Al-Azhar Med. J . (Surgery). *Vol. 52 (2), April, 2023, 601-616*
DOI: 10.21608/amj.2023.291652
https://amj.journals.ekb.eg/article_291652.html

THYROIDITIS AS ARISK FACTOR IN POLYCYSTIC OVARIAN SYNDROME WOMEN

By

Waleed Fawzy Mohamed Abo-Tahoon, Fahd Abd El-Aal El-Omda, Ahmed Taha Abd El-Fattah and Mahmoud Abd Elatif Hashish*

Department of Obstetrics and Gynecology and Clinical Pathology*, Faculty of Medicine, Al-Azhar University

E-mail: j17161452@gmail.com

ABSTRACT

Background: Polycystic ovary syndrome (PCOS) is a metabolic syndrome, characterized by anovulation, hyperandrogenism and polycystic ovary. PCOS exists commonly among women at reproductive age with an incidence rate of 6-10%.

Objective: To study thyroiditis as a risk factor in Polycystic Syndrome Patients.

Patients and Methods: This study was a cross sectional, observation study, this study included all consecutive PCOS patients with thyroiditis visiting the outpatient clinics of the Departments of Obstetrics and Gynecology Dar El-Shefa Damnhour Hospital, carried out on 60 patients divided into two groups: Group (A): 30 PCOS patients (Case group) and Group (B): (30) Non-PCOS patients (Control group). Between December 2019 to December 2020.

Results: Thyroid hormone in PCO group was significantly higher than non PCO group, also the Thyroglobulin antibody and Anti- thyroid peroxidase was significantly higher in PCO group more than non PCO. The Luteinizing hormone, Follicle stimulating hormone and Luteinizing hormone/ Follicle stimulating hormone ratio show insignificant difference between the two studied groups. The hormonal assay including estradiol, progesterone and free testosterone showed a significant increase in PCO patients more than non PCO group. The fasting blood sugar, HOMA Insulin resistance, lipid profile showed a significant increase in PCO group more than non PCO group. Regarding thyroid abnormalities, it was found that there was an increasing in goiter, overt hypothyroid, autoimmune thyroiditis and Graves disease in PCO group more than non PCO.

Conclusion: Thyroiditis considered a risk factor in polycystic syndrome patients and increase the symptoms of PCOs. Patients with thyroid peroxidase and thyroglobulin autoantibodies are likely to develop thyroid dysfunction later in life.

Key words: ACTH, AIT, DHEA, DHEAS and GnRH.

INTRODUCTION

Polycystic ovary syndrome (PCOS) is a metabolic syndrome, characterized by anovulation, hyperandrogenism and polycystic ovary. PCOS exists commonly among women at reproductive age with an incidence rate of 6-10% *(Sanchez-Garrido and TenaSempere, 2020)*. The clinical manifestation of PCOS includes oligomenorrhea, infertility. Acne, hirsutism, fat, and acanthosisnigricans and so on. In addition, these patients may develop with many other related endocrine and metabolic diseases, and have increased risk of suffering endometrial cancer, impaired glucose tolerance, diabetes, and cardiovascular disease *(Wild et al., 2010)*. Researches

about the pathogenesis of PCOS mainly focus on two interrelated metabolic elements-insulin resistance (IR) and hyperandrogenism *(Rosenfield Ehrmann 2016)*. Nevertheless, pathogenesis of PCOS still remains unclear *(Du and Li, 2013)*.

Several researchers suggested the relationship between PCOS and autoimmunity with controversial results, which showed that serologic makers of autoimmunity elevated in patients with PCOS. Hypothesized that functional autoantibodies could contribute to the development of PCOS, which represents hyperfunction of follicular recruitment in the ovaries, similar to hyperthyroidism in Graves' disease. So, can we regard PCOS as a self-immune disease? *(Hefler-Frischmuth et al., 2010)*.

Autoimmune thyroiditis (AIT), or named Hashi-moto's thyroiditis, or chronic lymphocytic thyroiditis, is the most prevalent autoimmune state that affects up to 5-20% of women during the age of fertility which is due to chronic inflammation of the thyroid and can lead to hypothyroidism finally. Most of the AIT patients show positivity for anti-TPO and/or anti-Tg and a typical hypoechogenic pattern in ultrasound scan *(Benetti-Pinto et al., 2013)*. The link between AIT and PCOS has been reported in several studies, but it's true pathogenesis is far from being elucidated *(Artini et al., 2013)*.

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. These cases have been given an eponym Van Wyk and Grumbach syndrome, after the scientist who first described the case *(Hefler-Frischmuth et al., 2010)*.

Are we right in saying, therefore that women with PCOS are more predisposed to autoimmune diseases? There seem to be some theoretical basis for this statement. PCOS is known to be a hyperestrogenic state. Hyperestrogenism has been proposed as one explanation for the occurrence of increased autoimmune diseases in females when compared to males. Estrogen receptors have a proliferative action on B-lymphocytes and estrogen receptors are also present on T-cell as well as macrophages *(Du and Li, 2013)*.

