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POLYCYSTIC OVARIAN SYNDROME AND HYPOTHYROIDISM

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ABSTRACT

Introduction: As the prevalence of these endocrine dysfunctions increases, the association of polycystic ovary syndrome (PCOS) and thyroid disease is increasingly being recognized. **Objective:** This study aimed to find out the relationship between hypothyroidism and polycystic ovary syndrome. **Materials and Methods:** This study was conducted on a sample of women who suffer from low fertility and hypothyroidism, attending to some health clinical serves in the Brak Al-Shati area from 1st of July 2021 to the end of December 2022. 60 women were participating in this study, they were divided in to: 1. patients' group 40 women (hypothyroidism and PCOS) and control group 20 healthy women. The ages of the women participating in the study were between 18 and 45 years. **Results:** PCOS was found to be more prevalent in participants with hypothyroidism (65% vs. 35%). Increased BMI (28.53 ± 5.05 kg/m2 vs. 23.20 ± 2.18 kg/m2; p-value: <0.05) and increased TSH was significantly more in participants with PCOS. **Conclusions:** This study concluded that there is an association between hypothyroidism and PCOS. Therefore, PCOS patients must be screened with a thyroid profile.

KEYWORDS: Hypothyroidism**,** Thyroid Stimulating Hormone, Prolactin, Polycystic Ovary Syndrome.

INTRODUCTION

Polycystic ovary syndrome (PCOS) was first described by scientists Stein and Leventhal in[1,2,3,4,5] as they defined this syndrome as a combination of signs and symptoms of hypertrichosis (hirsutism), menopause, hyperovulation, infertility, obesity, and cystic ovaries,[2] the definition of PCOS has subsequently been developed over time through various expert opinions created by leading health organizations. The three main diagnostic criteria currently in use are: the National Institutes of Health criteria, developed in 1990, the Rotterdam criteria proposed at the conference of the American Society for Reproductive Medicine (ASRM) and the European Society of Human Reproduction and Embryology (ESHRE in Rotterdam in 2003 and the Androgen Excess Society (AES) standards proposed in 2006. According to this criteria, the basic definition of PCOS revolves around the presence or absence of signs of androgen excess, anovulation, and polycystic ovary syndrome (PCOM) on ultrasound evaluation.[6,7,2,8,9,10,4,11,12,13,5]

Its clinical presentation is heterogeneous and can be classified into several phenotypes depending on the presence or absence of distinct features[11] that can have implications at all ages, not just in the reproductive years.[14] It is estimated to affect 3-15% of women,[13] and several studies have suggested the prevalence of polycystic ovary syndrome (PCOS) in 5%-10% of women of reproductive age, using the US National Institutes of Health diagnostic criteria. Health, which indicates that polycystic ovary syndrome is the most common cause of infertility, ovarian dysfunction, and irregular menstruation.[5,8]

Clinical signs of PCOS are heterogeneous and can be classified into several phenotypes[11] that can have implications at all ages, not just in the reproductive age.[14] It is estimated to affect 3-15% of women,[13] and several studies have suggested the prevalence of (PCOS) in 5%-10% of women of reproductive age. the polycystic ovary syndrome is the most common cause of infertility, ovarian dysfunction, and irregular menstruation.[5,8]

Other studies have shown that PCOS is affecting about 6%-25% of women of reproductive age worldwide, while in India it is 3.7%-22.5% in adult females and 9.13%-36% in adolescent girls,[16,15] Globally more than 105 million women (15 and 49 years) were diagnosed with PCOS.[17]

Thyroid gland is a butterfly-shaped gland at the base of the neck that weighs about 20 grams. However, the hormones it secretes are essential for growth and metabolism, as it is considered a regulator of all body functions. Thyroid disorders have been found in 5-8.0% of the population and are more common 4-7 times in

Women. Thyroid dysfunction and anatomical abnormalities are the most common endocrine diseases.[11]

Thyroid function and reproductive function are closely related. Hypothyroidism has a negative impact on the female reproductive system,[11] and. For example, hyperthyroidism and hypothyroidism are associated with menopause, so thyroid dysfunction is considered a cause of infertility.[19]

