

Thyroid Hormones and Autoantibodies in Iraqi Hyperthyroid Patients

Sarah T. Al-Mofarji^{1,*}, Hameed M. Jasim² and Sanad B. Mohammed³

¹Forensic DNA Center for Research and Training, Al-Nahrain University, Jadriya, Baghdad, Iraq

²College of Biotechnology, Al-Nahrain University, Jadriya, Baghdad, Iraq

³College of Science for Women, University of Baghdad

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Abstract

Hyperthyroidism can be defined as the status of over production of thyroid hormones: tri-iodothyronine (T3) and thyroxine (T4) as a results of thyroid gland dysfunction. The aim of the current study was to investigate the association between the abnormalities of thyroid hormones (T3 and T4) and serum levels of thyroid auto-antibodies: anti-thyroid peroxidase (TPO-Ab) and anti-thyroid stimulating hormone receptor (TR-Ab) and the state of hyperthyroidism. Blood samples were collected from 75 Iraqi individuals were early diagnosed as hyperthyroidism patients in addition to 25 Iraqi individuals as a healthy control group. Enzyme Linked Fluorescent Assay (ELFA) used to determine the levels of thyroid hormones (T3 and T4) and the level of thyroid stimulating hormone (TSH), Enzyme Linked Immuno-Sorbent Assay (ELISA) was used to determine the levels of auto-antibodies (TPO-Ab and TR-Ab). The results show that T3 levels and T4 levels in hyperthyroidism patients (2.07 nmol/L and 14.02 µg/dl respectively) increased significantly ($P < 0.01$) compared to healthy control levels (1.33 nmol/L and 6.4 µg/dl respectively). While the levels of thyroid stimulating hormone (TSH) in hyperthyroidism patient (0.17 µIU/ml) decreased significantly ($P < 0.01$) when compared with healthy control group (1.84 µIU/ml). The results also showed that levels of TPO-Ab and TR-Ab in hyperthyroidism patients (235.29 IU/mL and 32.05 IU/mL respectively) increased significantly ($P < 0.01$) when compared to healthy control group (20.76 IU/mL and 0.3 IU/mL respectively). This study revealed that there is an association between thyroid hormones disorders and the positivity of thyroid auto-antibodies in hyperthyroidism patients.

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*Corresponding author: sarahtkm88015@gmail.com



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1. Introduction

Thyroid gland is considered as one of the most important glands in the body because of its role in regulation of vital activity of the body through production of its hormones (thyroxine T4 and tri-iodothyronine T3) which regulate different metabolic activities: growth development, brain development, fetus development, heart function and many other different activities [1]. Most common thyroid disorder that may affect thyroid function as well as the thyroid hormones (T3 and T4) production includes hypothyroidism and hyperthyroidism [2]. Thyroid disorders were considered as the common causes of autoimmune thyroid disease (AITD), Hashimotos' thyroiditis and Graves' disease respectively [3]. In autoimmune thyroid disease (AITD) self-antigen (thyroid specific antigen) recognized as a foreign antigen results in autoantibodies formation and destruction of thyroid cells [4]. Autoimmune thyroid diseases (AITD) were classified as an organ specific autoimmune disease detected in 2-5 % of population. Its prevalence depending on different factors: gender, age,

environmental and genetic factors. Hashimotos' thyroiditis (HT) and Graves' disease (GD) were described by the presence of autoantibodies against thyroid antigen and infiltration of T and B cells, this infiltration lead to tissue damage and alter thyroid gland function [5]. Cell lysis occurs when autoantibodies or sensitize T cells react with thyroid cell causing inflammatory reaction. Graves' disease (GD) was considered as most common autoimmune disorders, that affect female more than male in a ratio 10:1. There is a genetic predisposition to Graves' disease, determined by alleles at the major histocompatibility complex, cytotoxic T-lymphocyte-associated antigen. In addition to that there are non-genetic factors that may lead to the development of hyperthyroidism which include: smoking, pregnancy, estrogen medicine, and stressful life events [6]. Auto-antibodies against thyroid stimulating hormone receptor (TR-Ab) caused excess production of thyroid hormones and thyroid gland enlargement. Auto-antibodies against thyroid peroxidase (TPO-Ab) also play an important role in thyrocyte destruction and development

