

Study the Association between the Thyroid Autoimmunity Markers and Polycystic Ovary Syndrome in Euthyroid Women

Nassrin Malik Aubead

Lecturer Department of Obs. & Gyn., College of Medicine/University of Babylon-Hilla-Iraq

Abstract

Polycystic ovary syndrome during childbearing age is considered as one of the commonest endocrine disease in reproductive age females, with a prevalence of 4% to 15%. The clinical expression of PCOS is variable, but mostly includes anovulation or oligo-ovulation, clinical or biochemical hyperandrogenism and ovarian polycystic picture in U\S. **Objective:** To determine the levels and prevalence of thyroid antibodies in euthyroid women has PCOS.

Patients and method: A case control study carried in the Infertility clinic of the Babylon Teaching Hospital for maternity and children in Al-Hila city, Babylon governorate, /Iraq in the period from October 1, 2018 to the end of Nov. 2019. **Results:** the current study found a highly statistically significant association between the studied group among the BMI ($P<0.001$), while no significant association between the studied groups regarding the age ($P>0.05$). Eighty percent of the patients (PCOS) group, and 20% in control group presented with family history with thyroid disease. Anti-TG were negative in (85.72%) of the PCOS group patients, 8.57% of the patients with borderline positive and only (5.71%) were positive (>110 IU/ml). TSH level in PCOS group (2.3 ± 0.5) were increase with significant association than that in control group (2.1 ± 0.8), highly significant increase were found in Anti-TPO, Anti-TG, free testosterone and LH in PCOS group than that in control group ($P<0.001$).

Conclusion: There is increased risk of thyroid disease with increase in thyroid Autoimmunity Markers in PCOS patients.

Keyword: PCOS, Anti-TPO, Anti-TG, Thyroid Autoimmunity Markers,

Introduction

Polycystic ovary syndrome during childbearing age is considered as one of the commonest endocrine disease in ladies, with a prevalence of 4% to 15% of the female population of childbearing age being estimated ⁽¹⁾.

The clinical expression of PCOS is variable, but mostly includes absence of ovulation or oligo-ovulation, clinical or biochemical hyperandrogenism and ovarian polycystic picture in U\S ⁽²⁾. Variability in phenotypic expression continues to be a reason for investigation and

should be considered at the time of the clinical approach ⁽³⁾.

The prevalence of thyroid pathology in patients who has PCOS remains a matter of debate. Several studies have shown a relationship between PCOS and the existence of hypothyroidism and autoimmune thyroid disease AITD ⁽⁴⁾. The AITD in PCOS is proposed to be related to genetic factors that also contribute to the pathophysiology of this syndrome, suggesting that autoimmune mechanisms are involved in the pathogenesis of PCOS ⁽⁵⁾.

While insulin resistance (IR) seems to be a fundamental event to initiate or perpetuate the most important pathological conditions of this syndrome, it is associated in obese patients with an increase in adipokines - cytokines and other inflammatory markers

Corresponding author:

Nassrin Malik Aubead

M.B.Ch.B, DOG, CABOG, FIBMS OG, FIRM.

E-mail: NassrinMalik123@yahoo.com

such as, tumor necrosis factor α (TNF α) and IL-6^(6,7). Moreover, its related to a defect in auto phosphorylation receptor, and phosphorylation of signaling molecules coupled to the insulin receptor independently of obesity and body mass index (BMI))⁽⁸⁾. Structural changes of the thyroid gland have been determined in different states of insulin resistance in relation to thyroid nodular disease⁽⁹⁾.

The effects described for insulin resistance establish phenomena of selectivity, maintaining the mitogenic pathways that involve this hormone as a vital factor of cellular growth and generation. The effect of insulin resistant on the thyroid gland recently has been evaluated, and demonstrating that patients with this condition have a greater thyroid mass, as well as a higher prevalence of thyroid nodules, and even recently has been related to early stages of thyroid carcinogenesis. In view of the overexpression of insulin receptors and insulin-like growth factors type 1 and 2 (IGF-1 and 2), with high structural homology and the existence of hybrid tetramers, in cell cultures of thyroid tumors, which They have also been isolated in granulosa and ovarian cells from PCOS patients^(9,10).

One of the common autoimmune disorders in childbearing women (5% to 20%) is the autoimmune thyroid diseases (AITD)⁽¹¹⁾. Previous studies have stated a relation between thyroid autoimmunity in pregnant women and adverse gestational outcomes like preterm labor and recurrent miscarriages⁽¹²⁾; moreover, recently many studies have described that there is an association with PCOS⁽¹³⁾.