The early stages of thyroid dysfunction can lead to a slight change in ovulation and a decrease in the uterine lining which may have a negative impact on fertility. Hypothyroidism in children if not treated leads to sexual immaturity, which leads to delayed onset of puberty.[11] In adults, severe hypothyroidism may be associated with decreased libido and failure to ovulate. In primary hypothyroidism, decreased pituitary function may lead to ovarian atrophy and menopause, so it is clear that both PCOS and thyroid disorder have a significant negative impact to procreate. Both polycystic ovary syndrome (PCOS) and thyroid disorders are two of the most common endocrine disorders in the population and in women of reproductive age, and both present with complaints of menstrual irregularity such as oligomenorrhea, amenorrhea, and sometimes menorrhagia.[20] The relationship between PCOS and thyroid disorders is not clearly understood, many studies tried to explore this.[11]

A study was conducted in Pakistan in 2019 showed that, a significant association between hypothyroidism and polycystic ovary syndrome. It was noted that hypothyroidism has a significant impact on the clinical, metabolic, and hormonal characteristics of polycystic ovary syndrome patients, and this may be due to increased exacerbation of insulin resistance in PCOS patients, which indicates that PCOS may be a type of autoimmune disease and has a close association with hypothyroidism. Therefore, it would be useful to routinely evaluate thyroid function to detect thyroid problem in PCOS patients even in the absence of symptoms related to hypothyroidism.[11,21]

Objective of the Study: As a result of the prevalence of polycystic ovary syndrome among women of reproductive age and there are many reasons for the appearance or incidence of polycystic ovary syndrome, this study aimed to find out the relationship between hypothyroidism and polycystic ovary syndrome.

MATERIALS AND METHODS

This study was conducted on a sample of women who suffer from low fertility and hypothyroidism, attending to some health clinical serves in the Brak Al-Shati area from 1st of July 2021 to the end of December 2022. 60 women were participating in this study, they were divided in to: 1. patients' group 40 women (hypothyroidism and PCOS) and control group 20 healthy women. The ages of the women participating in the study were between 18 and 45 years. They were not undergone treatment before and did not take any hormonal medications. All women agreed to participate in the research, signed consent form and filled a short questioner and their anthropometric measurements were taken.

Sample Collection

For the study, 5 ml of venous blood were collected from the women on the second or third day of the menstrual cycle. The samples were placed in the plain tube and the serum was used to measure TSH, PRO, LH, FSH, T3, and T4 by automated iFlash optical system analysis.

Statistical Analysis

The data were statistically analyzed using SPSS version 26, where the arithmetic mean, standard error, and percentages were calculated. The t-test for two independent samples was used to determine the differences between the different groups, the One-Way ANOVA test to measure the difference between the averages of more than 2 categories, and the Person Correlation test. P value < 0.05 was considered statistically significant, the results were represented graphically using Microsoft Excel 2019.

RESULTS

Results of Anthropometric Measurements

The results showed that, the average age of the control group was 31.50±9.41 years and in patient group was 34.53±8.68 years. By statistical analysis, it found that there were no significant differences between the two groups. While the Body Mass Index (BMI) showed a significant increase (P<0.05) in the patient group compared to the control group, the average of BMI was 27.76 ± 4.74 kg/m^2 and 22.82 ± 2.44 kg/m^2, in patient and control group; respectively (Table 1).

Table 1: Comparison Between the Patient and Control Group in Anthropometric Measurements.

Parameter	Patient group N= (40)	Control group N= (20)	P-value
	mean ± standard deviation		
Age (years)	34.53±8.68	31.50±9.41	**0.231**
BMI (kg/m^2)	27.76±4.74	22.82±2.44	**0.001**

Results of Thyroid Hormones

The level of TSH concentration was significantly higher (P>0.05) in the patient group compared to the control group, (8.13 ± 2.67 uIU/ml) and (2.4 ± 0.96 uIU/ml), respectively. statistical analysis showed a significant decrease ($P < 0.05$) in T3 and T4 (0.84 ±0.39 ng/ml) and (3.40 ± 1.16 ng/ml) respectively in the patient group compared to the control group, (2.39 ± 1.15 ng/ml) and (77.18 ± 18.06 ng/ml), respectively. (Table 2)

Table 2: Comparison Between the Patient and Control Group in Thyroid Hormones.