Thyroid disorders and polycystic ovary syndrome (PCOS) are two of the most common endocrine disorders in the general population. Although the etiopathogenesis of hypothyroidism and PCOS is completely different, these two entities have many features in common. An increase in ovarian volume and cystic changes in ovaries have been reported in primary hypothyroidism. In the other direction, it is increasingly realized that thyroid disorders are more common in women with PCOS as compared to the normal population *(Sinha et al., 2013)*.

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 purpose of descriptive and exploratory review is to explore the relationship between these two disorders. To generate

a hypothesis linking these disorders, terms "PCOS," "autoimmunity," "subclinical hypothyroidism "thyroid autoimmunity," "thyroid autoantibodies." "leptin," obesity" and "thyroiditis" were searched in various combination in PubMed. Google scholar and Embase. Relevant articles from this search as well as from cross references were retrieved and included. Elucidation of this relationship between thyroid disorders and PCOS requires answers to two questions: (1) What happens to ovaries in thyroid disorders? (2) What happens to thyroid in PCOS? *(Garelli et al., 2013).*

This question is relatively easier to answer, and pathways leading to change in ovarian morphology in hypothyroidism are well-known. In the presence of hypothyroidism, ovarian morphology becomes poly-cystic. Hence, thyroid disorders are one of the exclusion criteria before making a diagnosis of PCOS in any women. Rise in thyrotropin-releasing hormone (TRH) in primary hypothyroidism leads to increased prolactin and thyroid stimulating hormone (TSH) *(Ramanand et al., 2013).*

Prolactin contributes toward polycystic ovarian morphology by inhibiting ovulation as a result of the change in the ratio of follicle stimulating hormone (FSH) and luteinizing hormone and increased dehydroe-piandrosterone from the adrenal gland. Increased TSH also contributes due to its spill-over effect on FSH receptors. Increased collagen deposition in ovaries as a result of hypothyroidism has also been suggested. In a study, on somewhat less severe primary hypothyroidism, by Muderriset al., 26 treatment naïve females with primary hypothyroidism, with mean TSH 57.1 mcg/dl, underwent evaluation of ovarian volume before and after replacement with thyroxine *(Ganie et al., 2010).*

Twenty six healthy normal controls were also recruited. Ten of 26 hypothyroid females had polycystic appearing ovaries on ultrasound sonography test at baseline. All women with primary hypothyroidism had significantly higher ovarian volumes than controls. Even the subgroup without polycystic appearing ovaries had significantly higher ovarian volumes. However, there was no correlation of TSH levels with cyst formation. The most remarkable finding of this study was normalization of ovarian volume in all patients, with or without polycystic appearing ovaries, after replacement of thyroxine.

The pathophysiological pathway connecting these two disorders has not been clearly delineated as of 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. The link between thyroid functions and obesity is again an interesting one, with unclear pathophysiological mechanisms however, enough evidence to say that TSH is higher in people with high BMI *(Benetti-Pinto et al., 2013).*

The present work aimed to study the thyroiditis as a risk factor in Polycystic Syndrome Patients.

PATIENTS AND METHODS

This was a prospective study including consecutive PCOS patients with thyroiditis visiting the outpatient clinics of the Departments of Obstetrics and Gynecology, Dar El-Shefa Damnhour Hospital between December 2019 and December 2020.

Inclusion criteria: Patients with thyroid disorders having or did not have PCOS.

The PCOs patients were defined using Rotterdam criteria which included any 2 of following 3 to be present:

1. Abnormal menstruation including amenorrhea (absence of menstrual cycles in the last 6 months) or oligomenorrhea (cycles >35 days).
2. Hyperandrogenism either clinical (hirsutism defined by Ferriman and Gallwey score > 7 by physician and/or acne and/or alopecia (androgenic pattern)) or biochemical (testosterone > 2.0 nmol/L).
3. Presence of polycystic ovaries (follicles 2–9mm in diameter and ≥12 in number or ovarian volume ≥ 10 cm3) by ultarsonographic evaluation of the ovaries and antral follicle count (AFC) were performed trans vaginally in the lithotomy position with MINDRAY brand DE-7 T-model ultrasonographic device.

After ruling out other differential diagnoses as congenital adrenal hyperplasia (CAH), virilizing tumors, Cushing's syndrome and prolactinomas.

Adrenocorticotropin-stimulated 17-hydroxyprogesterone test and dexamethasone suppression test and/or 24-hour urinary cortisol excretion, if hypercortisolism is clinically suspected, were used to exclude other etiologies for hyperandrogenism. Subjects with known history of endocrine dysfunctions like Cushing's syndrome, hyperprolactinemia, and gonadal or adrenal neoplasm were excluded. 30 age-matched healthy females without the history of PCOS and known thyroid abnormality were selected as controls.

Sixty patients were divided into two groups:

- **Group (A):** Thirty PCOS patients (Case group).
- **Group (B):** Thirty non-PCOS patients (Control group).