of autoimmunity [7]. In Graves' disease thyrotropine receptor antibodies (TR-Ab) bind and activate TSH receptor leading to stimulation of follicle hypertrophy and hyperplasia and increasing the synthesis of thyroid hormones and the fraction of T3 relative to T4 [8]. Thyrocyte which is expressed HLA-R molecules can act as antigen presenting cell (APC) and lead to activation of local T cells by expression of co-stimulatory molecules. As a result, cytokines formed activates thyroid specific T cells and B cells to produce TR-Ab [9]. In light of the above, the objectives of the current study were to determine the association between serum levels of thyroid hormones (T3 and/or T4), thyroid stimulating hormone (TSH), and TPO-Ab and TR-Ab auto-antibodies.

2. Materials and Methods

2.1 Collection of blood samples:

A total of 75 Iraqi patients enrolled in this study were early diagnosed as hyperthyroidism attending the National Diabetes Center/Al-Mustansiriya University during the period from July to November/2021, 25 blood samples were collected from healthy volunteers as a control group. All patients and healthy control were from both genders with different age groups. Patient's history was recorded according to specific questionnaire form.

2.2 Inclusion and exclusion criteria:

Hyperthyroidism patients were diagnosed according to the early hormonal tests without any other symptoms, excluding hyperthyroidism patients with diabetes mellitus, hypertension, and cardiovascular diseases in addition to pregnant women.

2.3 Measurement of thyroid hormones and auto-antibodies:

The levels of tri-iodothyronine (T3), thyroxine (T4) and thyroid Stimulating hormone (TSH) were measured by Enzyme Linked Fluorescent Assay (ELFA) using Biomerx kit (France), while the level of autoantibodies (TPO-Ab and TR-Ab) were determined by Enzyme Linked Immuno Sorbent Assay (ELISA) using demiditec kit (Germany).

2.4 Statistical analysis:

The results were statistically analyzed using Statistical Analysis System-SAS (2018) program. Chi-square test was applied to find the significance for the variables. In addition to application of T-test to find the statistical significance ($P < 0.01$) at 95% confidence interval for the numerical variables.

3. Results and Discussion

The results illustrated in Figure 1 show that free T3 levels in hyperthyroidism patients (2.07 nmol/L) increased significantly ($P < 0.01$) as compared to healthy control group (1.33 nmol/L) this increase is an indicator for response to hyperthyroidism. In Figure 2, T4 concentration in hyperthyroidism patients (14.02 $\mu\text{g/dL}$) increased

significantly ($P < 0.01$) as compared to healthy control group (6.4 $\mu\text{g/dL}$). Results illustrated in the Figure 3 show a significant decrease at ($P < 0.01$) in concentration of TSH in hyperthyroidism patients (0.17 $\mu\text{IU/ml}$) when compared with its level in healthy control group (1.84 $\mu\text{IU/ml}$).

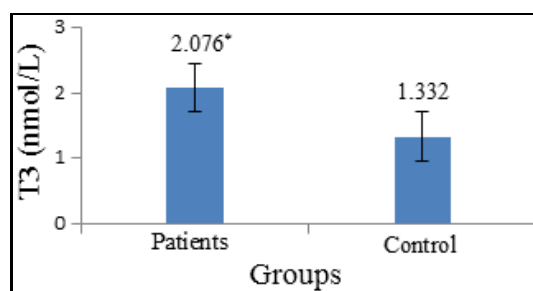


Figure 1. Serum concentration of free tri-iodothyronine in hyperthyroidism patients and healthy control groups. *: Significant at ($P < 0.01$).

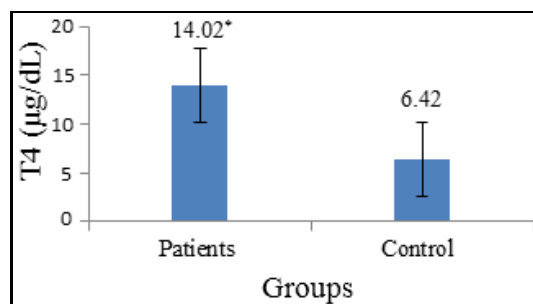


Figure 2. Serum concentration of thyroxine in hyperthyroidism patients and healthy control. *: Significant at ($P < 0.01$).

