results show that PCOS women with hypothyroidism are tending have a high body mass index (BMI). Forty-five percent of PCOS patients had hypothyroidism which was investigated in TSH and T4 tests by 35% and 10%, respectively. A high level of testosterone was found in females with PCOS. The cholesterol shows a significant correlation with the alteration in Thyroid Stimulating Hormone (TSH). **Conclusion:** There is a correlation between thyroid dysfunction especially hypothyroidism with the polycystic ovarian syndrome because both of them lead in features to metabolic syndrome and there is a high prevalence of hypothyroidism in women with PCOS.

KEYWORDS: Hypothyroidism, Poly-Cystic Ovarian Syndrome, Thyroid Stimulating Hormone, Rotterdam.

INTRODUCTION

One of the common endocrinal disorders is the Poly-Cystic Ovarian Syndrome (PCOS) which is also known as a syndrome of Stein and Leventhal that affect about 5 to 10 % of the female in reproductive age.[1] This disorder induces mainly a disturbance of the ministration period, hyperandrogenism, and infertility. These changes cause an increase in the risk factor of metabolic syndrome and cardiovascular disease due to increased insulin resistance and obesity.[2]–[4] 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.[5] 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:

1. Menstrual abnormalities like anovulation (or amenorrhea), oligomenorrhoea, or long cycle
2. Hyperandrogenism - Clinical or biochemical signs observed such as acne, hirsutism or high levels of testosterone
3. The polycystic appearance of ovaries by echographic such as ultrasound (US), containing multiple small follicles measuring from 2 to 9 mm

The main dysfunction of the thyroid is an irregularity of the menstrual period and also infertility which is caused by ovulatory dysfunction. These main dysfunctions had a serious effect on the female reproductive system.[6] Thyroid disease is one of the autoimmune diseases that can be recognized when the previously main dysfunction increased. A bidirectional association between the PCOS and the thyroid has been suggested but it is still uncertain. Most studies were performed on the pathophysiological incidence, cause and clinical features of the PCOS.[7]

A study performed by Diksha Goyal et. al[8], who found that the TSH in PCOS patients was higher than the

healthy subjects. Furthermore, Ding et. al.[9], demonstrated that the PCOS risk increased as a result of clinical hypothyroidism and depressive symptoms such as anxiety. 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.

The relationship between thyroid dysfunction and polycystic ovulatory syndrome is not widely discussed by the authors especially in Iraqi patients. This study aims to evaluate the prevalence of thyroid dysfunctions in women with PCOS in comparison with the control group. Also, to evaluate the relationship between PCOS and thyroid dysfunctions (ovarian hormones and thyroid hormone).

PATIENTS AND METHOD

This case-control research was conducted in the department of infertility of Al-Yarmouk teaching hospital, Baghdad, Iraq. The study was approved by the physiology department committee, College of Medicine, Al-Mustansiriyah University, Baghdad, Iraq. Eighty females selected in this study according to the declaration of Helsinki and divided equally into two groups: Forty with PCOS who were diagnosed by the Rotterdam criteria 2003[5], [10] and the other forty who are health control.

The complete history of all the subjects is assessed included the medical, surgical, menstrual. Then, a physical examination including weight and height was performed for measuring the BMI (weight in kg/(height)^2 in m^2). An ethical consent was obtained from the patients included in this study. Transabdominal ultrasound was done for both groups PCOS and normal women. A blood venous blood of 5 ml was collected from both PCOS and control groups of women to evaluate the thyroid function test such as TSH, T3, T4 and FSH, LH, testosterone and prolactin hormone. Also, the lipid profile, FBS, fasting insulin level was assessed. The SPSS-24 was used for statistical analysis purposes at significant level ≤0.5.

- **Inclusion criteria**

1. Irregular menstruation for PCOS women: no menses in the past 6 months or menstrual cycle prolonged for more than 35 days. Regular manse for the control group.
2. Increased androgen levels and/or acne and/or alopecia (androgenic pattern)11 or biochemical hyperandrogenism (testosterone level >2.0 nmol/L)
3. Polycystic ovaries (follicles 2–9 mm in diameter and ≥12 in number or ovarian volume ≥10 cm3) identified by transabdominal pelvic ultrasonography after excluding other diseases such as congenital adrenal hyperplasia and virilizing tumors.

- **Exclusion**

1. Patients use steroids.
2. Patients on contraceptive pills.
3. Pregnancy
4. Very low body mass index by measuring BMI.
5. Neoplasia: thyroid or adrenal.

RESULTS

A comparison between the characteristics and analysis of PCOS patients and control females selected in this study are illustrated in the table (1). A significant difference between the PCOS and control was found in length and BMI values.

The comparative analysis of lipid profile including the cholesterol, HDL, LDL, and VLDL. There was no significant difference between the PCOS and control women are shown in the results.

The comparison of glucose analysis was performed between the healthy and PCOS patients including the triglyceride (TG), fast blood sugar (FBS), and fast insulin. The statistically significant difference was found with FBS and fast insulin but not for TG.

Table 1: Characteristics of Female Patients with Pcos and Healthy Group Included In This Study.

