



Received: 19-08-2023  
Accepted: 29-09-2023

ISSN: 2583-049X

## **Biochemical Changes in Liver Enzymes in Patients with Thyroid Dysfunction**

<sup>1</sup> Adil Mohammed Hashim, <sup>2</sup> Raheem Tuama Al Mammori, <sup>3</sup> Ali Mohammed Abd-Alameer

<sup>1,3</sup> DNA Research Center, University of Babylon, Hillah-Najaf Street, Babylon State, 51001, Iraq

<sup>2</sup> Babylon Git and Liver Center, Babylon Directorate, Babylon State, 51001, Iraq

Corresponding Author: **Adil Mohammed Hashim**

### **Abstract**

The process of metabolising thyroid hormones is primarily regulated by the liver. In order for the liver to work properly, thyroid hormone levels must be normal. All cells, including hepatocytes, are subject to thyroid hormone regulation of their basal metabolic rate. Liver function may be affected by thyroid disorders. The current study's objectives are to identify the biochemical changes in liver function tests, which are aspartate amino transferase (AST), alanine amino transferase (ALT), and alkaline phosphatase (ALP), in people with thyroid dysfunction (both subclinical and overt hypothyroidism), as well as assess the impact of

changed thyroid hormones on these tests. Methodology The sample was tested for alkaline phosphatase (ALP), alanine transaminase (ALT), and aspartate transaminase (AST) using the calorimetric method and standard reagent kits. To measure the levels of serum T3, T4, and TSH, ELISA kits were employed. Data analysis was done. Results The results of our study show that serum levels of ALP, AST, and ALT were greater in hypothyroidism patients as compared to controls. Conclusions Patients with thyroid impairment have a regular correlation with the liver enzyme biochemical parameters examined.

**Keywords:** Hypothyroidism, Liver Function Tests, Free T3 and T4, TSH, ALP, AST, ALT

### **1. Introduction**

One of the largest endocrine glands in the body is the thyroid, which secretes hormones and controls metabolic rate in the body [1]. Thyroid-stimulating hormone (TSH) regulates how the thyroid gland functions. The anterior pituitary's propensity to produce thyroid follicular stimulating hormone (TSH) is controlled by thyroid releasing hormone (TRH). Thyroid stimulating hormone (TSH) regulates the thyroid's secretion of triiodothyronine (T3) and thyroxine (T4) [2]. Several types of thyroid dysfunction, varying from goiter to thyroid cancer, appear when the balance of thyroid hormones is abnormal [3]. The term "thyroid ailments" refers to a number of conditions linked to the thyroid hormones [4]. The two primary types of thyroid gland disorders, hyperthyroidism and hypothyroidism, are distinguished by either more or less in the levels of the thyroid hormones (T4 and T3). Congenital or acquired disorders may cause hypothyroidism. A thyroid or pituitary gland abnormality causes the acquired type. [5] Hyperthyroidism may result from thyroid autoimmunity [6]. Both hyperthyroidism and hypothyroidism first manifest as autoimmune thyroiditis, which causes the thyroid gland to swell and fibrose over time, reducing the thyroid gland's capacity to release thyroid hormone. A thyroid goitre, which enlarges the thyroid gland, is the first sign of numerous different types of hypothyroidism [7]. Thyroid hormones are necessary for normal cell development and growth. The resting metabolic rates of all cells are regulated by thyroid hormones; hence, variations in their amount can affect the body's overall metabolism [8, 9]. The thyroid gland secretes 110 nmol of T4 and 10 nmol of T3 daily in healthy individual [10]. Thyroxine's affinity and effectiveness for the nuclear receptor are both ten times larger for triiodothyronine than they are for thyroxine. As a regular part of the initial blood test performed to identify hypothyroidism, TSH levels are measured in the blood. If the TSH levels are high and the T4 levels are low, hypothyroidism is diagnosed. Subclinical hypothyroidism is the diagnosis if the second test indicates high TSH levels but normal T-4 and T-3 results. Usually, there are no visible signs as a result. Thyroid gland disorders are regularly observed in the general population [11].

