

Influence of Thyroid Stimulating Hormone on Liver Enzymes Levels in Serum of Thyroid Disorder Iraqi Patients

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Abstract

Thyroid hormones are essential element in body growth and influence the formation of many enzymatic proteins. These hormones regulate and have a major role in controlling the metabolism of the entire body. They also play an important role in the normal hepatic function. Thyroid diseases are linked with liver enzymes levels irregularities, cholestatic jaundice resulted from low bilirubin level and bile excretion, hepatic lipid homeostasis, viral hepatitis, an increase in alanine aminotransferase, aspartate transferase and alkaline phosphatase. Thyroid stimulating hormone and serum liver enzymes were analyzed using standard kits. Results showed that hyperthyroidism and hypothyroidism patients had an elevation in the levels of serum alkaline phosphatase, aspartate transferase and alanine aminotransferase when compared to controls. However, the values were higher in hyperthyroidism patients. This work aims to study the effect of thyroid stimulating hormone on the level of liver enzymes in a group of local Iraqi patients with thyroid disorder.

[DOI: [10.22401/ANJS.22.3.07](https://doi.org/10.22401/ANJS.22.3.07)]

Keyword: TSH, liver enzyme, thyroid disorder, ALP, AST, ALT.

Introduction

The endocrine system is a group of ductless glands that excrete their hormones to all organs through blood, these hormones play vital role in regulating the metabolism, growth, function, stress conditions and cell permeability of these organs [1]. Thyroid gland is considered one of the most substantial glands in the endocrine system that excretes hormones and controls the metabolism of the body [2]. Thyroid stimulating hormone (TSH) regulates the thyroid gland function. Thyroid releasing hormone (TRH) controls the secretion of thyroid stimulating hormone (TSH) from the pituitary gland. Thyroid stimulating hormone (TSH) has a major role in regulating 7% tri-iodothyronine (T3) and 93% thyroxine (T4) secretion from thyroid gland [3].

When the regulation of thyroid hormones is imbalanced, different types of thyroid dysfunctions appear ranging from goiter to thyroid cancer [4]. Thyroid disorder is a common idiom for many disorders related to the thyroid gland and thyroid hormones. According to the elevation and reduction in the thyroid hormones levels (T4 and T3), the thyroid gland disorders are divided to two main forms of disorders, hyperthyroidism and hypothyroidism, respectively [5].

Hypothyroidism may be either acquired disorder or congenital disorder. The acquired form results from a defect in thyroid gland or pituitary gland [6]. Autoimmunity to the thyroid gland may cause hyperthyroidism [7]. Hyperthyroidism and hypothyroidism starts first as thyroid gland inflammation (autoimmune Thyroiditis), which results in a gradual impairment and fibrosis of the gland leading to lack in thyroid hormone secretion. Different types of Hypothyroidism start to appear with the enlargement of the thyroid gland as thyroid goiter [8]. Thyroid hormones levels are essential in the metabolism of bilirubin and normal hepatic function [9]. On the other hand, liver plays a fundamental role in the metabolism of thyroid hormones.

Liver is considered the main position for the peripheral metabolism of thyroid hormones, oxidative deamination and the extra thyroidal de-iodination of thyroxine (T4) to triiodothyronine (T3) and biliary excretion [10]. Liver is involved in the composition of the proteins that connects thyroid hormone like albumin, pre-albumin and thyroxine-binding globulin (TBG). The elevation of liver enzymes may be linked with thyroid dysfunction. The increased levels of alkaline phosphatase and alanine aminotransferase were associated hyperthyroidism, while the

increase of aspartate aminotransferase is associated with hypothyroidism [11].

On the other hand, liver diseases are repeatedly connected to thyroid hormones variations and thyroid disorders, specially thyroxine and thyroxine-binding globulin increment. Hepatitis C viral infection was associated with thyroid abnormalities [11]. The prevalence of autoimmune thyroid disease is increased in cases of chronic hepatitis associated with primary biliary cirrhosis (PBC) or chronic autoimmune hepatitis [12,13].

As a result of an increase in thyroid-binding globulin levels, the levels of T4 is mostly increased in cases of primary biliary cirrhosis (PBC), mild or moderate severity of acute hepatitis [14]. In some cases of acute hepatic failure (especially viral hepatitis), patients were experiencing goiters, which resolved with an improvement in liver function [15].

Graves' hyperthyroidism probability linked with acute Hepatitis B viral infection (HBV), which influences the hepatocytes at first, causing a series of hepatic complications which includes cirrhosis, fibrosis and hepatocellular carcinoma [16]. In patients of Hepatitis C viral infection (HCV), there was a high prevalence of anti-thyroid antibodies. That means that HCV may be included in the list of predisposing triggers for the onset of auto-immune thyroid diseases (AITD) [17].