All patients were subjected to the following:

Thyroid ultrasound: USG of the thyroid was done in presence of goiter. USG thyroid was performed using a 7.5 MHz transducer with duplex sonography. The thyroid was considered hypoechoic when its signal was equal or below the echogenicity of the surrounding neck muscles.

Physical Examination: Height (cms), Weight (kg) and BMI.

Biochemical Investigations:

1. Fasting Blood Glucose.
2. Two hours post glucose.
3. Fasting (TSH) Thyroid Stimulating Hormone.
4. Fasting Insulin.
5. Total Testosterone.
6. Free T3 and Free T4.
7. Anti-thyroperoxidase antibody (anti-TPO ab).

8. HOMA IR.
9. LH, FSH and LH/FSH ratio.
10. Progesterone (P).
11. Estrogen (E2).
12. Total cholesterol.
13. Triglycerides.
14. LDH.
15. HDL.

Calculated Parameters:

A valid method of assessing Insulin Resistance was HOMA-IR.

Homeostatic Assessment Model of Insulin Resistance (HOMA-IR) = Fasting plasma Insulin (μU/mL)* Fasting plasma glucose (mmol 22.5).

Patient was advised to come in 8-10 hrs fasting. They were adviced to take their dinner by 8 PM on the previous day, then no food should (carbohydrate diet) be taken. Next day morning tea / coffee / any carbohydrate drink should avoided. Patient was to sit in a chair calmly and with stretched forearm. Blood was drawn by 7-8AM under aseptic precaution. Fasting sample was collected for Glucose, Insulin, Testosterone, TSH, then 75gm of glucose dissolved in 300ml of water was given to the patients and allowed to take for a period of 5 min. Post glucose sugar sample was taken 2 hrs after drinking glucose. In the mean time patients were instructed not to do exercise or walking for long distance.

Statistical analysis:

Data were fed to the computer using IBM SPSS software package version 24.0.

Qualitative data were described using number and percent. Comparison between different groups regarding categorical variables was tested using Chi-square test.

For normally distributed data, comparison between two independent populations was done using independent t-test, as for the abnormality distributed data were done using Mann-Whitney test.

The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant as the following P-value <0.05 was considered significant.

RESULTS

Age in group I ranged from 24-35 with mean value 29.30-3.25 and in group II ranged from 25-36 with mean value 30.4-3.74. BMI in group I ranged from 26.3-31.9 with mean value 29.07-1.86 and in group II ranged from 23.932.2 with mean value 28.1-2.73. There was no statistically significant difference between the two studied groups regarding age and BMI **(Table 1)**.

Table (1): Comparison between the two studied groups regarding demographic and anthropometric data

Groups / Parameters	Group I "Patients with PCO" "n=30"	Group II "Patients without PCO" "n=30"	P value
Age (years)			
Range	24.0-35	25-36	0.229
Mean	29.30	30.4	
S.D.	3.25	3.74	
BMI (Kg/m2)			
Range	26.3-31.9	23.9-32.2	0.113
Mean	29.07	28.1	
S.D.	1.86	2.73	

Using: Independent Sample t-test; p-value >0.05 NS

TSH in group I ranged from 0.9-15.9 with mean value 7.34-5.29 and in group II ranged from 0.5-7 with mean value 3.7-1.76. T3 in group I ranged from 3-13 with mean value 7.51-3.11 and in group II ranged from 1.8-5.2 with mean value 3.7-1.11. T4 in group I ranged from 0.2-18.9 with mean value 5.75-3.63 and in group II ranged from 0.4-7 with mean value 2.8-2.28. There was highly statistically significant difference between the two studied groups regarding TSH, free T3 and free T4 ($P < 0.05$). That anti-TPO in group I ranged from 10-49 with mean value 38-13.82 and in group II ranged from 9-38 with mean value 27.8-7.86. TG antibody in group I ranged from 20-2200 with mean value 237.67-485.12 and in group II ranged from 0.0-120 with mean value 22-31.05. There was statistically significant difference between two studied groups regarding TG antibody ($P<0.05$) Also, there was a statistically significant difference regarding anti-TPO **(Table 2)**.

Table (2): Comparison between the two studied groups regarding thyroid function and Anti-TPO and TG antibody

Parameters \ Groups	Group I "Patients with PCO" "n=30"	Group II "Patients without PCO" "n=30"	P value
TSH (mIU/mL)			
Range	0.9-15.9	0.5-7	<0.001
Mean ±S.D.	7.34±5.29	3.7±1.76	
Free T3 (pg/mL)			
Range	3.0-13	1.8-5.2	<0.001
Mean ±S.D.	7.51±3.11	3.7±1.11	
Free T4 (ng/dL)			
Range	0.2-18.9	0.4-7	<0.001
Mean ±S.D.	5.75±3.63	2.8±2.28	
Anti-TPO (IU/mL)			
Range	10.0-49	9.0-38	0.014
Mean ±S.D.	38.00±13.82	27.8±7.86	
TG antibody (U/I)			
Range	20.0-2200	0.0-120	0.022
Mean ±S.D.	237.67±485.12	22.0±31.05	

Using: Mann-Whitney test;
p-value >0.05 NS; p-value <0.05 S; p-value <0.001 HS

LH in group I ranged from 5-29 with mean value 13.12-7.6 and in group II ranged from 5-24 with mean value 5.81-3.7. FSH in group I ranged from 2-7 with mean value 4.30-1.76 and in group II ranged from 1.7-5.9 with mean value 3.7-1.10. LH/FSH in group I ranged from 0.9-14 with mean value 4.98-3.70 and in group II ranged from 0.9-10.58 with mean value 4.5-2.55. There was statistically significant difference between the two studied groups regarding LH, while there is no statistically significant difference between groups as regard FSH and LH/FSH ratio **(Table 3)**.

