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Comparison of the Relationship between Thyroid Autoimmune Markers and Polycystic Ovary Syndrome in Women with Hypothyroidism versus Healthy Subjects

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ABSTRACT

Background and Objective: Polycystic ovarian syndrome (PCOS) is associated with autoimmune thyroid disease and is thought to be one of the most frequent endocrine diseases in women of reproductive age. This research aims to compare the levels of TSH, LH, Insulin, HOMA-IR, and testosterone in women with polycystic ovary syndrome (PCOS) versus healthy subjects of same age and BMI.

Methods: This case control study was conducted among 100 patients who referred to Al-elwyah Teaching Hospital. The samples were selected on the basis of symptoms of hypothyroidism, and fertility problems, and polycystic ovary syndrome in two groups of 50. They were diagnosed by specialized doctors in the hospital. The first group consisted of fifty healthy women, and the second group also consisted of fifty women with polycystic ovary syndrome, reproductive problems, and hypothyroidism. Hormonal analyses were performed using a ready-made kit according to the manufacturer's instructions, Roche Cobas, using an ELISA microplate analyzer.

Findings: Mean body mass index, insulin, HOMA-IR, testosterone, anti-TPO, anti-TG, thyroid stimulating hormone, and luteinizing hormone, as well as age group (31-40) were respectively as follows: (35.96±0.34, 23.12±0.31, 6.64±0.07, 98.80±0.75, 7.70±0.10, 10.27±0.30). LH and anti-TG insulin levels were positively correlated with their BMI. There was also an inverse relationship between body mass index and HOMA-IR, and between anti-TG and testosterone.

Conclusion: The results of the study showed that in patients with polycystic ovary syndrome, increased risk of thyroid disease is related to increased thyroid autoantibody markers and measured hormones, insulin and HOMA-IR.

Keywords: *Polycystic Ovary Syndrome, Insulin, Homeostasis Model Assessment of Insulin Resistance (HOMA-IR), Thyroid Autoimmune Markers, Anti-TPO, Anti-TG.*

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Introduction

It is believed that between 4 and 15 percent of women of reproductive age have polycystic ovary syndrome, making it one of the most frequent endocrine disorders affecting women (1, 2). Polycystic ovarian syndrome (PCOS) is characterized by prolonged anovulation, hyperandrogenemia, and insulin resistance (IR), and may appear clinically as abnormal uterine hemorrhage, hirsutism, infertility, and other symptoms. Ultrasound detection of polycystic ovaries in the absence of other reasons; presence of oligo- or an-ovulation; presence of clinical and/or biochemical hyperandrogenemia; existence of polycystic ovaries (3), constitutes diagnostic criteria for this illness. It is still unclear how common thyroid pathology is in PCOS individuals. PCOS has been linked to hypothyroidism and autoimmune thyroid disease (AITD), according to a number of studies (4, 5, 6). Serum autoantibody testing confirms that a number of factors contribute to the development of AITD (5, 6). It has been hypothesized that the autoimmune triad in polycystic ovary syndrome (PCOS) is linked to the hereditary variables that also contribute to the pathophysiology of this condition (7).

Patients with polycystic ovary syndrome (PCOS) exhibit the same symptoms, including irregular periods, hyperandrogenism symptoms, and elevated testosterone levels, regardless of their body mass index. Subclinical thyroid dysfunction and an increase in androstenedione conversion to testosterone may disrupt gonadal function and cause anovulatory cycles (8, 9). Thyroid hormone replacement treatment, on the other hand, decreases blood testosterone levels and improves the appearance of polycystic ovaries in women with PCOS (10). To maintain the mitogenic pathways that rely on this hormone for cellular synthesis and proliferation, insulin resistance is defined as a selective phenomenon. Recently, researchers have started looking at the link between insulin resistance and the thyroid, and their findings suggest that those with insulin resistance tend to have a larger thyroid, more thyroid nodules, and a higher risk of developing thyroid cancer. Insulin receptors, insulin-like growth factors types 1 and 2, and hybrid tetrameters are overexpressed in thyroid tumor cell cultures, much as they are in the granular and ovarian cells of polycystic ovary syndrome (PCOS) patients (11, 12).