Variable	PCOS Median (Range) Mean ± SD	Control Median (Range) Mean ± SD	*p*-value
Age (years)	29 (19 – 42) 29.7 2± 6.71	35 (17 – 45) 33.35 ± 7.73	0.1243
BMI(Kg/m^2)	29.86 (24.03 – 39.14) 29.13 ± 3.76	27.19 (24.38 – 32.31) 27.31 ± 1.88	0.0490*
Cholesterol	178.85 ± 16.98	170.05 ± 13.26	0.0756
TG	130.3 ± 32.51	128.25 ± 17.41	0.8050
HDL	47.95 ±3.94	50.15 ± 5.26	0.1428
LDL	95.20 ± 21.24	95.25 ± 8.50	0.9922
VLDL	17.05 ± 3.54	17 ± 2.37	0.9919
FBS	98.35 ± 3.66	92.9 ± 4.84	0.0002*
Fast Insulin	17.52 ± 2.18	11.46 ± 2.54	<0.00001*
*Unpaired T-Test for Significant difference test at ≤0.05			

The clinical features such as the presence or absence of acne, hirsutism, and hair falling were investigated for both PCOS patients and control groups as presented in figure (1). It shows that 50 %of PCOS groups had acne, while it was 12.5 % for the control group. For hirsutism, a higher percentage was found for PCOS (80%) than the control group (10%). Furthermore, 90% of a female with PCOS shows to had a hair falling rather than the control who had 15% in normal condition.

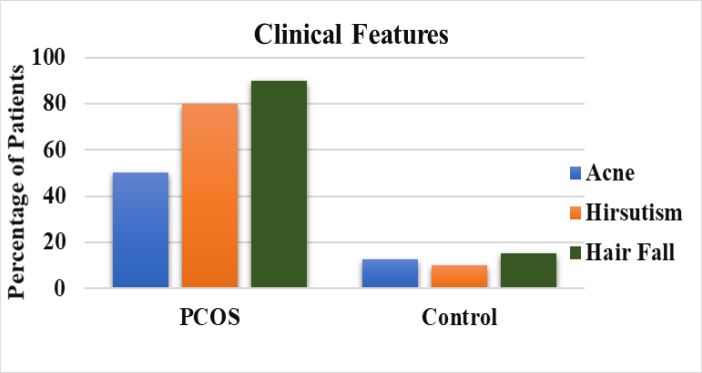

Figure 1: Clinical features of PCOS patients and control.

We show the statistical results of sex hormones tests in the table (2) for the LH, FSH, prolactin, and testosterone. It shows a significant difference for LH between the PCOS and control. Where both LH and testosterone show a high level of PCOS.

Table 2: Sex hormones analysis comparison between the PCOS and healthy control.

Variable	PCOS	Control	*p* - value
LH mIU/ml	8.98 ±2.84	6.67 ± 1.19	0.0450*
FSH mlU/ml	8.75 ± 1.73	6.58 ± 1.90	0.5435
Prolactin	24.66 ± 3.05	14.48 ± 9.71	0.1823
Testosterone	0.64 ± 0.02	0.36 ± 0.01	<0.00001*
*Unpaired T-Test for Significant difference test at ≤0.05			

The results of the thyroid function tests are listed in the table (3). The tests including T3, T4, and TSH. We found the TSH levels to be significantly higher in PCOS patients than in the control.

The percentage of PCOS female patients with hypothyroidism shows that the TSH test of a patient with hypothyroidism is 14 (35%), and 4 (10%) patients have low T4 levels. It should be noticed that there was no abnormal value was found with the T3 hormone.

Table 3: A Comparative Analysis of Thyroid Function Between The Pcos and Healthy Control Female.

Variable	PCOS	Control	*p* - value
T3 nmol/L	1.40 ± 0.30	2.89 ± 0.22	0.3168
T4 nmol/L	88.18 ± 13.90	100.38 ± 9.93	0.1116
TSH µIU/L	4.66 ± 0.28	1.68 ±0.33	0.0035*
*Unpaired T-Test for Significant difference test at ≤0.05			

We performed a statistical correlation test to investigate the relationship between the thyroid analysis (TSH, T3, and T4) with all the studied parameters, such as lipid, FBS insulin level, sex hormones for PCOS females. The results show a significant correlation between the TSH and cholesterol only, as illustrated in the table (4).

Table (4): Correlation between the TSH, T3, T4 and other variables.