Table (3): Comparison between the two studied groups regarding LH, FSH and LH/FSH ratio

Parameters \ Groups	Group I "Patients with PCO" "n=30"	Group II "Patients without PCO" "n=30"	P-value
LH (mIU/mL)			
Range	5.0-29	5.0-24	<0.001
Mean±S.D.	13.12±7.6	5.81±3.7	
FSH (mIU/mL)			
Range	2.0-7	1.7-5.9	0.227
Mean ±S.D.	4.30±1.76	3.7±1.10	
LH/FSH			
Range	0.9-14	0.9-10.588	0.519
Mean ±S.D.	4.98±3.70	4.5±2.55	

Using: Mann-Whitney test;
p-value >0.05 NS; p-value <0.05 S; p-value <0.001 HS

Estradiol in group I ranged from 30-86 with mean value 52.90-16.22 and in group II ranged from 24-112 with mean value 63.1-26.38. Progesterone in group I ranged from 0.6-4.2 with mean value 2.22-1.18 and in group II ranged from 3.9-14.2 with mean value 7.6-3.34. Free testosterone in group I ranged from 8-40 with mean value 24.33-9.26 and in group II ranged from7-20 with mean value 13.8-4.36. There was statistically significant difference between two studied groups regarding progesterone and free testosterone (P<0.05) while there was no statistically significant difference regarding estradiol **(Table 4)**.

Table (4): Comparison between the two studied groups regarding hormonal assay

Parameters \ Groups	Group I "Patients with PCO" "n=30"	Group II "Patients without PCO" "n=30"	P value
Estradiol (pg/ml)			
Range	30.0-86	24.0-112	0.019
Mean ±S.D.	52.90±16.22	63.1±26.38	
Progesterone (ng/mL)			
Range	0.6-4.2	3.9-14.2	<0.001
Mean ±S.D.	2.22±1.18	7.6±3.34	
Free testosterone (pg/mL)			
Range	8.0-40	7.0-20	<0.001
Mean ±S.D.	24.33±9.26	13.8±4.36	

Using: Mann-Whitney test;
p-value >0.05 NS; p-value <0.05 S; p-value <0.001 HS

FBS in group I ranged from 76-124 with mean value 99.53-12.92 and in group II ranged from 71-120 with mean value 92.5-15.50. HOMA IR in group I ranged from 1-4.5 with mean value 2.87-0.92 and in group II ranged from 0.93.5 with mean value 2.3-0.73. There was statistically significant difference between the two studied groups regarding HOMA-IR while FBS insignificant difference between groups **(Table 5)**.

Table (5): Comparison between the two studied groups regarding FBS and HOMA-IR

Parameters \ Groups	Group I "Patients with PCO" "n=30"	Group II "Patients without PCO" "n=30"	P value
FBS≠			
Range	76.0-124	71.0-120	0.061
Mean ±S.D.	99.53±12.92	92.5±15.50	
HOMA -IR (mU mmol/l)#			
Range	1.0-4.5	0.9-3.5	0.024
Mean ±S.D.	2.87±0.92	2.3±0.73	

Using: ≠Independent Sample t-test; #Mann-Whitney test;
p-value >0.05 NS; p-value <0.05 S; p-value <0.001 HS

Total cholesterol in group I ranged from 126-273 with mean value 200-45.33 and in group II ranged from 121-235 with mean value 170.6-32.69. Triglycerides in group I ranged from 95-154 with mean value 126.33-16.58 and in group II ranged from 75-109 with mean value 91-11.7. LDH in group I ranged from 105-178 with mean value 144.13-18.18 and in group II ranged from 85-139 with mean value 110.5-15.61. HDL in group I ranged from 25-55 with mean value 38.63-8.60 and in group II ranged from 40-70 with mean value 53.4-8.92. There was statistically significant difference between the two studied groups regarding total cholesterol, triglycerides, LDH and HDL **(Table 6)**.

