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Polycystic ovarian syndrome and thyroid disorders

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***Abstract*— Background and objectives:**
Polycystic ovary syndrome (PCOS) is the most common endocrinopathy of women in the reproductive age group, characterized by chronic anovulation, hyperandrogenism and polycystic ovarian features on ultrasound. Thyroid dysfunction and PCOS are linked to each other since several years both of them pose independent risk of ovarian failure and pregnancy related complications. The present study aimed to investigate the association between polycystic ovarian syndrome and thyroid disorders by determining the polycystic ovarian women with abnormal thyroid function test (T3, T4, TSH) and identifying the demographic features of the study participants.
Patients and methods:
This study was conducted from the first of April/2015 to the first of April/2016 in the Maternity Teaching Hospital in Erbil City/ Kurdistan region/ Iraq. Total of 50 women in reproductive age/ (15-45) years had been enrolled in the study including women who had PCOS (2 of 3 Rotterdams criteria) .Thyroid function test (T3, T4, TSH) was done for them at the hospital laboratory and the results were recorded. These data entered into excel separate sheet and analyzed.
Results:
About half of PCOS patients were between 26-35 years old. Thyroid disorders were detected in 16% of patients and the rest were euthyroid. Hypothyroidism constitutes the major proportion of thyroid disorders in (PCOS).
Conclusion:
1-There is a possibility of causational relationship between thyroid dysfunction and PCOS.
2-The most common thyroid disorder in PCOS is hypothyroidism.
3-Thyroid function test is necessary in patient with PCOS.
Keywords: **Polycystic ovary syndrome (PCOS), thyroid disorder, hypothyroidism.**

I. INTRODUCTION

PCOS is a complex disorder affecting approximately 5-10% of all women in reproductive age. It is a multifactor endocrine disorder which demonstrates menstrual disturbance, infertility, anovulation, hirsutism and hyperandrogenism (1). There is no unique cause for PCOS as there is numerous genetic, variants and environmental factors interact and contribute to the pathophysiology of PCOS (1 ,2,3). Genetic factors play a part, put the exact mechanisms are unclear. Some evidence of familial aggregation of hyperandrogenaemia with or without oligomenorrhoea in the first degree relatives of women with PCOS. The diagnosis should exclude the secondary causes such as androgen producing neoplasm, hyperprolactinemia and adult onset congenital adrenal hyperplasia (2).

PCOS is also associated with increase metabolic and cardiovascular risk factors due to increase insulin resistance that compounded by the common occurrence of obesity, although insulin resistance is also present in non-obese women with PCOS. A meta-analysis found a two fold increase risk of coronary heart disease and stroke in women with PCOS. Although, there is an increased risk of cardiovascular disorders, but there is no apparent risk of increase mortality (4,5).

We can diagnose PCOS depending on Rotterdam criteria. The presence of 2 of 3 of these criteria is essential to diagnose PCOS (reduced or anovulation, biochemical or clinical signs of androgen excess and or polycystic ovaries on ultrasound (the presence of at least 12 follicles measuring 2-9 mm in diameter and ovarian volume in excess of 10 ml) (32).

Three main phenotypes of PCOS have been proposed, classical PCOS with hyperandrogenism and anovulation with or without PCOS ovaries, ovulatory PCOS with hyperandrogenism and PCOS ovaries and an-ovulatory PCOS without hyperandrogenism with PCOS ovaries on ultrasound .several phenotypes are associated with variable degree of metabolic and fertility irregularities (7,8,9).

Thyroid gland is a butterfly – shaped gland at base of the neck weights only about 20 gram, However the hormones it secrets are essential to the growth and metabolism. The gland is a regulator of all body functions. Thyroid disorders are found in 0.8 -5% of the population and are 4-7 times more common in women .Dysfunction and anatomic abnormalities of the thyroid hormone are among the most common disease of the endocrine gland. Thyroid disorders are often insidious in their presentations and it have long been recognized that thyroid dysfunction has a profound effect on the female reproductive system. Although the reason is not understood, the high prevalence of thyroid disorder in women is possibly due to the autoimmune nature of the thyroid disorder. The abnormalities of the thyroid hormone supply to the peripheral tissues are associated with a number of metabolic processes (11,12,13 ,14).

Early stages of thyroid dysfunction can lead to subtle change in ovulation and endometrial receptivity which may have a profound effect on fertility. Infantile hypothyroidism if untreated leads to sexual immaturity. Untreated juvenile hypothyroidism causes delay in the onset of puberty followed by an-ovulatory cycles. In adults sever hypothyroidism may

be associated with diminished libido and failure of ovulation. Primary ovarian failure can also be seen in patients with hashimotos thyroditis as a part of autoimmune polyglandular syndrome. Rarely, in primary hypothyroidism secondary depression of pituitary function may led to ovarian atrophy and amenorrhoea (16,17,18) .