Some of PCOS's reproductive and metabolic symptoms are worsened by being overweight. Thyroid diseases, on the other hand, affect women at a higher rate than men and may have serious ramifications for reproductive health and menstrual regularity (13). Weight gain due to mucus accumulation and salt and water retention are additional symptoms of hypothyroidism (14). Current medical consensus confirms that hypothyroidism and polycystic ovary syndrome constitute a systemic endocrine and metabolic disease. The aim of the study is to evaluate the relationship between thyroid autoimmune markers and polycystic ovary syndrome in women with hypothyroidism.

Methods

This case-control study was conducted in Al-elwyah Teaching Hospital, situated in Baghdad, Iraq. The Ethics Committee of the College of Medicine at Iraqi University duly approved the research protocol for this study, in compliance with the stipulations set forth in the 2013 Helsinki Declaration. All study participants provided informed consent prior to their involvement (Ethics Approval Code: 158639). The study population comprised 50 female patients diagnosed with polycystic ovary syndrome and

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hypothyroidism, and a control group of 50 healthy individuals. The age range of all participants was between 20 to 40 years. The diagnoses were made by specialists at the hospital, based on manifest signs and symptoms of the diseases.

Blood samples, approximately five milliliters each, were obtained from both the patients and the healthy controls via venipuncture. The collected blood was left to clot at room temperature for about 20 minutes in a gel tube, after which it was centrifuged at 3000 revolutions per minute for a duration of 10 minutes. The extracted serum was stored at a temperature of -20°C for ensuing analysis. Serum concentrations of HOMA-IR, Insulin, Testosterone, TSH, and LH were ascertained using an automated ELISA microplate reader analyzer (Bio-Rad Mark Microplate Absorbance Reader) (S6850, Germany). The procedure was carried out as per the instructions of the Roche Cobas E411 Modular Elisa kit provided by Roche (Germany).

Data were organized and analyzed using the Statistical Package for the Social Sciences (SPSS), version 23. Descriptive statistics are conveyed as mean±standard error. A T-test analysis was conducted for comparison between the two groups. For all statistical assessments, the level of significance, or the p-value, was set at≤0.05. The results are represented in the form of tables and graphs.

Results

The results showed a clear relationship between the age stages of females with PCOS and hypothyroidism. The highest rate of infection is in the age group (31-40), as shown in Figure 1.

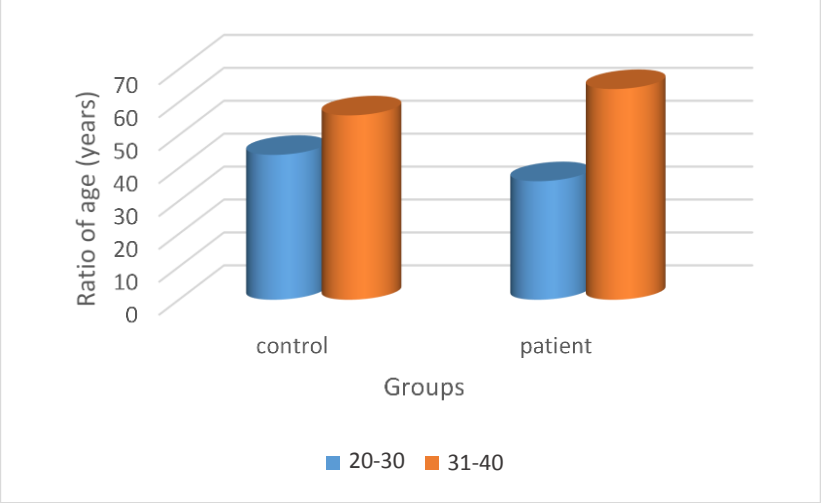

Figure 1. Age-stages for the two study groups

A total of 50 patients diagnosed PCOS with autoimmune thyroid disease and 50 controls were assessed in current study. Based on the collected information, we were able to determine the Mean±SD of each parameter (body mass index, insulin, HOMA-IR, testosterone, anti-TPO, anti-TG, thyrotropin, and luteinizing hormone) (Table 1).