Table (6): Comparison between the two studied groups regarding lipid profile

Parameters \ Groups	Group I "Patients with PCO" "n=30"	Group II "Patients without PCO" "n=30"	P value
Total cholesterol (mg/dL)			
Range	126.0-273	121.0-235	0.014
Mean	200.00	170.6	
S.D.	45.33	32.69	
Triglycerides (mg/dL)			
Range	95.0-154	75.0-109	0.0001
Mean	126.33	91.0	
S.D.	16.58	11.70	
LDH (mg/dL)			
Range	105.0-178	85.0-139	0.0001
Mean	144.13	110.5	
S.D.	18.18	15.61	
HDL (mg/dL)			
Range	25.0-55	40.0-70	0.0001
Mean	38.63	53.4	
S.D.	8.60	8.92	

In group I, goiter was 9(30%), overt hypothyroid was 4(13.3%), autoimmune thyroiditis was 3(10%) and graves disease was 2(6.7%) while in group II was 2(6.7%), 1(3.3%), 1(3.3%) and none respectively. There was statistically significant difference between the two studied groups regarding goiter, while there was no statistically significant difference regarding overt hypothyroid, autoimmune thyroiditis and graves disease **(Table 7)**.

Table (7): Comparison between the two studied groups regarding thyroid abnormalities

Parameters \ Groups	Group I "Patients with PCO" "n=30"		Group II "Patients without PCO" "n=30"		P value
	No.	%	No.	%	
Goiter	9	30.0	2	6.7	0.024
Overt hypothyroid	4	13.3	1	3.3	0.161
Autoimmune thyroiditis	3	10.0	1	3.3	0.301
Graves disease	2	6.7	0	0.0	0.492

DISCUSSION

The results of our study showed that the basic demographic data age and anthropometric data (BMI) in the two groups were matched without significant difference, these results were important to eliminate the effect of demographic data on the net results and the only affected factor was the PCOs.

Thyroid hormone including TSH, free T3 and T4 showed a significant increase in PCO patients group more than the non PCO group. The anti TPO showed insignificant difference between the two groups, while TG antibody and Anti-TPO show a significant increase in PCOs.

In agreement with our study, *Sinha et al. (2013)* in a study on thyroid disorders in polycystic ovarian syndrome Subjects, found that PCOS patients higher mean TSH level than control group. Also, they found that there was a significant increase in both T3 and T4 in PCOs patients more than the non PCO.

Kachuei et al. (2012) showed that the prevalence of autoimmune thyroiditis in patients with polycystic ovary syndrome were significantly higher in PCOS patients.

TPO Ab were significantly higher in PCOS patients. Our current Wnding conWrms the observation has shown elevated a threefold higher prevalence of AIT in patients with PCOS *(Ott et al., 2010).*

It was shown that TSH anti-TPO and anti-Tg levels were significantly higher in PCOS woman than control, which was in accordance with the results of *Singh et al. (2020).* Explanation for the high incidence of thyroid autoimmunity in PCOS is open to speculation. The cause of AIT is thought to be a combination of genetic susceptibility and environmental factors.

In our study, the level of LH showed insignificant difference between the two studied groups, while FSH showed a significant increase in patients with PCO. The LH/FSH ratio showed and insignificant difference between the two groups. On the other hand, the levels of estradiol and progesterone showed significant decreases in patients with PCO, while the free testosterone showed a significant increase in patients with PCO.

In agreement with our study, *Alawneh et al. (2012)* study the Hypothyroidism A possible Risk Factor for Polycystic Ovary Syndrome among Jordanian Women, found that a large differences in mean FSH levels were found that not significantly different between any groups.

Similar results were obtained for estradiol and progesterone between all groups. Our results agreed with *Marques et al. (2018)* who observed that when puberty begins, the anterior pituitary gland reacts to increased estrogen levels by increasing LH concentrations and reducing FSH production, which causes irregular stimulation of ovarian-derived estradiol and androgens as well as abnormal maturation of ovarian follicles and a state of chronic anovulation.

Estradiol levels can be slightly raised or normal in PCOS patients and in patients with other hyperandrogenism conditions. *Stefano et al. (2015)* found that increasing estradiol is among hormonal changes associated with overt hypothyroidism. Our results regarding estradiol disagreed with them as we found

a negative effect between free tri-iodothyronine and estradiol in the control group.

The results of our study showed that the lipid profile including total cholesterol, triglycerides and LDH showed a significant increase in patients with PCO more than the patients without PCO; On the other hand, LDL showed a significant decrease in patients with PCO less than the patients without PCO.

Many studies have identified variations in cholesterol, TG, and LDL in patients with subclinical hypothyroidism, but the results are not consistent these was an increase was total cholesterol and LDL in patients with subclinical hypothyroidism without any change in TG or HDL compared with controls. Observed similar results in Kuwaiti women *(Elizabeth, 2012).*

In a study carried by *Alawneh et al. (2012),* they found that an increased LDL concentrations were noted with increasing total cholesterol in both hypothyroidism and PCOS groups, and differences between them were not significant statistically.

However, differences were significant between either hypothyroidism or PCOS group as compared with the control group. In contrast, *de-Medeiros et al. (2017)* found that there was no change in lipid levels among patients with subclinical hypothyroidism compared with controls.

