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Comparing the values of anti-TPO and IL-17 among patients with thyroid disorders and comparing them with healthy controls in Ramadi City

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Abstract---Even though most thyroid subjects are undiagnosed due to nonspecific symptoms, universal screening for thyroid disease is not recommended for the general population. In this study, our motive is to compare thyroid autoantibody anti-TPO and IL-17 in addition to traditional thyroid markers TSH, T4, and T3 between two patients' groups (patients with hypothyroidism (TSH) > 6 mIU/L and patients with hyperthyroidism TSH between 0.3 and 6 mIU/L) with a control group. Here a total of 45 subjects were divided into three groups, the first group consisted of 15 patients with hypothyroidism. The second group consisted of 15 individuals with hypothyroidism, and the control group consisted of 15 healthy individuals. According to our results, an increase in TPO values was observed in all study groups, and the highest increase was recorded in the hyperthyroidism (386.672±116.924), and with regard to interleukin-17 values, a high value was observed in patients with hyperthyroidism (38.1033±5.44) compared to other groups. Our results showcase that anti-TPO appear prior to the onset of thyroid hormone dysfunction in control group And this is an indication of future disorders in the thyroid gland, in addition to the high levels of interleukin in the pathological groups and the high levels of interleukin in the height group, indicating the role of immune disorders in thyroid disorders.

Keywords---IL-17, thyroid, healthy controls.

Introduction

Dysfunction of thyroid, defined as a wide range of related -thyroid disorders, has a significant impact on human health. In the United States, approximately 20 million people suffer from thyroid disease in some form. [1]. Thyroid dysfunction prevalence varies by population, which can be related to environmental/geographical factors, age, ethnicity, gender, and so on. Hypothyroidism (decreased activity of the gland) and hyperthyroidism (increased activity of the gland) are the two main kind of functional thyroid disease, which are divided into many diseases subclinical and overt. Previous studies have indicated that 1.3 percent of the population in the United States have hyperthyroidism, and 4.6 percent has hypothyroidism. [2]. Many people with thyroid disease go undiagnosed because symptoms are nonspecific and develop gradually. Although it is important, a comprehensive thyroid scan has not been approved due to the lack of available studies and clinical trials demonstrating the effectiveness of screening and subsequent treatments [3]. Graves' disease (HYPOTHYROIDISM), the most famous cause of spontaneous hyperthyroidism in the world [4] It is an autoimmune disease that affects the thyroid gland and is characterized by increased secretion of thyroid hormones stimulated by thyroid-stimulating hormone. (TSH) [4]. Hashimoto's thyroiditis (HT) is a common autoimmune endocrine disorder that is characterized by lymphocytic infiltration and thyroid gland fibrosis. [5]. Although Hashimoto's thyroiditis can cause overt hypothyroidism, the majority of patients have subclinical hypothyroidism with normal thyroid hormone levels and elevated TSH [6]. The most common type of thyroid dysfunction is autoimmune thyroid disease, which causes hyperthyroidism (Graves' disease) and hypothyroidism (Hashimoto's thyroiditis). Autoantibodies of thyroid, particularly anti-Thyroid Peroxidase (anti-TPO) and anti-Tg (anti-thyroglobulin), characterize thyroid autoimmunity [7]. Thyroid peroxidase is a poorly glycosylated membrane-bound enzyme that is responsible for the iodination and oxidation of tyrosyl residues on Tg molecules [8]. It was dubbed of microsomal due to its intracellular location. Anti-thyroid peroxidase antibody (anti-TPO antibody) is a type of thyroid autoantibody that can cause and diagnose autoimmune thyroid disease. Thyroid autoimmunity can result in abnormal thyroid and thyroiditis function ranging from hyperthyroidism to hypothyroidism. Unfortunately, thyroid autoantibodies are only routinely tested when there is an abnormality in thyroid hormones, particularly TSH and FT4. However, their presence prior to the TSH marker, which is the primary marker, has not been recognized. [9] [10]. Anti-TPO antibodies can be of any IgG class, though many studies show a higher prevalence of IgG1 (70%) and IgG4 (66.1%) compared to IgG2 (35.1%) and IgG3 (19.6%). Low IgA antibody levels have also been reported. Anti-Tg antibodies are less common than anti-TPO antibodies, and anti-TPO are associated with disease of thyroid. [11]. Anti-TPO antibodies cause oxidative stress in the blood, as demonstrated by decreased potential of antioxidant, advanced products of glycosylation, and oxygen metabolites [12]. However, their contribution to damage of thyroid is minor when compared to T lymphocytes and cytokine-mediated apoptosis [13]. The newly discovered Th17 cells, as a subset of T cells, play an important role in the immune response, and this comes mainly by producing IL-17. [14]. many Previous studies have revealed that Th17 cells and IL-17 play an crucial role in the pathogenesis of autoimmune diseases like, Graves' ophthalmopathy (GO) and Hashimoto's thyroiditis [15]. The

most common autoimmune thyroid diseases are Graves' disease in young adults and Hashimoto's disease in children and young women (AITD). AITD patients had a higher proportion of perivascular Th17 cells than controls, and it was affected by disease activity and severity. [16][17][9]. As a result, the project's goal was to see if the levels of Th17-related cytokines IL-17 were different and anti-TPO antibody in patients with hypothyroidism and hyperthyroidism in comparison to healthy controls.