Materials and method:

Study groups

In this study, the samples were taken from the Center of Endocrine and Diabetes/ Department of Biochemistry at Al-kindy teaching hospital. Thyroid gland patients were divided into two groups. The patients in each group were already diagnosed with hypo and hyperthyroidism. Group1 consisted of 26 hypothyroidism patients; the ages of the patients were ranged from 22 to 48 years old with mean age of 34.8 ± 7.8 years. Nine of the patients were males while 17 were females. Group 2 consisted of 33 hyperthyroidism patients, the ages of the patients were ranged from 25 to 46 years old with mean age of 36 ± 6.9 years, and 19 of the patients were males while 14 were females. Control group

was selected from the same region and their ages were in the same range of patients. The patients in this study have neither hypertension nor diabetes mellitus.

Blood collection and separation of serum

A volume of 5 ml of venous blood samples was drawn from the study groups with disposable plastic syringe and transferred to plain test tubes. All tubes were centrifuged at 3500-4000 (Revolutions per minute) rpm for 10 min. Serum samples were separated and transferred in a plain container and stored at -20°C until use.

Biochemical analysis

Determination of serum Thyroid-stimulating hormone (TSH):

Thyroid-stimulating hormone was determined by using Enzyme immunoassay test kit according to the procedure provided by manufacture' instructor (Linear chemicals S.L. Joaquim Costa 18 2^a planta. 08390 Montgat, Barcelona, Spain). The test sample is allowed to react simultaneously with the two antibodies, resulting in the TSH molecules being sandwiched between the solid phase and enzyme-linked antibodies. After 60-minute incubation at room temperature, the wells are washed with water to remove unbound labeled antibodies. A solution of TMB Reagent is added and incubated for 20 minutes, resulting in the development of a blue color. The color development is stopped with the addition of Stop Solution, changing the color to yellow. The concentration of TSH is directly proportional to the color intensity of the test

Determination of serum alkaline phosphatase (ALP):

Alkaline phosphatase was measured by Kinetic method using alkaline phosphatase (ALP) Liquizyme kit provided by spectrum company (MDSS GmbH Schiffgraben 4130175 Hannover, Germany). The ALP determination was done by pipetting 1 ml of the working reagent in a test tube then adding a 10 μl of the sample to the test tube. Then the contents of the test tube were mixed and read its initial absorbance after 1 minute at 405 nm, then repeat the absorbance reading after 1, 2, 3 minutes. The mean absorbance was

determined per minute ($\Delta A/\text{min}$) and the mean was multiplied by 5454 to obtain the serum ALP.

Determination of serum Aspartate aminotransferase (AST/GOT):

Serum Aspartate aminotransferase was measured according to colorimetric method kit provided by spectrum company (MDSS GmbH Schiffgraben 4130175 Hannover, Germany). 0.5 ml of buffer solution and 100 μl of the sample were pipetted into a test tube. The contents were mixed and incubated for 30 minutes at 37°C . then 0.5ml of another reagent was added to the test tube for 20 minutes at $20\text{-}25^\circ\text{C}$. Then 5ml of sodium hydroxide solution was added to the test tube and the contents were mixed and after 5 minutes the absorbance was measured at 546nm against reagent blank.

Determination of serum Alanine aminotransferase (ALT/GPT):

Serum Alanine aminotransferase was also determined by colorimetric method kit provided by spectrum company (MDSS GmbH Schiffgraben 4130175 Hannover, Germany). 0.5 ml of buffer solution and 100 μl of the sample were pipetted into a test tube. The contents were mixed and incubated for 30 minutes at 37°C . then 0.5ml of another reagent was added to the test tube for 20 minutes at $20\text{-}25^\circ\text{C}$. Then 5ml of sodium hydroxide solution was added to the test tube and the contents were mixed and after 5 minutes the absorbance was measured at 546nm against reagent blank.

Statistical analysis

The findings were expressed as the mean \pm SD with standard error. Statistical and correlation analyses were performed using the student t-test, and spearman correlation test respectively, P value < 0.001 was accepted as statistically significant. SPSS (for windows, version 10.0) was used for statistical analyses.

Results

In the present study differences appeared between males and females among patients with thyroid dysfunction. It was found that females (52%) are more susceptible than men (48%) to thyroid dysfunction. As it was shown in table (1), levels of serum TSH in patients with hypothyroidism increased significantly ($p < 0.001$) when compared to control.

Also a significant elevation ($p < 0.001$) in the levels of serum ALP, ALT, and AST is shown in hypothyroidism patients when compared to control group.

Table (1)

The serum levels of TSH, ALP, ALT and AST in hypothyroidism patients and control groups expressed as (mean \pm standard deviation).

Groups	No.	TSH ($\mu\text{IU}/\text{ml}$)	ALP (U/L)	ALT (U/L)	AST (U/L)
Control	25	3.8 ± 1.27	83.6 ± 16.9	43.96 ± 26.9	49.6 ± 23.5
Hypothyroidism	26	8.67 ± 1.1	121.5 ± 12.3	111.38 ± 9	99.65 ± 8.4
P-value		< 0.001	< 0.001	< 0.001	< 0.001

The levels of serum TSH were expressed as micro-international unit per milliliter ($\mu\text{IU}/\text{ml}$), while the levels of serum ALP, ALT, and AST were expressed as international unit per liter (U/L); P-value less than 0.001 is significant.