The most common thyroid disease that affects people in the world is hypothyroidism [12]. It results from decreased T4 and T3 production [13]. The commonly occurring disease hypothyroidism has a negative impact on lipid metabolism [14]. According to the biochemistry, a decline in T4 and T3 levels causes a rise in pituitary TSH release and a quicker increase in blood TSH levels. This test result is important, especially in terms of early thyroid dysfunction identification [15]. The most prevalent lipid abnormality in hypothyroid patients is hypercholesterolemia, mostly as a result of an increased level of low-density lipoproteins (LDL). Additionally, reports of increased HDL, LDL, and (VLDL) cholesterol due to increased hepatic fatty acid esterification have been made [16]. There are a number of reasons for the lack of thyroid activity or low activity. Previous

thyroid operations, exposure to radiation, inflammatory thyroiditis, micronutrient deficiencies, a lack of enzymes necessary for the production of thyroid hormone, and numerous medications are some of the causes [17]. Women are more inclined than men to experience thyroid dysfunction and age-related increases in TSH levels [18]. The blood TSH levels are elevated in sub-clinical hypothyroidism (SH), and the FT4 and FT3 values are within normal limits. Additionally, SH may progress to overt hypothyroidism. There is a connection between SH and elevated TC and LDL-C values. [19, 20] HDL-c levels may be normal or elevated, although overt and SH levels are associated with hypercholesterolemia, primarily because LDL-c levels are elevated. On the other hand, a decrease in total LDL-c and HDL-c levels in the serum, which are used to measure their excretion, is linked to hyperthyroidism [21]. According to whether the serum levels of the (T4 and T3) are elevated or lowered, the two main types of thyroid disorders are hyperthyroidism and hypothyroidism [22]. Aspartate transaminase (AST). The metabolism of amino acids is aided by an enzyme known as AST. Similar to ALT, AST is frequently seen in low amounts in blood. An illness, damage to the liver, or even a muscle injury, could all be indicators of elevated AST levels. An inorganic Hunger, tachycardia, and weariness are signs of hyperthyroidism, which results in an accelerated metabolism.

Edoema, dry skin, and diarrhoea, on the other hand, are signs of a sluggish metabolism brought on by hypothyroidism. In thyroid disease, hypothyroidism is more common than hyperthyroidism, and subclinical thyroid dysfunction is common. Stereospecific transfer mechanism. The process is energy-demanding, and intracellular amounts of the free hormone exceed plasma levels [28].

A vast, the liver produces a readily exchangeable pool of blood hormones in the form of many plasma proteins that connect the hydrophilic thyroid hormones. The hormone's biological effects are caused about by its plasma free hormone component, which is in equilibrium with the hormone's protein-bound equivalent. Since the plasma concentrations of both hormones are steady, Same amounts of free T4 and T3 are absorbed by the tissues. However, the activity of the deiodinase and the transport systems in different tissues affect the levels of free hormone in those tissues [29].

**2. Materials and Methods**

**Sample Collection**

Samples for this investigation were collected from the Margan Medical Centre in Hilla City. Two categories of thyroid gland patients were created (subclinical and overt hypothyroidism). There were 165 subjects in all, ranging in age from 32 to 59. The possibility of diabetes, liver disorders, people taking thyroxin supplements, any other acute inflammatory conditions, and any serious illnesses, a brief medical history and physical were conducted. Among them, the study included (95 sample) 50 subclinical and 45 overt hypothyroid) patients and 70 healthy controls who had no outward signs of illness. A venous blood sample of five millilitres was taken. From the chosen subjects and put in an unadorned test tube. Before being centrifuged for five minutes at 3000 rpm, Blood was drawn and left to clot at room temperature in a simple tube. The serum that was then taken was used to measure the levels of the hormones TSH, FT3, and FT4 as well as the serum enzymes ALT, AST, and

ALP. A deep freezer at a temperature of -40°C is where the serum is kept. T3, T4, and TSH were measured using the ELISA method. By using a fully automated auto analyzer and the kinetic spectrophotometric technique, serum AST, ALT, and ALP concentrations were estimated. Subclinical and overt hypothyroidism used to be classified by thyroid profile tests (FT3, FT4, and TSH).

**Inclusion Standards**

Study on hypothyroid cases, regardless of treatment and disease duration, in the 32–59 age range. Healthy adults between the ages of are used as the control group.