Pregnancy complications are associated with overt and subclinical hypothyroidism. So, it is evident that both PCOS and thyroid disorder have profound effect on reproductive biology and PCOS –thyroid relationship affects fertility. Therefore different studies from various parts of the world have tried to explore that correlation (34).

With this background, the present study has been contemplated to investigate the prevalence of different thyroid disorders in PCOS patients attending consultation department of Erbil at maternity teaching hospital in Kurdistan region.

II. Patients and methods

This study was conducted as observational analytic (cross-sectional) study from the first of April 2015 to the first of April 2016, at Maternity Teaching Hospital in Erbil city/Kurdistan Region/ Iraq .Total of 50 women in the reproductive age (15-45) years has been enrolled in the study including women who had a diagnosed PCOS . The diagnosis was made by 2 of 3 Rotterdam criteria. Normal female without PCOS, premenarche, menopause were exclude from the study. Informed verbal consent was taken from each women involved in the study. The study protocol includes a thorough history taking, full clinical examination and investigations.

Each woman was asked about age, marital state, history of sub fertility (primary or secondary), menstrual history including any history of oligomenorrhea or amenorrhea and any previous sonographic studies documented PCOS .Each woman was examined for the presence and the distribution of hirsutism and acne with a calculation of body mass index .At the same time, thyroid function test (serum level of TSH, T3, T4) were done for them.

A. Reference values:

The reference normal values used in our study are according to governmental hospital laboratory of Erbil Maternity Teaching Hospital:

Serum level of T4: (66 – 181) nmol/L
Serum level of T3: (1.30 – 3.10) nmol/L
Serum level of TSH: (0.27 – 4.20) nmol/L

Criteria for diagnosis of hypothyroidism:
TSH measurement depended on:
Patients with serum TSH level > 4.20 nmol/L considered to have hypothyroidism.

III. Criteria for diagnosis of hyperthyroidism:

Because of free T4 test was not available in the laboratory, TSH and total T4 and T3 measurements were used for the diagnosis of hyperthyroidism.

A. Statistical analysis:

Data were analyzed using the Statistical Package for Social Sciences (SPSS, version 19). Chi square test of association was used to compare between proportions. When the expected count of more than 20% of the cells of the table was less than 5, Fisher's exact test was used. Student's t test was used to compare between means of two groups.

IV. Approval and Ethical Consideration:

This study was approved by Scientific Committee of the College of Medicine of Hawler Medical University. The purpose and the procedure of the study were explained to all participants and they were given the right to participate or not, verbal consent was taken with interpret gained will be kept confidentially and not to be used for other than the research object.

V. Results

The 50 women who participated in the study were confirmed by (2 of 3 Rotterdam's criteria) to have PCOS. The demographical features of our study participants were as seen in our results below.

In this study we looked for the demographical characters of the study participants, nearly half of them were in the age group 26-35 years (48%) with PCOS presented were from 26-35 years of age, followed by less than 25 years old patients. The majority of women (80%) were living in urban areas and only 20% of them were living in rural areas. 44% them had a primary school level of education and 36% had the secondary level of education, while the illiterate and university level was equal to 10% of all cases.

Regarding the BMI, 64% of our cases were overweight, 32%were normal weight and 4% were obese. Most of our study participants were housewives by 88% and just 12 were employee. 76% of our patients were married and 24% were single. In this study thyroid function test was abnormal in 16% of the study participants while the remaining 84% have a normal thyroid function test as seen in the table below

Table 1: Thyroid function test distribution.

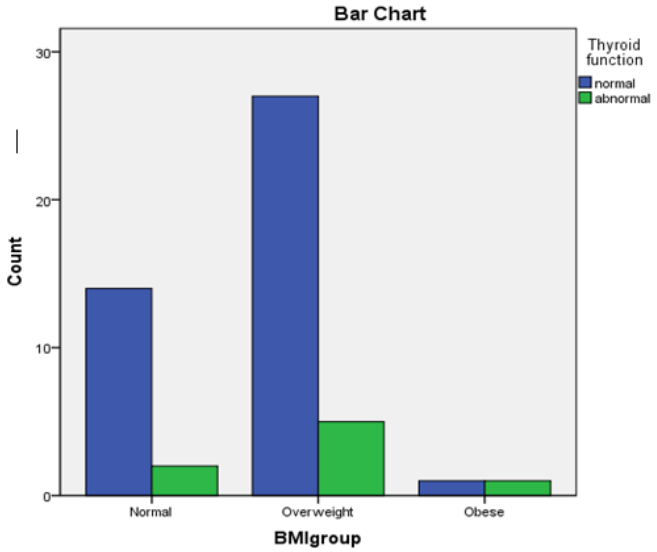
Thyroid function	Frequency	Percent	Valid Percent	Cumulative Percent
normal	42	84.0	84.0	84.0
abnormal	8	16.0	16.0	100.0
Total	50	100.0	100.0	100.0

Primary infertility was the highest percentage by 32% followed by the normal fertility status by 30% and 14% for secondary infertility as illustrated in table2.