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Table 1. The levels of parameters examined for patients and healthy volunteers

Parameters	Control (n=50) Mean±SE	Patients (n=50) Mean±SE	p-value
BMI (Kg/m^2)	24.16±0.29	35.96±0.34	0.0001
Insulin (IU/ml)	16.13±0.17	23.12±0.31	0.0001
HOMA-IR (mlU/L)	4.21±0.26	6.64±0.07	0.0001
Testosterone (ng/dl)	36.54±0.30	98.80±0.75	0.0001
TSH (mIU/l)	1.94±0.06	7.70±0.10	0.0001
LH (IU/ml)	5.55±0.12	10.27±0.30	0.0001
Anti-TPO (IU/ml)	32.82±0.36	45±1.24	0.0001
Anti-TG (IU/ml)	34.46±0.43	96.22±2.90	0.0001

The result indicated the presence of a significant increase in all parameters in patients compared with control group (p=0.0001) as shown in figures 2-5.

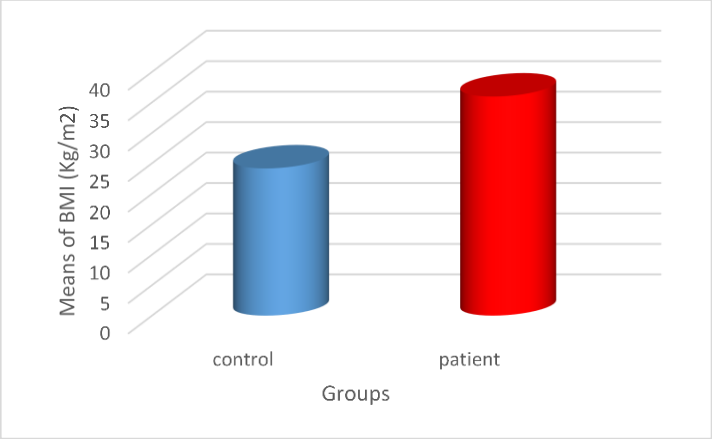

Figure 2. BMI in PCOS compared with control subjects

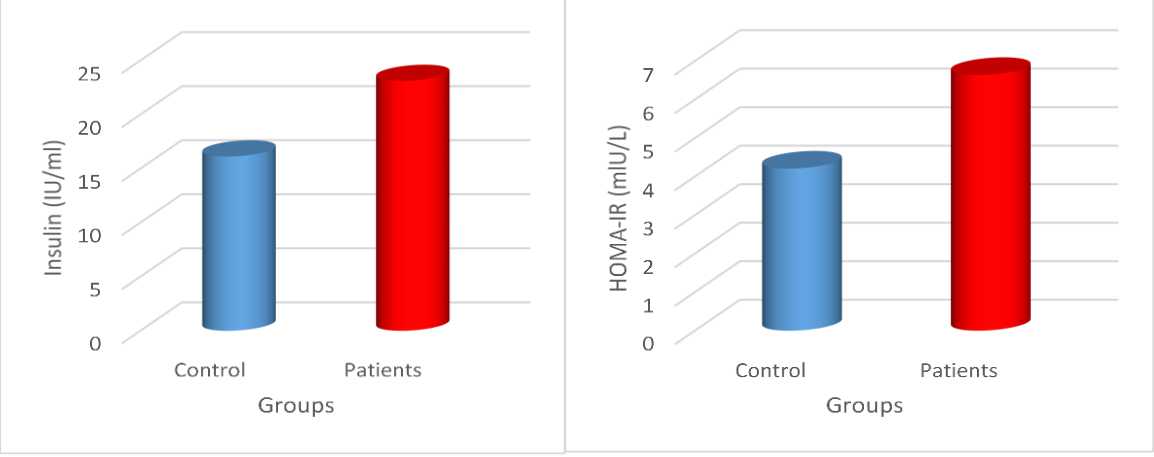

Figure 3. Serum of Insulin and HOMA-IR of PCOS patients with autoimmune thyroid disease in comparison with control subjects