**Exclusion Standards**

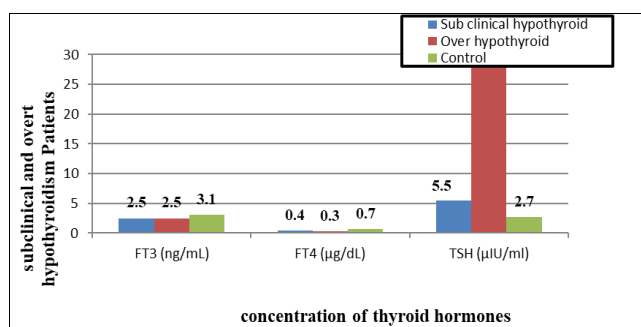
Exclusion criteria for the study included those with previous history of liver disease, persistent drinking, active or recent infections, such as kidneys disease, cardiac conditions, bone and muscle disease, pancreatic disease, pregnancy, as well as diabetes, cancer, high blood pressure, and users of drugs.

**3. Result and Discussion**

In Table 1 of this study, there was a highly significant difference in serum TSH ( $2.7 \pm 0.2$  IU/ml). TSH levels significantly increased in patients with subclinical hypothyroidism ( $5.5 \pm 0.03$  IU/ml), and they significantly increased in patients with overt hypothyroidism ( $28 \pm 0.05$  IU/ml). Also it was statistically significant that the levels of ft4 ( $0.4 \pm 0.2$  g/dL) and ft3 ( $2.5 \pm 0.02$  ng/ml) were lower in subclinical hypothyroid patients than they were in controls ( $0.7 \pm 3.2$  g/dL and  $3.1 \pm 0.02$  ng/ml, respectively). When compared to the control group, ft4 and ft3 levels in overt hypothyroid patients ( $0.3 \pm 0.6$  g/dL and  $2.5 \pm 0.05$  ng/ml, respectively) exhibited a statistically significant decline in value.

**Table 1:** TSH, ft3, and ft4 results were compared between healthy controls and people who had subclinical and overt hypothyroidism

Parameter	Subclinical hypothyroid	Overt hypothyroid	Control	P value
ft3 (ng/mL)	$2.5 \pm 0.02$	$2.5 \pm 0.05$	$3.1 \pm 0.02$	0.001
ft4 (µg/dL)	$0.4 \pm 0.2$	$0.3 \pm 0.6$	$0.7 \pm 3.2$	0.001
TSH (µIU/ml)	$5.5 \pm 0.03$	$28 \pm 0.05$	$2.7 \pm 0.2$	0.001



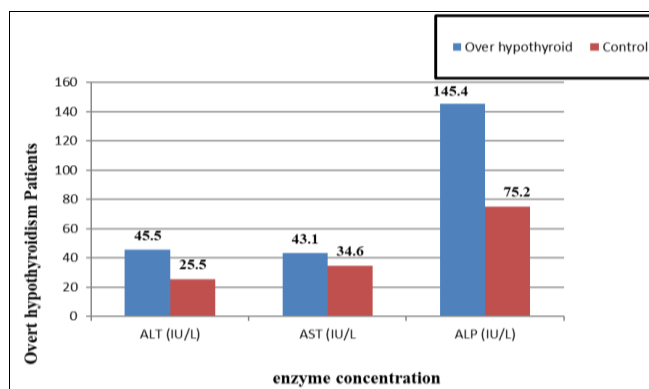
**Fig 1:** TSH, ft3, and ft4 results were compared between healthy controls and people who had subclinical and overt hypothyroidism

In (Table 2, 3) the liver enzyme ALP increased statistically significantly in individuals with overt hypothyroidism ( $145.4 \pm 3.1$  IU/L) and subclinical hypothyroidism ( $134.16 \pm 5.8$  IU/L) when compared to controls ( $75.4 \pm 5.7$  IU/L).

Subclinical hypothyroid subjects had higher AST levels than controls ( $40.5 \pm 1.5$  IU/L), while overt hypothyroid cases had significantly higher values ( $43.1 \pm 2.5$  IU/L). When control ( $25.1 \pm 0.9$  IU/L) was compared to subclinical hypothyroid cases ( $35.3 \pm 0.9$  IU/L) Additionally, the changes in ALT readings were statistically significant in overt hypothyroid patients ( $45.5 \pm 2.8$  IU/L) as well.