Parameter	patient group N= (40)	Control group N= (20)	P-value
	Mean ± SD		
TSH (uIU/ml)	8.13 ± 2.67	2.40 ± 0.96	**0.001**
Total T3 (ng/ml)	0.84 ± 0.39	2.39 ± 1.15	**0.001**
Total T4 (ng/ml)	3.40 ± 1.16	77.18 ± 18.06	**0.001**

RESULTS OF FEMALE HORMONES

Table No. (3) shows the concentration of female hormones at the patient group and the control group. It is clear from it that, the prolactin, FSH, and LH concentration were astatically higher in the patient group (48.76 ± 36.11 ng/ml, 10.35 ± 7.45 mIU/ml, 17.04 ± 9.67 mIU/ml; respectively) compared to the control group (11.49 ± 5.50 ng/ml, 6.72 ± 2.23 mIU/ml, 4.35 ± 1.84 mIU/ml; respectively).

Table 3: Comparison Between the Patient and Control Group in Female Hormones.

Parameter	patient group N= (40)	Control group N= (20)	P-value
	Mean ± SD		
Prolactin(ng/ml)	38.67 ± 14.11	11.49 ± 5.50	**0.001**
FSH(mIU/ml)	10.35 ± 7.45	6.72 ± 2.23	**0.001**
LH(mIU/ml)	17.04 ± 9.67	4.35 ± 1.84	**0.001**

Polycystic Ovary Syndrome Among the Patient Group (N=40)

The results showed that, 26 (65%) of the patient group had PCOS and 14 (35%) of them no had polycystic ovary syndrome (Non PCOS), as shown in Figure (1).

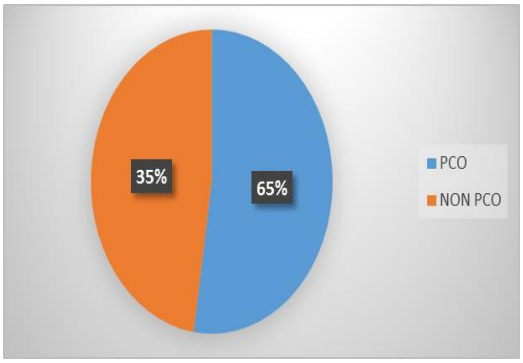

Figure 1: Distribution of polycystic ovary syndrome in patient group.

Comparing between women with and without polycystic ovary syndrome showed that, there was a significant increase in the BMI and TSH, while there was non-significant increase in FSH and prolactin. Also, the result showed that, there was a significant decrease in T4 and FSH, while there was non-significant decrease in T3. as shown in Table (4).

Table 4: Comparison of the Studied Variables Between PCOS and Non PCOS Groups.

Parameter	PCOS group N= (26)	NON PCO group N= (16)	P-value
	Mean ± SD		
Age (years)	34.79±9.1	32.7±8.87	**0.255**
BMI (kg/m^2)	28.53±5.05	23.20±2.18	**0.012**
TSH (uIU/ml)	8.79 ± 2.73	6.59 ± 2.90	***0.05**
Total T3(ng/ml)	0.82 ± 0.35	0.95 ± 0.51	**0.65**
Total T4(ng/ml)	3.10 ± 1.05	4.29 ± 0.716	***0.002**
Prolactin(ng/ml)	40.28 ± 13.32	33.46 ± 16.75	**0.105**
FSH (mIU/ml)	9.02 ± 3.36	10.37 ± 8.44	***0.04**
LH (mIU/ml)	17.52 ± 8.82	13.58 ± 6.82	**0.09**

DISCUSSION

The relationship between PCOS and thyroid disorders is still under study and no conclusive findings have yet been reached on the relationship between these two common disorders among women who are at reproductive age. Several studies are still investigating this relationship to understand the pathophysiological mechanism and the factors contributing to the existence of this relationship.[22,23]

Both disorders cause dysfunction of female sex hormones and thus dysfunction of the menstrual cycle resulting in infertility in women as well as metabolic disorders. From here comes the relationship between them and the likelihood of a causal relationship between them.[24,25]

Many studies suggest that changing the balance between estrogen and androgen in PCOS may lead to hypothyroidism, but this mechanism is categorically uncertain. On the other hand, hypothyroidism was not associated in all cases with PCOS.[26]