Materials and Methods

Sampling

Blood samples were taken from newly diagnosed and naïve patients suffering from hyperthyroidism, with 15 increased samples, 15 hypothyroidism samples, and 15 normal controls. Centrifugation was used to separate serum specimens, which were then stored at -20°C until the assay. Individuals are classified as having hyperthyroidism, hypothyroidism based on their thyroid status. hypothyroidism was described as an increased level of thyroid stimulating hormone (TSH) > 6 mIU/L while hyperthyroidism was defined as a TSH between 0.3 and 6 mIU/L . Exclusion criteria included (1) Age (2) Gender (3) breastfeeding mothers or pregnant women (4) known cases of previously existing thyroid disease or surgery, and (5) previous thyroid dysfunction or surgery. Except for HT, the presence of cancer, autoimmune diseases, and chronic inflammatory diseases is required. (6) the presence of both acute and chronic infection, with or without fever (7) a history of immunosuppressive therapy or drug use that may have an impact on thyroid function, such as lithium or iodide.

Thyroid function assessment

TSH, T₃ and T₄ levels were determined using the Roche e411 Analyzer (Roche professional diagnostics Switzerland) according to the manufacturer's specifications. Roche Diagnostics was used to obtain the reagents (Roche professional diagnostics Switzerland).

Immune parameters

Anti-TPO was determined using the Roche e411 Analyzer (Roche professional diagnostics Switzerland) according to the manufacturer's specifications. Roche Diagnostics was used to obtain the reagents (Roche professional diagnostics Switzerland), values greater than 40 IU/ml were regarded as positive for the presence of anti-TPO. IL-17 serum measurements were determined using an ELISA method as directed by the manufacturer (Fine test, Wuhan Fine Biotech.).

Statistical Evaluation.

SPSS 19.0 (SPSS Inc., Chicago, IL, USA) and Microsoft excel 2016 were used for the statistical analysis (GraphPad Inc., San Diego, CA, USA). The continuous variables were represented by the mean ±standard error (SE).

Results

Parameters	Hypothyroidism	Hyperthyroidism	control
Number	15	15	15
TSH mIU/L	24.255±6.348	2.716±0.704	2.728±0.463
T4 µg/dL	3.968±0.372	11.518±1.527	5.809±0.328
T3 ng/dL	1.032±0.114	3.120±0.502	1.525±0.078
Anti-TPO IU/ml	282.2025±89.10833	386.672±116.924	137.5334±7.553
IL-17 pg/ml	22.4676±1.7899	38.1033±5.44	22.335±1.200

*p≥0.05

As presented in Table 1, patients according to TSH level were divide to Hypothyroidism and Hyperthyroidism according to TSH values .patients with Hyperthyroidism had a significant higher of T4 and T3 concentrations than control and Hypothyroidism . Regarding the immunological indicators, the outcomes of TPO revealed no significant differences between the three groups, in addition there was no significant differences between each disease group with the control group also no difference between the two groups of patients (p<0.05).

On the other the IL-17 results revealed that There were notable differences. when comparing the three groups, as well as statistically significant differences between the two pathological groups and the Hyperthyroidism group and the healthy controls (p≥0.05). However, no significant differences were observed between the Hypothyroidism group and the healthy control.