Another study by *El-Hafez et al. (2013)* did not reveal any alterations in levels of total cholesterol, TG, or LDL among euthyroid PCOS subjects who were stratified on the basis of a TSH cutoff of 2 IU/L. Whether hypothyroidism alters the phenotypic expression of PCOS, and whether subclinical hypothyroidism has any effect on PCOS in these patients is not apparent. In our study, we did not measure clinical or biochemical parameters for comparing between groups, but we found differences and similarities in hormone and lipid parameters between groups. Based on our results, we conclude that, except for minor changes in lipid profile, PCOS is not altered in the presence of subclinical hypothyroidism.

In this study, regarding the thyroid abnormalities, it was found that in group I, goiter was in 30%, overt hypothyroid in 13.3%, autoimmune thyroiditis in 10%, and graves disease in 6.7%. In group II, was 6.7%, 3.3%, 3.3% and none respectively. There was a statistically significant difference between the two studied groups regarding goiter, while there was no statistically significant difference regarding overt hypothyroid, autoimmune thyroiditis and graves disease.

In agreement without study, *Sinha et al. (2013)* found that goiter was present in 27.5% patient, subclinical hypothyroidism was present in 22.5%, and clinical hypothyroidism in 2.5% cases. Among these hypothyroid patients, autoimmune hypothyroidism was present in 22.5% patient.

Thus, this prospective case-control revealed significant higher prevalence of thyroid disorders among young PCOS patients compared to age matched controls. These findings were very close to the study done by *Singh et al. (2020)* where they observed a prevalence of autoimmune thyroiditis (biochemically)

first prospective multicenter studies done by Singh, et al. from Germany on this very issue. Some other studies reported even higher prevalence of autoimmune thyroiditis in PCOS subjects.

Didem et al. (2011) found that thyroid nodules were detected in 27.1% of patients, 10 had solitary and 19 had multiple nodules.

Thyroid pathologies were observed in half of the patients with PCOS. *Kachuei et al. (2012)* has also shown significantly higher prevalence of autoimmune thyroiditis and goiter in PCOS patients than that in control subjects, i. e. goiter 62.3% vs. 35.7%.

CONCLUSION

Thyroiditis considered a risk factor in polycystic syndrome patients and increase the symptoms of PCOs. Our data suggested that all patients with PCOS should be screened for thyroid function and thyroid-specific autoantibodies even without evidence of overt thyroid dysfunction, as patients with TPO and TG autoantibodies are likely to develop thyroid dysfunction later in life.

REFERENCES

1. **Alawneh SM, Hananeh WM, Ahmed D and Qar J (2012):** Hypothyroidism A possible Risk Factor for Polycystic Ovary Syndrome among Jordanian Women. Journal of Advanced Biomedical and Pathobiology Research, 2(4):155-64.
2. **Artini PG, Uccelli A, Papini F, Simi G, Di Berardino OM, Ruggiero M and Cela V (2013):** Infertility and pregnancy loss in euthyroid women with thyroid autoimmunity. Gynecol Endocrinol, 29: 11-17.
3. **Benetti-Pinto CL, Berini VR, Garmes HM and Teatin CR (2013):** Subclinical hypothyroidism in young women with polycystic ovary syndrome: An analysis of clinical, hormonal, and metabolic parameters. Fertil Steril. 99: 588-92.
4. **Cai J, Zhang Y, Wang Y, Li S, Wang L, Zheng J, Jiang Y, Dong Y, Zhou H, Hu Y, Ma J, Liu W and Tao T (2019):** High thyroid stimulating hormone level is associated with Hyperandrogenism in Euthyroid polycystic ovary syndrome (PCOS) women, independent of age, BMI, and thyroid autoimmunity: a cross- sectional analysis. Front Endocrinol. 10: 222- 231.
5. **De-Medeiros SF, Yamamoto MMW, de-Medeiros MAS, Barbosa JS and Norman RJ (2017):** Should Subclinical Hypothy-roidism Be an Exclusion Criterion for the Diagnosis of Polycystic Ovary Syndrome?. J Reprod Infertil. 18 (2): 242-250.
6. **Didem O, Neslihan C, Fevzi B, Alper U, Reyhan E and Bekir C (2011):** Prevalence of thyroid pathologies in patients with polycystic ovary syndrome. Endocrine Abstracts. 26: 92.
7. **Du D and Xuelian L (2013):** The relationship between thyroiditis and polycystic ovary syndrome: a meta-analysis. International Journal of Clinical and Experimental Medicine. 6: 880–889.
8. **El-Hafez HA, Elrakhawy MM, El-Aziz SA and El-Eshmawy MM**

(2013): Thyroid function and volume are associated with anthropometric measurements and insulin resistance in Egyptian women with polycystic ovary syndrome. J Diabetes Metab. 4: 1–5.