Variable	TSH		T3		T4	
	r_s	*p- value*	r_s	*p- value*	r_s	*p- value*
FSH mIU/mL	0.25434	0.2792	-0.15008	0.52769	-0.0535	0.82273
LH mIU/mL	0.25434	0.2792	-0.03849	0.87201	0.20664	0.38207
Prolactin ng/ml	0.07154	0.7644	-0.28539	0.22258	0.0143	0.9523
Testosterone ng/ml	0.12145	0.61	-0.09232	0.69867	-0.0552	0.81721
Cholesterol mg/dl	0.47062	0.03624*	0.01365	0.95445	0.12581	0.59714
TG mmol/L	-0.08574	0.71929	0.14113	0.55286	0.20622	0.38304

Fast Insulin µU/ml	0.15011	0.52761	-0.06134	0.79726	-0.01142	0.96188
LDL mg/dl	0.36838	0.11	-0.3143	0.17715	-0.03326	0.8893
HDL mg/dl	-0.17603	0.45787	0.29414	0.20809	0.09734	0.6831
VLDL mg/dl	0.00038	0.99871	-0.25238	0.28305	-0.40427	0.07708
FBS mg/dl	0.15449	0.51548	-0.37426	0.10402	-0.06159	0.79646
Fast Insulin µU/ml	0.15011	0.52761	-0.06134	0.79726	-0.01142	0.96188
*Correlation Test at ≤0.05 level.						

DISCUSSION

The median female age of this study is 29 and the range is within the reproductive age. The PCOS group tends to be overweight or obese with a higher BMI other than the control. The increase in BMI is maybe related to two causes, the first one is PCOS and the second cause may be hypothyroidism. Forty-five percent of PCOS in this study are obese. Deepa et al[6] are in coordination with these findings. They had a mean age is 26 ± 4.2 and a BMI of 29 ± 4.4 with 32% of PCOS patients are obese. Rahul et al[11] studied the correlation of thyroid dysfunction with the PCOS prevalence and found spatially hypothyroidism increased in PCOS incidence and obese women. Mayada et. al.[12] found an increase in BMIO in PCOS women.

Women with PCOS complain of many symptoms and clinical features, such as amenorrhea, hirsutism, obesity, enlarged ovaries and infertility. It is associated with increased cardiovascular disease risk factors, such as increased blood pressure, dyslipidemia, insulin resistance, and impaired glucose tolerance.[13]

The clinical feature of the PCOS group of patients presented a higher incidence than the healthy women. These findings are agreed with Deepa et al.[6] who found out that 52% of patients suffer from these clinical features. The result in the current research agrees with their study as shown in table (2) and we noticed that there is an increase in testosterone and hormone levels in PCOS females rather than healthy women. Also, Najem et al.[14] reported that all PCOS women included in their study are shown hyperandrogenism clinical features.

When the thyroid analysis was investigated for PCOS women in this study, it appears that 45% had hypothyroidism and 35% out of them were shown in the TSH test. Sinha et. al.[15] showed that 27.5 % of the PCOS females had thyroid disorder where 22% of them suffering hypothyroidism. Furthermore, they reported that TSH levels in the PCOS group were significantly higher than in the control group.

Many authors studied the relationship between the metabolic analysis for PCOS women and thyroid dysfunction[6],[8],[11] and pathologies[16]–[18] such as Pinto et al.[19] who found that 19 out of 168 PCOS women had subclinical hypothyroidism and showed higher levels of cholesterol, prolactin, and LDL than the control women. Previous findings agree with our results, except that the LDL levels in PCOS women are almost similar to the healthy control levels.

The association test of TSH, T3, and T4 with parameters involved in this study shows a significance of TSH with cholesterol only. These results disagreed with Dittrich et. al.[20] who found a significant association between insulin and TSH. They reported that PCOS women with TSH less than 2.5 mIU/L had a significant alteration of metabolic condition and endocrine hormonal level.

Simona Gabers et. al., 2015[21] performed a study on PCOS females within reproductive age correlation with Hashimoto's Thyroiditis (HT). the data are very scarce concerning clinical consequences, joint etiology, or pathogenesis. Probably, these results are a complex etiology of both PCOS and HT. there is no doubt that genetic suspectable contributes to the development of both disorders in more than 70% as shown by family and twin studies.

The diagnosis of PCOS by ultrasound (US) is not precise and dependable. Further investigations need to be performed in order to gain an accurate diagnosis. We should mention that when hypothyroidism affects PCOS women, it worsens their symptoms by lowering the level of binding globulin belongs to sex hormone, which converts the androstenedione into testosterone and aromatization to estradiol. Also, it reduces the metabolic clearance rates of androstenedione and estrone.[22],[23]

CONCLUSION

In conclusion, the prevalence of thyroid dysfunctions, especially hypothyroidism, is increased in women with PCOS patients. There is an association between polycystic and hypothyroidism in metabolic conditions. For accurate diagnosing, lipid profile and thyroid function should be performed for PCOS patients.

*** Ethical approval:** "We conform that all **procedures** performed in studies involving human participants were in accordance with the ethical standards of the physiology department committee, College of Medicine, Al-Mustansiriyah University, Baghdad, Iraq research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

DECLARATIONS

All manuscripts must contain the following sections under the heading 'Declarations':

Ethics approval and consent to participate

- **Patients statement:** I choose and consent to participate in this research
- The study was approved by the physiology department committee, College of Medicine, Al-Mustansiriyah University, Baghdad, Iraq.

Consent for publication

Not applicable

Availability of data and materials

Not applicable

Competing interests

The authors declare that they have no competing interests

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The authors fund the paper equally

Authors' contributions

The authors share the conception, design of the work, the acquisition, analysis, interpretation of data; writing equally.

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