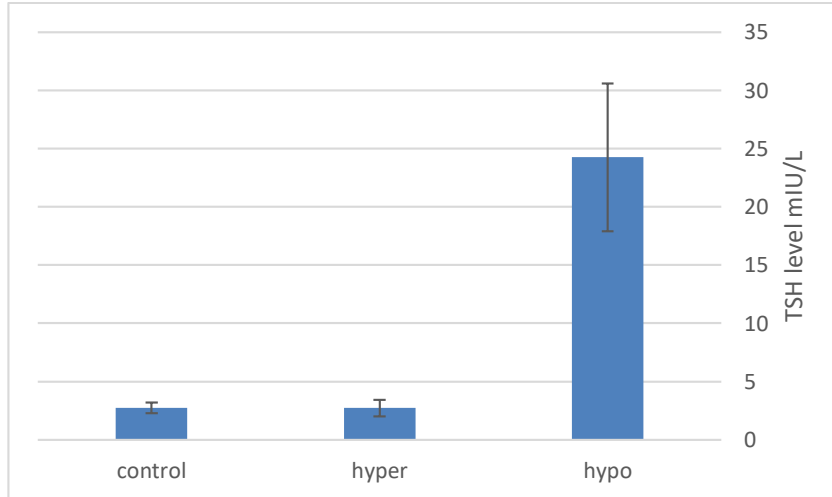


Figure 1: Serum TSH levels in study groups

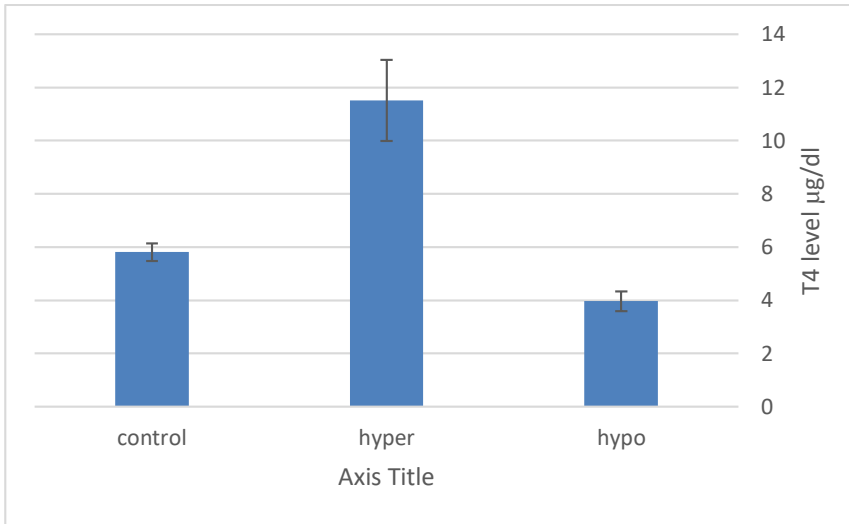


Figure 2: Serum T4 levels in study groups

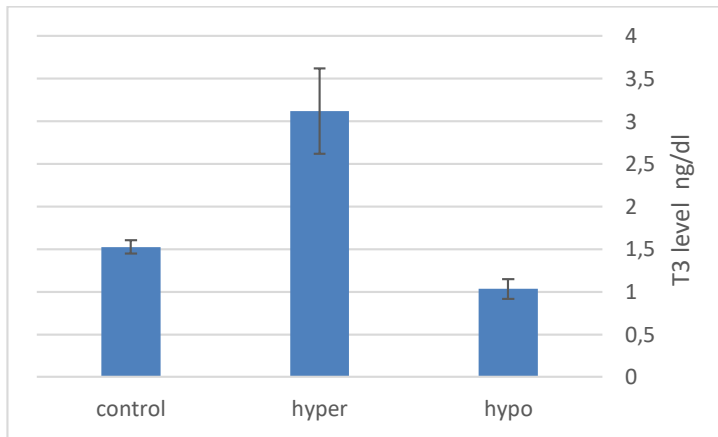


Figure 3: Serum T3 levels in study groups

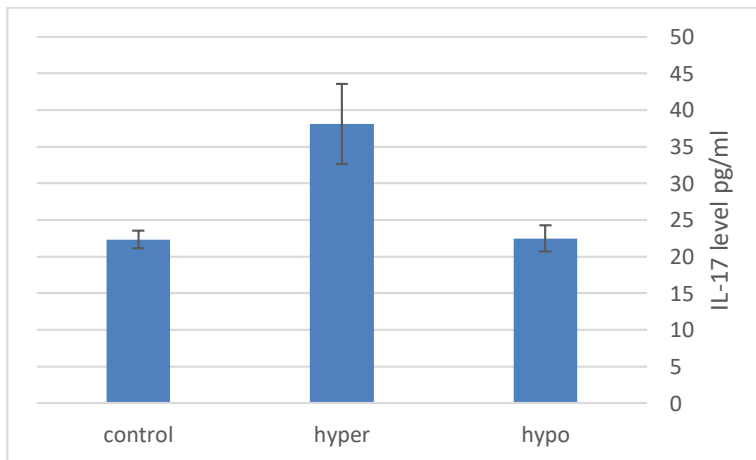


Figure 4: Serum interleukin-17 levels in study groups

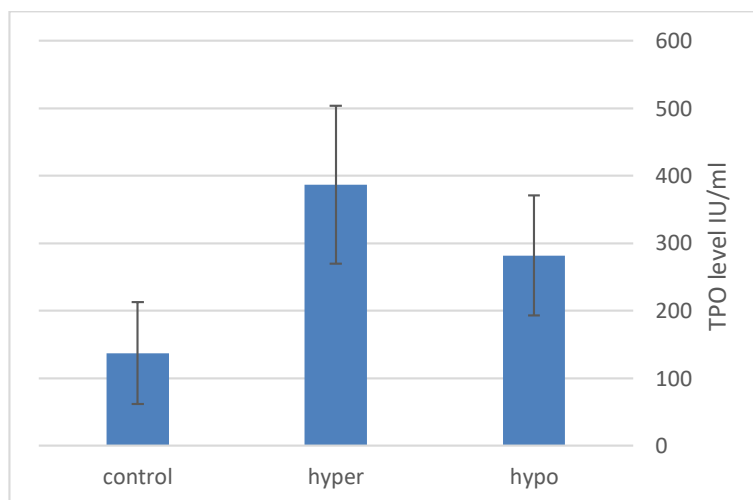


Figure 5: Serum TPO levels in study groups

Discussion

Recent developments in molecular techniques have transformed our knowledge of the main immune system cellular components that decide the outcome of immune responses. These methods showed the presence of distinct subsets of lymphocytes, each with a distinct function, distinct cell surface markers, cytokine profiles, and distinct developmental requirements. Th17 cells are a newly discovered and distinct lineage of CD4⁺ T-cells. The discovery of these cells, which have both defensive and offensive capabilities, sheds new light on the autoimmune diseases pathogenesis, particularly those thought to be caused by abnormal Th1 responses. [18]. As a result, quantifying cytokines required for Th17 cell development and function in disease and health may be necessary in order to understand the complex molecular mechanisms that underlie thyroid disease. The current study's data showed that no high up IL-17 levels were related with HPOTHYROIDISM relapse, shedding new light on the etiology and relapse of HPOTHYROIDISM and in the same time the results also the current study's results indicate that serum IL-17 levels in HT patients are significantly higher., implying that this cytokine may play a role in pathogenesis of disease. It should be indicated that IL17 is a proinflammatory cytokine that can also stimulate the expression of other proinflammatory cytokines and chemokines [19]. These inflammatory molecules are responsible for the creation of an inflammatory milieu, which helps disease progression through different pathways such as the development of fibrosis. Scientists such as Li *et al.* have confirmed the link between thyroid fibrosis and increased inflammatory mediators. [20] They discovered a link between IL17 expression and stromal fibrosis in patients' thyroid glands. [21]. Quantification of cytokines required for Th17 cell development and function Understanding the complex molecular mechanisms underlying hyperthyroidism may require research in both health and disease. The current study's findings show a significant rise in serum IL17 levels in HT patients in compare with control healthy group, implying that this cytokine may play a role in disease pathogenesis. It should be noted that IL17 is a proinflammatory cytokine that can also induce the expression of a variety of