9. **Elizabeth N (2012):** Pearce, Update in Lipid Alterations in Subclinical Hypothyroidism. The Journal of Clinical Endocrinology and Metabolism. 97 (2): 326– 333.
10. **Escobar-Morreale HF (2018):** Polycystic ovary syndrome: definition, aetiology, diagnosis and treatment. Nature Reviews Endocrinology. 14(5): 270-84.
11. **Ganie MA, Marwaha RK, Aggarwal R and Singh S (2010):** High prevalence of polycystic ovary syndrome characteristics in girls with euthyroid chronic lymphocytic thyroiditis: A casecontrol study. Eur J Endocrinol. 162: 1117-22.
12. **Garelli S, Masiero S, Plebani M, Chen S, Furmaniak J, Armanini D and Betterle C (2013):** High prevalence of chronic thyroiditis in patients with polycystic ovary syndrome. European Journal of Obstetrics, Gynecology, and Reproductive Biology. 169: 248–251.
13. **Hefler-Frischmuth K, Walch K, Huebl W, Baumuehlner K, Tempfer C and Hefler L (2010):** Serologic markers of autoimmunity in women with polycystic ovary syndrome. Fertility and Sterility. 93(7): 2291-4.
14. **Hepşen S, Karaköse M, Çakal E, Öztekin S, Ünsal İ, Akhanlı P, Uçan B and Özbek M (2018):** The assessment of thyroid autoantibody levels in euthyroid patients with polycystic ovary syndrome. J Turk Ger Gynecol Assoc. 19: 215–9.
15. **Kachuei M, Jafari F and Kachuei A (2012):** Prevalence of autoimmune thyroiditis in patients with polycystic ovary syndrome. Arch Gynecol Obstet. 285: 853–856.
16. **Marques P, Skorupskaite K, George JT and Anderson RA (2018):** Physiology of GNRH and gonadotropin secretion. Endotext. 19 (1): 246-253.
17. **Monteleone P, Parrini D, Faviana P, Carletti E, Casarosa E and Uccelli A (2011):** Female infertility related to thyroid autoimmunity: the ovarian follicle hypothesis. Am J Reprod Immunol. 66(2): 108–14.
18. **Ott J, Aust S, Kurz C, Nouri K, Wirth S and Huber JC (2010):** Elevated antithyroid peroxidase antibodies indicating Hashim- oto's thyroiditis are associated with the treatment response in infertile women with polycystic ovary syndrome. Fertil Steril. 94: 2895–2897.
19. **Otusanya AD (2020):** If You Never Came in and Saw Me, You Would Probably Be Dead: Exploring Intercultural Communication and Health Communication Issues Surrounding Pcos (Doctoral dissertation, George Mason University). 2(6): 111-124.
20. **Ramanand GB, Ramanand JB, Patwardhan MII, Changhas RR and Jain SS (2013):** Clinical characteristics of polycystic ovary syndrome in Indian women Indian Endocrinol Metab. 17: 13815- 13822.

21. **Rosenfield RL and Ehrmann DA (2016):** The Pathogenesis of Polycystic Ovary Syndrome (PCOS): The Hypothesis of PCOS as Functional Ovarian Hyperandrogenism Revisited. Endocr Rev. 37(5): 467-520.

22. **Sanchez-Garrido MA and Tena-Sempere M (2020):** Metabolic dysfunction in polycystic ovary syndrome: Pathogenic role of androgen excess and potential therapeutic strategies. Mol Metab. 35: 100937.

23. **Serin AN, Birge Ö, Uysal A, Görar S and Tekeli F (2021):** Hashimoto's thyroiditis worsens ovaries in polycystic ovary syndrome patients compared to Anti-Müllerian hormone levels. BMC Endocr Disord. 21(1): 44- 51.

24. **Singh J, Wong H, Ahluwalia N, Go RM and Guerrero-Go MA (2020):** Metabolic, Hormonal, Immunologic, and Genetic Factors Associated With the Incidence of Thyroid Disorders in Polycystic Ovarian Syndrome Patients. Cureus. 12(11): e11681-e11689.

25. **Sinha U, Sinharay K, Saha S, Longkumer TA, Baul SN and Pal M (2013):** Thyroid disorders in polycystic ovarian syndrome subjects: a tertiary hospital based cross-sectional study from Eastern India. Indian Journal of Endocrinology and Metabolism. 17: 304–309.

26. **Stefano P and Marlieke A (2015):** De Wilde, Angela Falbo, Maria P.H. Koster, Giovanni Battista La Sala, Bart C.J.M. Fauser, Pregnancy complications in women with polycystic ovary syndrome, Human Reproduction Update. 21 (5): 575–592.

27. **Twig G, Shina A, Amital H, Shoenfeld Y (2012):** Pathogenesis of infertility and recurrent pregnancy loss in thyroid autoimmunity. J Autoimmun. 38: 275–81.

28. **Unuane D and Velkeniers B (2020):** Impact of thyroid disease on fertility and assisted conception. Best Practice and Research Clinical Endocrinology and Metabolism. 34: 4- 15.

29. **Wild RA, Carmina E, Diamanti KE, Dokras A, Escobar Morreale HF, Futterweit W, Lobo R, Norman RJ, Talbott E and Dumesie DA (2010):** Assessment of cardiovascular risk and prevention of cardiovascular disease in women with the polycystic ovary syndrome: a consensus statement by the Androgen Excess and Polycystic Ovary Syndrome (AE-PCOS) Society. J Clin Endocrinol Metab. 95: 2038-2049.