Aim of the study: To determine the levels and prevalence of thyroid antibodies in euthyroid ladies with PCOS.

Patients and method:

A case control study carried in the in the Infertility clinic of the Babylon Teaching Hospital for maternity and children in Al-Hila city, Babylon governorate, / Iraq in the period from October 1, 2018 to the end of Nov. 2019. For this study, each patient presented with hypertrichosis and menstrual disturbance with in the age in between 18-40 years who visited the infertility clinic at same period. For determining of PCOS we depend on The Rotterdam Classification in the case of: (1) menstrual disorders such as amenorrhea (no menses for the last six months), oligomenorrhea (cycles of >35 days), (2) clinical and / or biochemical hyperandrogenism, (3) U\ S

pictures show PCO (more than 12 follicles, 2-9 mm in size).

The presence of 2 of these 3 criteria was necessary to determine poly cystic ovarian syndrome when all other diagnoses, such as congenital adrenal hyperplasia, androgen secreting tumors, Cushing's syndrome, and hyperprolactinemia, were excluded⁽¹⁴⁾. Clinical hyper-androgenism (hypertrichosis) with Ferriman-Galway score more than (7) and / or acne and/or androgenic(male) pattern of alopecia⁽¹⁵⁾. Biochemical hyperandrogenemia was determined by increased testosterone. The proportion of luteinizing hormone to follicle stimulating hormone more than two found to be high. To detect the presence of cystic ovaries, ultrasound performed on the transabdominal pelvis. Other causes of hyperandrogenism excluded by 17-OH progesterone stimulated with adrenocorticotropin, a test for dexamethasone suppression, and / or urinary cortisol excretion for 24 hours. Ladies with similar age group who visited the infertility clinics with complains not related to poly cystic ovarian syndrome or thyroid problems, with normal menstruation enrolled as controls (N=35).

Medical history taken in detail, developed physical examination, Age, BMI were recorded.

Laboratory parameters measurement:

Five cc of venous blood samples were collected in the morning from each participants using clot activator tube during menstrual cycle (2-5th days of MC). By using centrifuge the separation of serum were done after standardized time needed and then put in a special refrigerator to frozen at temperature below -80°C to do further analysis. The following serum measurements were achieved: TSH, free thyroxin level (FT4 and FT3), anti-thyroid peroxidase antibody (anti-TPO), anti-thyroglobulin antibody (anti-TG), fasting blood glucose, fasting insulin, LH, FSH, free testosterone.

As we measured the blood glucose in mg/dL so we use can calculate the HOMA-IR (mIU/L) as follow:

Fasting insulin mIU/L multiply by fasting glucose mg/dL divided by (405).

Insulin resistance readings range:

- Normal (less than 3)
- Borderline (3-5)

- Severe IR (more than 5)

Statistical Analysis

Data entered by the researcher by use of computerized statistical software; Statistical Package of the Social Sciences (SPSS) version 23. Descriptive statistics are presented in the form (mean ± standard deviation). One-way ANOVA analysis was used to compare more than two means. In all statistical analyzes,

the significance level (p-value) was set at ≤ 0.05 and the result was presented in tables and / or graphs.

Results

Seventy participants enrolled in the current study with response rate of 100%. Table 1 show that the BMI in PCOS group were highly significant than BMI in healthy control group (P<0.001). The age in case group were less than that in control group but with no statistically difference were found (P>0.05)

Table 1: Socio demographic criteria			
Domains	PCOS group (No=35)	Control group (No=35)	P value
Age (year)	27.2±6.7	28.3±7.2	NS
BMI	29.4±3.1	27.7±3.6	<0.001

As shown in figure 1, 80% of the patients in case group (PCOS) and 20% in control group presented with family history with thyroid disease.