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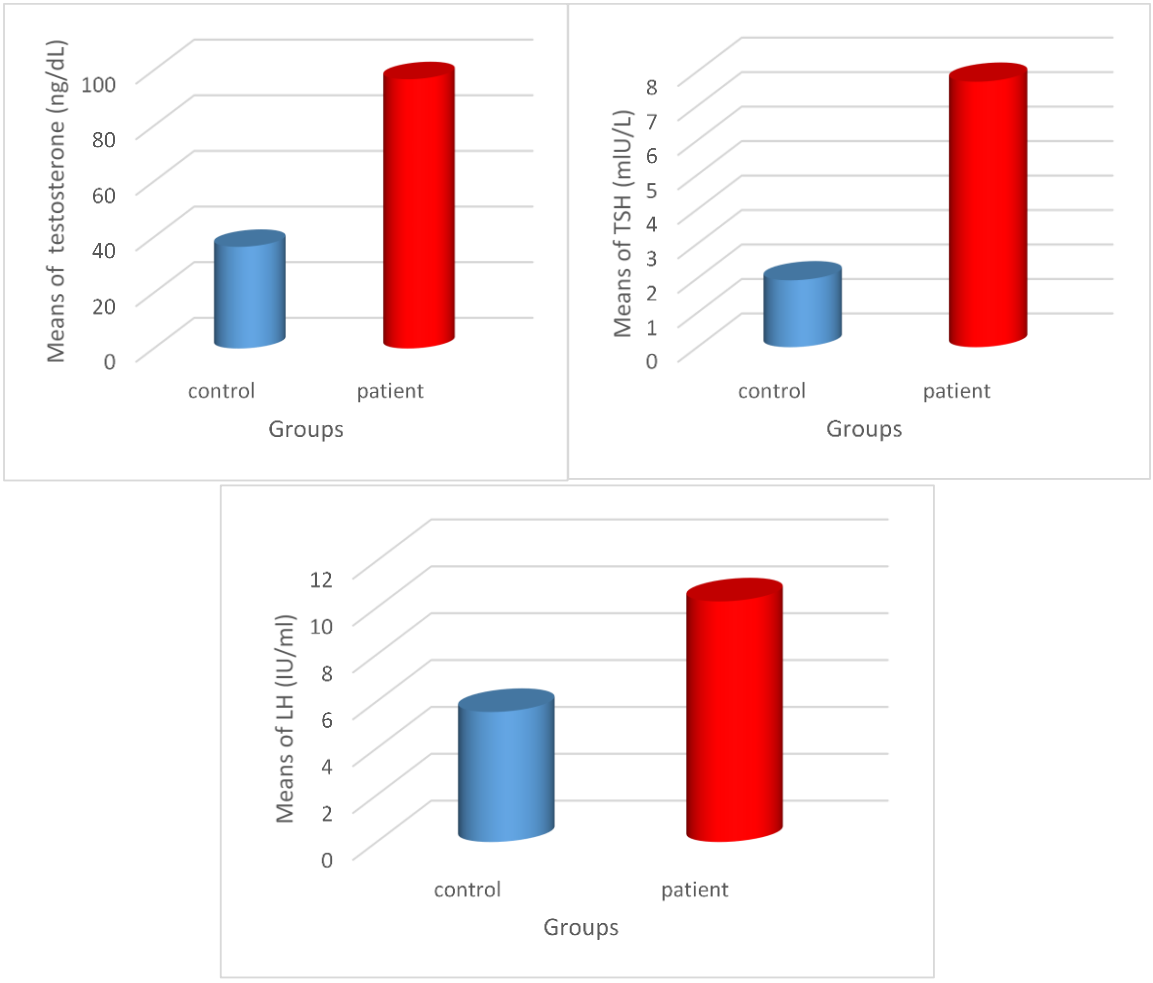