This study showed an increase in the mean of TSH and a decrease in the mean of T4 and T3 in women with hypothyroidism compared to the control group. This rise is due to the loss of negative feedback mechanism by thyroid hormones on the thyroid stimulating hormone, increasing its concentration, which is the first indicator of primary hypothyroidism and this was confirmed by other studies on the investigation of hypothyroidism.[27,28]

The results of this study also showed an increase in the mean BMI in the patient group compared to the control group. This is also consistent with other studies suggesting that hypothyroidism leads to a rise in BMI, which is attributable to a decrease in metabolic rate.[29]

The results showed a significant difference in the mean concentration of LH, FSH, and prolactin between the patient group and the control group. These findings are consistent with other studies that have shown an increase in the concentration of these hormones in thyroid hypothyroidism. Some reports indicate that TRH can also induce the production of prolactin, which is thought to have adverse effects on the biosynthesis of sex hormones, thereby leading to infertility. Insufficient production of gonadotropin-releasing hormone (GnRH) is accompanied with suppressed production of luteinizing hormone (LH) and follicle-stimulating hormone (FSH).[30,31]

The results of this study showed that 65% of women with hypothyroidism involved in this study had PCOS, which was confirmed using an ultrasound, and 35% did not have PCOS. When compared to the anthropometric and biochemical variables between the two groups, there were significant differences between the two groups in the mean of BMI, where they were higher in the group with PCOS. This is consistent with other studies that showed a high BMI in women with PCOS.[32,33]

While the results did not show a significant difference between the two groups in age. where the two groups were of the same age group and considered to be of young ages, This is consistent with another study that indicated that the PCOS decreases as age.[34,35] When comparing the two groups in biochemical variables, the results showed that there were significant differences in the concentration of TSH, T4 and FSH, where the mean TSH was higher (accompanied by a decrease in average T4) in women with hypothyroidism and polycystic ovaries compared to those with hypothyroidism and free PCOS. These results are consistent with studies that showed that TSH levels were higher in women with PCOS.[36] The results have shown an increase in the mean concentration of LH and prolactin in the group of hypothyroidism with PCOS compared group of hypothyroidism without PCOS, this agreed with many studies that showed an increase in LH and prolactin levels in PCOS.[37,38]

These results also showed that FSH mean was lower in the group of hypothyroidism with PCOS compared group of hypothyroidism without PCOS, it is consistent with studies showed that FSH level is low in PCOS compared LH level,[39] this is due to a disturbance in the secretion pattern of the goadotrophin-releasing hormone (GnRH) results in the relative increase in LH to FSH release. Ovarian estrogen is responsible for causing an abnormal feedback mechanism that caused an increase in LH release.[40]

A Previous study indicat that The severity of ovarian morphology also depends on duration and severity of underlying primary hypothyroidism. In most severe cases like long standing untreated cases of congenital hypothyroidism ovarian morphology can be very striking and can even be mistaken for ovarian malignancies.[41] Based on our findings we can conclude that hypothyroidism may play a role in the occurrence of PCOS. Because in our results there was a difference in severity of hypothyroidism which was indicated by the difference in TSH level between the two groups(with PCOS higher than without PCOS). On the other hand, hypothyroidism was accompanied by an increase in BMI, and the mean of BMI was higher in the group of hypothyroidism with PCOS compared to the group of hypothyroidism without PCOS group, increasing BMI is one of the contributing factors to the occurrence of polycystic ovaries, On the other hand, increasing BMI is one of the factors causing insulin resistance and many studies have indicated that insulin resistance is a risk factor for PCOS. High concentration of insulin leads to disorders in hypothalamus and pituitary function resulting in increased production of androgens that cause PCOS.[42] If the increase in BMI is caused by hypothyroidism as a major cause, this increase may be the cause of insulin resistance, which later causes PCOS.

However, the lack of insulin concentration and the calculation of insulin resistance in this study prevented clarification of the relationship between insulin resistance, BMI and hypothyroidism and their effects on the occurrence of polycystic ovaries.

CONCLUSIONS

This study concluded hypothyroidism significantly correlated with PCOS patients. A significant effect of hypothyroidism on clinical, metabolic, and hormonal characteristics of PCOS patients was seen in our study. Hence, screening for a thyroid problem in PCOS patients is recommended, even in the absence of symptoms related to thyroid dysfunction, which may benefit the patient clinically. The limitation of our study that it was a single-centered study, so future studies should be carried on large numbers of patients with and without PCOS.

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