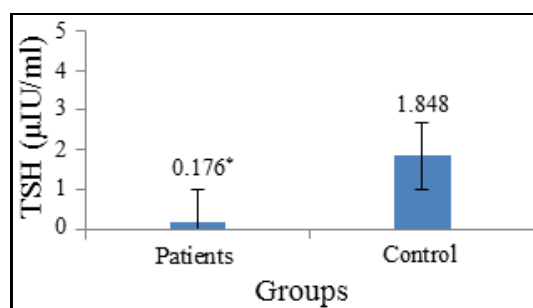


Figure 3. Serum concentration of thyroid stimulating hormone in hyperthyroid patients and in healthy control group. * Significant at ($P < 0.01$).

The results in Figure 4 demonstrate a significant increase at ($P < 0.01$) in TPO-Ab in serum samples of hyperthyroidism patients (235.29 IU/ml) as compared with healthy control (20.7 IU/ml) which was within a normal level (less than 35 IU/ml). According to these results, TPO-Ab reflects thyroid autoimmunity and hyperthyroidism.

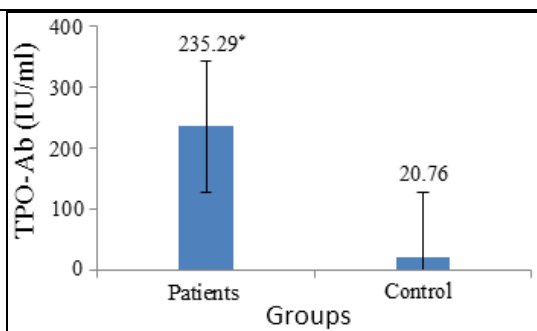


Figure 4. Serum concentration of thyroid peroxidase autoantibodies in hyperthyroidism patients and healthy control group. * Significant at ($P < 0.01$).

The results illustrated in the Figure 5 found that the concentration of TR-Ab significantly increased ($P < 0.01$) in hyperthyroidism group (32.0 IU/L) compared with their levels in normal healthy controls (0.3 IU/L).

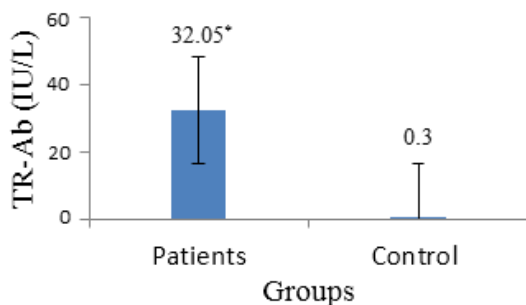


Figure 5. Serum level of thyrotropin receptor antibodies (TR-Ab) in hyperthyroidism patients and healthy control group. * Significant at ($P < 0.01$).

The results illustrated in the Figure 1 found that there is significant difference between healthy and patients according to T3 levels and there is a highly significant differences among the studied groups depending on the levels of T4 and TSH. Thyroid gland is responsible for the T3 and T4 production under the control of TSH hormone produced by the pituitary gland. In hyperthyroidism patients the level of thyroid hormones (T4 and T3) can be recorded a high level with low level of TSH hormone [14]. The main product of thyroid gland is T4 but the biologically active is T3 [15]. Thyroid gland often produces T4 that is converted to T3 by TPO enzyme, while any defect in TPO enzyme, T4 never converted to T3 so that, T4 level will increase. Our findings are in agreement with Ali *et al.* [16] who reported that T3 recorded significant change in hyperthyroidism group compared with healthy controls but they recorded a significant difference in T4 and TSH levels. In contrast, Fawzi *et al.* [17] found that T3, T4 and TSH are recorded a high significant difference between healthy and hyperthyroidism patients. On the other hand, our results seem to agree with those obtained by Nadhaif *et al.* [18] who found significant differences in TPO antibodies levels between healthy and hyperthyroidism patients. Other studies found a slight increase in TPO antibodies level in

hyperthyroidism patients [18]. High levels of TR-Ab recorded in this study agree with Fawzi *et al.* [17] who found that TR-Ab recorded a high level in hyperthyroidism patients.

4. Conclusions

There is an association between auto-antibodies against thyroid antigenic determinant and abnormal level of thyroid hormones in early diagnosed hyperthyroidism patients and play role in development of disease.

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