proinflammatory cytokines and chemokines. [19] Scientists such as Li et al. have confirmed the link between thyroid fibrosis and increased inflammatory mediators [20].

They discovered a link between IL17 expression and stromal fibrosis in patients' thyroid glands. Different clinical trials have confirmed the importance of IL17 in the pathogenesis of HT, which is also supported by disease experimental models. Thyroid accumulation of Th17 cells, for example, in the murine experimental model of human HT with IL17+/+ T-cells but not in those with IL-17-/-T-cells, suggests a role for IL17 in HT pathophysiology [21]. With regard to the values of interleukin-17 in deficient patients, the results of the study revealed that there is no notable difference in its values when compared with the control group. But when looking at the results of anti-TPO values, there are no notable differences between the groups of patients and the control group, but depending on the instructions of the manufacturer of the work substance, any value higher than 40 is considered a positive value, and therefore all groups have an increase in the concentration of anti-TPO.

Thyroid function and thyroid profile testing have long been known to be affected by anti-thyroid antibodies. We theorized that people with a faulty thyroid profile have more anti-thyroid antibodies. In that study, we discovered that anti-TPO antibodies are more common in people with abnormal TSH than in people with normal TSH [22]. Brown et al. discovered that anti-TPO positivity is linked to a 60% increase in TSH [23]. Ghoraishian et al. discovered similar results in Iran. They examine the relation of anti-TPO with T3, T4, and TSH in 2425 people and discovered that it was notably deranged in the antibody positive group. [24]. Elevated anti-TPO values in the control group with normal TSS values indicate that these people are prone to developing thyroid disorders in the future. [3] Our goal in this study was to show the value of using anti-TPO as a first-tier test in conjunction with TSH and FT4; thus, subjects with normal TSH but raised autoantibodies would not be ignored, but rather referred for frequent follow-ups due to the short duration of our study.

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