Figure 4. Means of hormones (Testosterone, TSH and LH) in the studied groups

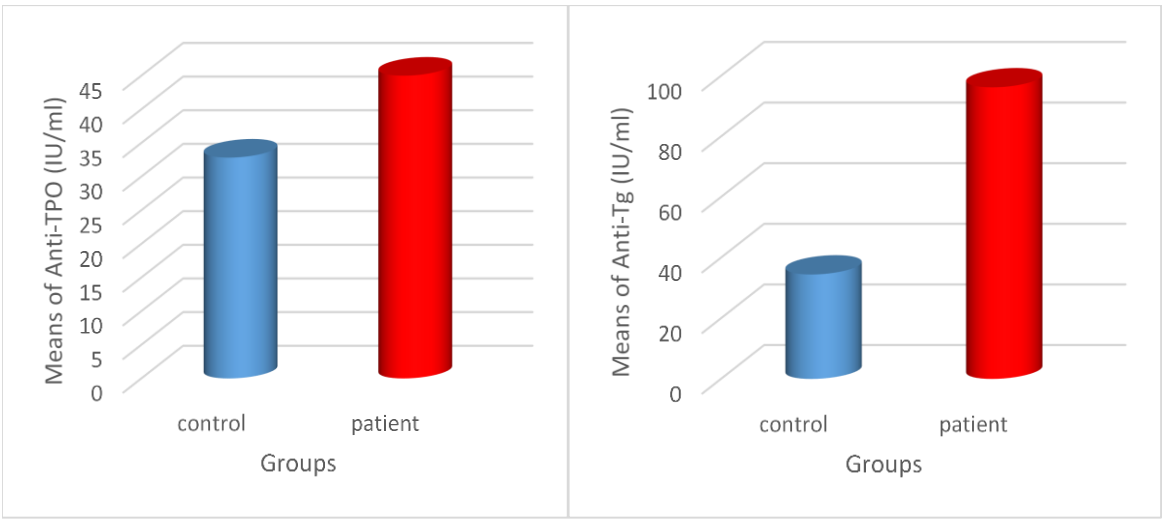

Figure 5. Means of thyroid autoimmunity (Anti-TPO and Anti-TG) in the studied groups

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Pearson correlation analysis was used to investigate the connection between all factors included in the present study and their respective chemical analyses and physical measurements. Table 2 summarizes the data collected.

Table 2. Correlations between variables in patients group (r-value)

Parameters	BMI	Testosterone	Anti-TPO	Anti-TG	TSH	LH	Insulin	HOMA-IR
BMI								
R	1	0.157	0.041	0.213	0.210	0.347*	0.095	-0.422**
P		0.277	0.778	0.137	0.144	0.013	0.510	0.002
Testosterone								
R	0.157	1	0.001	-0.286*	0.107	0.043	-0.042	-0.056
P	0.277		0.992	0.044	0.461	0.767	0.774	0.701
Anti-TPO								
R	0.041	0.001	1	-0.060	-0.124	-0.005	-0.072	-0.070
P	0.778	0.992		0.679	0.390	0.973	0.621	0.631
Anti-TG								
R	0.213	-0.286*	-0.060	1	0.036	0.086	0.290*	-0.055
P	0.137	0.044	0.679		0.806	0.554	0.041	0.704
TSH								
R	0.210	0.107	-0.124	0.036	1	0.050	-0.177	0.052
P	0.144	0.461	0.390	0.806		0.728	0.219	0.719
LH								
R	0.347*	0.043	-0.005	0.086	0.050	1	0.204	-0.040
P	0.013	0.767	0.973	0.554	0.728		0.155	0.782
Insulin								
R	0.095	-0.042	-0.072	0.290*	-0.177	0.204	1	0.077
P	0.510	0.774	0.621	0.041	0.219	0.155		0.597
HOMA-IR								
R	-0.422**	-0.056	-0.070	-0.055	0.052	-0.040	0.077	1
P	0.002	0.701	0.631	0.704	0.719	0.782	0.597	

***Correlation is significant at the 0.05 level. **Correlation is significant at the 0.01 level. R: Pearson Correlation.**

Table 2 shows that there is a positive relationship between patients' body mass index (BMI) and their LH and insulin level. The investigation also found that the higher the BMI, the lower the HOMA-IR. Furthermore, statistical research revealed an inverse relationship between anti-TG and testosterone.