إلتهاب الغدة الدرقية المرتبط بالمناعة الذاتية كعامل خطر لدى السيدات اللاتي تعانين من متلازمة تكيسات المبيض

وليد فوزي أبو طاحون، فهد عبد العال العمدة، أحمد طه عبد الفتاح، محمود عبداللطيف حشيش*

قسمي النساء والتوليد والباثولوجية الاكلينيكية*، كلية الطب، جامعة الأزهر

E-mail: j17161452@gmail.com

خلفيـــة البحـــث: متلازمـــة تكـــيس المبـــايض هـــي متلازمـــة أيضـــية تتميـــز بانقطـــاع الإباضـــة وفـــرط الأنـــدروجين وتكـــيس المبـــايض. توجـــد متلازمـــة تكـــيس المبـــايض بشـــكل شائع بين النساء في سن الإنجاب بمعدل حدوث 6-10٪.

الهـــدف مـــن البحـــث: دراســـة التهـــاب الغـــدة الدرقيـــة كعامـــل خطـــر فـــي مرضـــى متلازمـــة تكيس المبايض.

المرضـــى وطـــرق البحـــث: كانـــت هـــذه الدراســـة مقطعيـــة، دراســـة مراقبـــة، شـــملت هـــذه الدراســـة جميـــع مرضـــى متلازمـــة تكـــيس المبـــايض المتعـــاقبين المصـــابين بالتهـــاب الغـــدة الدرقيـــة الـــذين يـــزورون العيـــادات الخارجيـــة لأقســـام النســـاء والـــولادة بمستشـــفى دار الشـــفاء دمنهـــور، وأجريـــت علـــى 60 مريضـــاً مقســـمة إلـــى مجموعتـــان: **المجموعـــة (أ):** 30 مريضـــة بمتلازمـــة تكـــيس المبـــايض (مجموعـــة الحالـــة) و**المجموعـــة (ب):** 30 مريضـــة بمتلازمـــة تكـــيس المبـــايض غيـــر المتعـــدد الكيســـات (المجموعـــة الضـــابطة). نتـــائج البحـــث: أظهـــرت نتـــائج هـــذه الدراســـة أن هرمـــون الغـــدة الدرقيـــة فـــي مجموعـــة متلازمـــة تكـــيس المبـــايض كـــان أعلـــى بشـــكل ملحـــوظ مـــن مجموعـــة متلازمـــة المبـــيض غيـــر المتعـــدد الكيســـات، كمـــا أن الأجســـام المضـــادة للثيروجلوبـــولين ومضـــادات الغـــدة الدرقيـــة كانـــت أعلـــى بشـــكل ملحـــوظ فـــي المبـــيض المتعـــدد الكيســـات مجموعـــة المتلازمـــة أكثـــر مـــن متلازمـــة المبـــيض غيـــر المتعـــدد الكيســـات. يُظهـــر كـــل مـــن الهرمـــون اللـــوتيني والهرمـــون المنبـــه للجريـــب والهرمـــون الملـــوتن نســـبة الهرمـــون المحفـــز للجريـــب فرقًـــا ضـــئيلًا بـــين المجمـــوعتين المدروســـتين. يُظهـــر الفحـــص الهرمـــوني بمـــا فـــي ذلـــك الاســـتراديول والبروجســـتيرون والتستوســـتيرون الحـــر زيـــادة كبيـــرة فـــي مرضـــى متلازمـــة تكـــيس المبـــايض أكثـــر مـــن مجموعـــة متلازمـــة المبـــيض غيـــر المتعـــدد

الكيسات. يُظهر سكر الدم الصائم ومقاومة الأنسولين ونسبة الدهون زيادة كبيرة في مجموعة متلازمة تكيس المبايض أكثر من مجموعة متلازمة المبيض غير المتعدد الكيسات. فيما يتعلق باضطرابات الغدة الدرقية ، فقد وجد أن هناك زيادة في تضخم الغدة الدرقية ، قصور الغدة الدرقية الصريح ، التهاب الغدة الدرقية المناعي الذاتي ومرض جريفز في مجموعة متلازمة تكيس المبايض أكثر من متلازمة المبيض غير المتعدد الكيسات.

الإستنتاج: يعتبر التهاب الغدة الدرقية عامل خطر في مرضى متلازمة تكيس المبيض ويزيد من أعراض متلازمة تكيس المبايض. من المرجح أن يصاب المرضى الذين يعانون من بيروكسيداز الغدة الدرقية والأجسام المضادة الذاتية لهرمون الغدة الدرقية بخلل وظيفي في الغدة الدرقية في وقت لاحق من الحياة.

الكلمات الدالة: موجه قشر الكظر، التهاب الغدة الدرقية المناعي الذاتي، ديهيدرو إيبياندروستيرون، كبريتات ديهيدرو إيبياندروستيرون، الهرمون المطلق لموجهة الغدد التناسلية.