Figure 1: family history of thyroid disease in the studied group (case and control)

Anti-TG-IgG were negative in (85.72%) of the PCOS group patients, 8.57% of the patients with borderline positive and only (5.71%) were positive (>110 IU/ml)

Table 2: Distribution of thyroid Autoimmunity Markers according to their level			
Domain		No.	%
Anti-TG IgG	Positive (> 110 IU/ml)	2	5.71
	Borderline positive (90 - 110 IU/ml)	3	8.57
	Negative (< 90 IU/ml)	30	85.72
		No.	%
Anti-TPO IgG	Positive (> 55 IU/ml)	4	11.42
	Borderline positive (45 - 55 IU/ml)	4	11.42
	Negative (< 45 IU/ml)	27	77.16

Table 3 revealed that TSH level in PCOS group (2.3 ± 0.5) were increase with significant association than that in control group (2.1 ± 0.8), highly significant increase were found in FBG, Fasting insulin, HOMA-IR, Anti-TPO, Anti-TG, free testosterone and LH in poly cystic ovary group than that in healthy group (P<0.001), while difference between FT4, and FSH was not significant.

Table 3: The relation of many domains and the studied groups

Domain	PCOS group	Control healthy group	P-value
FBG(mg/dL)	108.57±11.27	98.68±15.1	<0.001
Insulin(IU/ml)	22.7±3.4	17.20±5.3	<0.001
HOMA-IR (mIU/L)	6.08±2.51	4.19±1.81	<0.001
TSH μ IU/ml	2.3 \pm 0.5	2.1 \pm 0.8	0.03
FT4 nmol/L	78.23 \pm 21.4	76.9 \pm 22.2	NS
Anti-TPO IU/ml	46.5 \pm 16.9	32.9 \pm 10.2	<0.001
Anti-TG IU/ml	92.3±23.4	34.8±6.20	<0.001
Free testosterone	0.98 \pm 0.44	0.36 \pm 0.14	<0.001
LH	9.7 \pm 6.5	5.4 \pm 2.8	<0.001
FSH	6.4 \pm 4.2	6.8 \pm 1.5	NS

Discussion

One of the most common connection between PCOS and thyroid disease is the increase level of insulin resistance and BMI⁽¹⁶⁾. The current study revealed that there is increase in BMI of the PCOS group, which is very common in women with this disease. As mentioned by Lim S et al, this prevalence was between 54–68% of cases⁽¹⁷⁾. Moreover, many studies were in agreement with current study. Nevertheless, it is not in agreement with Duntas L et al, and with Harpsoe M et al, when they concludes that there is no association between thyroid autoimmunity and BMI^(18,19).

Prevalence of thyroid disorders (Td) in women With the PCOS, this is still a matter of debate. Different studies demonstrated a link between PCOS and attendance hypothyroidism and antithyroid antibodies⁽²⁰⁾.

In a retrospective study of 197 women With PCOS, reported a high prevalence of subclinical hypothyroidism and thyroid autoimmunity, with frequencies of 26.3 and 20.3%, respectively

Ganie and colleagues reported a significantly higher prevalence of PCOS in euthyroid adolescents with

chronic lymphocytic thyroiditis (CLT) compared to healthy controls (46.8 vs. 4.3%)⁽²¹⁾.

In addition, a recent meta-analysis study indicates that the occurrence of autoimmune thyroiditis and Plasma TSH levels in patients with poly cystic ovarian syndrome was significantly higher than those of healthy group⁽¹⁵⁾.

While in the current study we found that positive anti TPO were found in 11.42% of the patients with PCOS, this is less than (37.8%) that found in a study carried by Ozdemir D et al, in Turkey⁽²²⁾. Moreover, it is less than that found by Indian study done by Sinah U et al, when positive anti-TPO were found in 22.5% of the PCOS patients included his study⁽¹⁵⁾. This may be due to differences in sample size collection and different in cutoff value of the markers used in the studies.

The current study show that LH/FSH were increase >2 times in 24% of the PCOS patients and < 2 times in 76%, while in Banaszewska B et al, study they revealed that the raised was in 45.4% in LH/FSH ratio and the raised was 64% in Anlakash A et al^(23,24).

The mean serum of anti TPO in PCOS group was significantly elevated than that in healthy group ($p < 0.001$), also the anti-TG serum levels were higher increase in PCOS group than that in control group. In agreement with Syrian study regarding the anti-TPO but this study that carried by Al-Saab R et al, mentioned that serum level of anti-TG were more elevated in PCOS group than that in control healthy group but with no significant association ⁽²⁵⁾. In addition to that, Kachuei et al, in Iranian study were in agreement with Al-Saab R et al finding ⁽¹³⁾.

Conclusion

There is increased risk of thyroid disease with increase in thyroid Autoimmunity Markers in PCOS patients.

No Conflicts of Interest

Self-funding Source: Ethical clearance: from the Ministry of health and Environment/ scientific committee

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