Discussion

In our current study, we discovered a positive correlation between LH with body mass index, anti-TG with insulin levels in patients. In addition, HOMA-IR has a negative correlation with BMI, and testosterone has a negative correlation with anti-TG. Results for mean±standard deviation (SD) are as follows:

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(35.960±0.34, 23.12±0.31, 6.64±0.07, 98.80±0.75, 7.70±0.10, 10.27±0.30, 45±1.24, 96.22±2.90) for age group 31-40 and all parameters (body mass index, insulin, HOMA-IR, testosterone, TSH, LH, anti-TPO, anti-TG). Insulin resistance and obesity are often linked in patients with PCOS and thyroid illness (15).

The new research confirmed what has long been suspected: that women with PCOS tend to have higher body mass indexes. Lim et al. (16) reported a prevalence of between 56% and 68%. In addition, numerous other investigations mirrored the results of this one. However, it does not agree with the findings of Duntas et al and Harpsøe et al, who found that thyroid autoimmunity was not linked to body mass index (17, 18) in obese PCOS patients, who had higher levels of free testosterone in their blood than their leaner PCOS counterparts (19).

Two of the most common connections between polycystic ovary syndrome (PCOS) and thyroid disease are increased insulin resistance and obesity (20). This matches the results of our research in which a significant elevation in HOMA-IR was seen between euthyroid PCOS and euthyroid controls. After controlling for body mass index, Matta et al. and Benetti-Pinto et al. (21, 22) observed no statistically significant difference in IR between the hypothyroid and PCOS populations in Turkey. Although the studies did not agree on a common IR cutoff, they did find that people with PCOS and subclinical hypothyroidism had greater HOMA-IRs than those with euthyroid PCOS (23). Researchers have shown that TSH is greater in patients with a high BMI, suggesting a link between hypothyroidism and obesity. Increased TSH levels cause obesity because inflammatory mediators or another hormone called leptin stimulate the fast creation of fat cells (14).

The question of whether or not PCOS women are at an increased risk of developing thyroid diseases (Td) remains open. Several studies have shown an association between PCOS and antithyroid antibodies and hypothyroidism in women (24). Subclinical hypothyroidism and thyroid autoimmunity were shown to be very prevalent in a retrospective analysis of 197 women with PCOS, with reported rates of 26.3% and 20.3%, respectively (25). Research by Ganie et al. shows that the prevalence of polycystic ovarian syndrome (PCOS) is 46.8% in euthyroid adolescents with chronic lymphocytic thyroiditis (CLT), compared to 4.3% in healthy controls (26). Patients with polycystic ovary syndrome also had a greater prevalence of autoimmune thyroiditis and Plasma TSH levels than the healthy control group, according to a recent meta-analysis research (21). This is also lower than the percentage of PCOS patients with positive anti-TPO observed in an Indian research by Sinha et al (27). While we did find elevated anti TPO levels in PCOS patients, it was lower than a research done in Turkey by Ozdemir et al. (28). Possible causes for this discrepancy include variations in study designs and cutoff values for the markers. Anti-TG serum levels also increased more rapidly in the PCOS group compared to the control group, and the mean serum anti-TPO level was substantially greater in the PCOS group than in the healthy group ($p=0.001$). While this research agrees with the Syrian one in terms of anti-TPO, it differs in that it found no statistically significant link between PCOS and an increased blood level of anti-TG. The findings of Al-Saab et al. (29) were corroborated by those of an Iranian investigation conducted by Kachuei et al (30).

In conclusion, the results of this study showed that elevated serum thyroid autoantibody markers in PCOS patients and in connection with the measured hormones and Insulin, HOMA-IR, were related to an increased risk of thyroid illness.

Conflict of interest: The authors declare that there is no conflict of interest.

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