Table (2) show that there is a significant decrease ($p < 0.001$) in the levels of serum TSH in hyperthyroidism patients when compared to control.

The levels of serum ALP, ALT, and AST in hyperthyroidism group were found to increase significantly ($p < 0.001$) when compared to the control group.

Table (2)
The serum levels of TSH, ALP, ALT and AST in hyperthyroidism patients and control groups expressed as (mean± standard deviation).

Groups	No.	TSH (μIU/ml)	ALP (U/L)	ALT (U/L)	AST (U/L)
Control	25	3.8±1.27	83.6 ± 16.9	43.96 ± 26.9	49.6 ± 23.56
Hyperthyroidism	33	0.21±0.1	132.12 ±16.4	106.48±7.35	103.69±8.91
P-value		< 0.001	< 0.001	< 0.001	< 0.001

The levels of serum TSH were expressed as micro-international unit per milliliter (μIU/ml), while the levels of serum ALP, ALT, and AST were expressed as international unit per liter (U/L); P-value less than 0.001 is significant.

Discussion

The metabolism rate of tissues is regulated by thyroid hormones, thus when a change occur in the action of these hormones, various organs and enzymes levels will be influenced by this change [18]. The present study confirmed that thyroid disorder causes significant effect on metabolism of various cells of the body that was reflected by increased level of serum enzymes to a varying extent. Thyroid dysfunction shows a strong female preponderance. Menstrual irregularities, subfertility, ovulatory function and higher repeated miscarriage rates have been connected to hypothyroidism [18].

This study also showed that patients with hypothyroidism suffered from a significant increase ($p < 0.001$) in the levels of liver enzymes ALP, ALT and AST as their values were (121.5 ± 12.3), (111.38 ± 9) and (99.65 ± 8.4) respectively when compared to control group. These results can be explained by the fact that thyroid hormones are essential for organ growth, development and function, and any disorder affecting the thyroid gland will affect the level of the thyroid gland will affect the level of their hormones, leading to imbalance in the metabolism of various organs [19].

The heart and liver are considered the most affected organs by any thyroid dysfunction, so changes the levels of hepatic enzymes ALP,

ALT, AST and GGT [20, 21]. The results conducted in this study were in agreement with the results of other studies [21, 22], as these studies have shown that the levels of liver enzymes (ALP, ALT and AST) elevated in patients with hypothyroidism. While another study conducted by Martinez-Triguero et al., found that the level of AST significantly elevated in patients with hypothyroidism [23].

The present study also showed that the levels of liver enzymes ALP, ALT and AST in hyperthyroidism patients were found to significantly increase ($p < 0.001$) when compared to control group as it was illustrated in Table (2). Thyroid hormones are necessary for the growth and regulation of the metabolic rate of all body cells, so the presence of any abnormality in the thyroid gland will affect cellular metabolism [19]. The liver is the most influenced organ by any defect may occur in the cellular metabolism process, thus the effectiveness of liver enzymes ALP, ALT and AST is affected consequently [20].

Thyroid disease causes relative oxygen deficiency in periventricular regions of the liver. The demand for hepatic oxygen will increase without an appropriate increase in blood flow, as a result the increased levels of liver enzymes in the blood [21]. Excess thyroid hormone can cause hepatic tissue

hypoxia by increased demand of hepatic and splanchnic oxygen [18].

As a result, the current study is in agreement with previous study which was done by Miah and co-workers [24] where the ALP enzyme level was found to elevate significantly in hyperthyroidism patients, while Martinez-Triguero et al., concluded that patients with hyperthyroidism suffered from significant increase in AST enzyme levels. Another study conducted by Pandey et al., [21] found that the levels of liver enzymes ALP, ALT and AST were generally increased in hyperthyroidism patients, the study also showed that the levels of liver enzymes were also increased in cases of hypothyroidism.

A study done by Hasan et al., [18] also showed that the levels of ALP, AST and ALT were increased significantly in both hyperthyroidism and hypothyroidism cases; these results were also in agreement with this current study.

Conclusion

The results of this study, in association with other studies, has shown that there is a relation between thyroid hormone (TSH) and liver enzymes (ALP, ALT, AST) as any thyroid disorder and a TSH deficiency affect the levels of liver enzymes. The liver enzymes ALP, AST and ALT were increased significantly in patients with hyperthyroidism and there was a significant increase in the levels of these enzymes in hypothyroidism patients. This study was a hospital based cross-sectional study involving small number of patients visiting a single hospital in Baghdad. Therefore, the observation might not be true representative of the thyroid disease patients in Iraq. In the future the initiation of a routine screening program should be considered for thyroid alteration and its effect on other organs.

Acknowledgment

The authors would like to thank the workers in the Center of Endocrine and Diabetes/ Department of Biochemistry at Al-kindy teaching hospital for their cooperation.

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