Table 2: Fertility status

fertility status	Frequency	Percent	Valid Percent	Cumulative Percent
Fertile	15	30.0	39.5	39.5
Primary infertility	16	32.0	42.0	81.6
Secondary infertility	7	14.0	18.4	100.0
Total	38	76.0	100.0	
Missing System	12	24.0		
Total	50	100.0		

In this study there is no obvious association between the age and thyroid abnormalities since P value was 0.988 which is more than 0,05 and there is no significant association between BMI and thyroid abnormalities since P value is 0.393 which is more than 0.05 as demonstrated in the figure below .



There was no significant association between thyroid abnormalities and fertility state as P value is 0.096 which is more than 0.05 as illustrated in the table below.

Table3: Thyroid function relation with fertility

fertility status * Thyroid function Cross tabulation

			Thyroid function		
			Normal	Abnormal	Total
fertility status	Fertile	Count	15	0	15
		% within fertility status	100.0%	.0%	100.0%
	Primary infertility	Count	12	4	16
		% within fertility status	75.0%	25.0%	100.0%
	Secondary infertility	Count	5	2	7
		% within fertility status	71.4%	28.6%	100.0%
Total		Count	32	6	38
		% within fertility status	84.2%	15.8%	100.0%

Chi-Square Tests

	Value	DF	Asymp. Sig. (2-sided)
Pearson Chi-Square	4.693[a]	2	.096
Likelihood Ratio	6.778	2	.034
Linear-by-Linear Association	3.838	1	.050
N of Valid Cases	38		

a. 3 cells (50.0%) have expected count less than 5. The minimum expected count is 1.

VI. DISCUSSION:

There are enough literatures support to argue that subclinical hypothyroidism, thyroid autoimmunity is increased in women with PCOS patients since both of PCOS and thyroid disorders are two of the most common endocrine disorders in the general population and are closely associated (30,31,32,33).

The pathophysiological pathways and contributing factors behind this association are yet be elucidated. Long term studies are required to assess the significance of thyroid dysfunction in patient with PCOS, especially with infertility.

The pathogenesis of hypothyroidism and PCOS is completely different. But these two entities have many features in common (45) (1-44).

64% of the cases were overweight which is also similar to other studies which state a prevalence of obesity in approximately 50%, in a Delhi based study with 33 PCOS subjects, obesity was observed in 46%. The prevalence of obesity among 318 PCOS patients as observed by Najem was 57% and 54% overweight in the study of Gomathicetal in 2008. However, obesity varies significantly with the country of origin .the increase of' BMI in PCOS is obvious in the majority of cases, which is also noticed in patients with high level of TSH with unclear path physiological mechanism (45).

Obesity is a common finding in PCOS and aggravates many of its reproductive abnormalities and features. The relationship between them is complex .not well understood, and most likely involves interaction of genetic and environmental factors (48). About fertility state 76% of our study participants were married with 30% of them fertile without medical intervention. In contrast, the overall prevalence of sub fertility 46% in which 32% of them have a primary infertility and 14% of cases had secondary infertility.

The prevalence of sub fertility could be higher because more than a quarter of the total number was not sexually active. The thyroid function test of 50 women with PCOS revealed 16% incidence of thyroid dysfunction as isolated elevation in thyroid stimulating hormone, while 84% were euthyroid.

Other studies in the literatures such as retrospective analysis of patients recorded at the endocrine clinic in Benghazi was undertaken and showed that thyroid disease was noticed among 5.3% of the patient. Additionally, Muderrisetal (2011) stated that sever prolong hyopthyroidism contributes to bigger ovarian size and or cyst formation. Moreover, restoration in serum hormone level accomplishment of euthyroidism, induces a reduction in ovarian size, resolve of ovarian cyst together with reversal of the polycystic ovary syndrome – like characteristics (50).

At the same time, the study was consistent with Ghosh et al (1993) who in intending to analyze the part of hypothyroidism resulted in reduction of sex hormone binding globulin level and increment of testosterone level (51).

CONCLUSION

1.There is a possibility of causational relationship between thyroid dysfunction and PCOS.

2.The most common thyroid disorder in PCOS is hypothyroidism.

3.Thyroid function test is necessary in patient with PCOS.

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