**Table 2:** Comparison of liver enzyme data obtained in people with overt hypothyroidism and controls

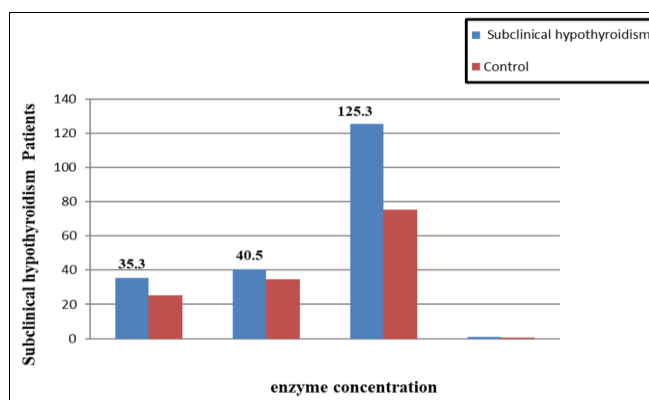
Parameter	Overt Hypothyroid	control	P value
ALT (IU/L)	$45.5 \pm 2.8$	$25.5 \pm 0.9$	0.002
AST (IU/L)	$43.1 \pm 2.5$	$34.6 \pm 1.9$	0.003
ALP (IU/L)	$145.4 \pm 2$	$75.2 \pm 5.7$	0.002



**Fig 2:** Comparison of liver enzyme data obtained in people with overt hypothyroidism and controls

**Table 3:** Comparison of liver enzyme data obtained in people with subclinical hypothyroidism and controls

Parameter	Subclinical hypothyroid	control	P Value
ALT(IU/L)	$35.3 \pm 0.9$	$25.1 \pm 0.9$	0.005
AST(IU/L)	$40.5 \pm 1.5$	$34.6 \pm 1.9$	0.130
ALP(IU/L)	$125.3 \pm 5.8$	$75.4 \pm 5.7$	0.010



**Fig 3:** Comparison of liver enzyme data obtained in people with subclinical hypothyroidism and controls

## Discussion

Thyroid hormones control the rate of tissue metabolism; as a result, changes in the activity of these hormones will have an impact on the levels of various organs and enzymes<sup>[30]</sup>.

Our findings demonstrated that the levels of AST, ALT, and ALP in hypothyroid people were significantly higher when compared to healthy controls. Both overt and subclinical hypothyroid patients had this rise. Thyroid hormones are metabolised by the liver, muscle, and kidney, which also controls their endocrine systemic effects. Therefore, liver,

muscle, and other organ functioning may be affected by thyroid disease, and vice versa<sup>[31]</sup>. ALP, ALT, and AST values in hypothyroid individuals increased significantly ( $p < 0.001$ ) more than those in the control group, according to the study's findings. ALP, ALT, and AST values in hypothyroid individuals increased significantly ( $p < 0.001$ ) more than those in the control group, according to the study's findings. All of these effects could be caused by an imbalance in the metabolism of numerous organs, since thyroid hormones are essential for their formation, growth, and functioning<sup>[32]</sup>. The findings of this investigation were consistent with those of prior studies. Relatively low oxygen levels are brought on by thyroid illness in the periventricular liver. The need for hepatic oxygen will increase due to the increased levels of liver enzymes in the blood without a corresponding increase in blood flow<sup>[33]</sup>.

## 4. Conclusion

The current investigation provided evidence that thyroid disorders had considerable effects on the metabolism of different bodily cells, which were reflected in variable degrees by elevated serum enzyme levels. Liver enzymes (ALP, ALT, AST) and thyroid hormone (TSH) are related because both thyroid disorders and low TSH levels affect the levels of these enzymes. Whereas patients with hypothyroidism had significantly higher levels of same enzymes.

## 5. References

- Skarulis MC, Stack BC Jr. Thyroid disease, e-publication; Office on Women's Health (OWH), USA, Washington DC: Department of Health and Human Services, 2015.
- Lynn WR, Lynn JA. Hypothyroidism is easily overlooked, *Practitioner*. 2007; 22(4):224-231.
- Al Shahrani AS, El-Metwally A, Al-Surimi K, Salih SB, Saleh Y, Al-Shehri A, *et al*. The epidemiology of thyroid diseases in the Arab world: A systematic review, *Journal of Public health and Epidemiology*. 2016; 8(2):17-26.
- Abdullah JA, Abdulkalek H, Haider S, Aamer A. Study of the relationship between calcium ion and thyroid hormones, liver enzymes in some patients of hypocalcaemia and hypercalcaemia, *Journal of Contemporary Medical Sciences*. 2015; 1(3):27-30.
- Segni M. Disorders of the thyroid gland in infancy, childhood and adolescence. In *Endotext* [Internet]. MDText.com, Inc, 2017.
- Zabczyńska M, Kozłowska K, Pocheć E. Glycosylation in the thyroid gland: Vital aspects of glycoprotein function in thyrocyte physiology and thyroid disorders, *International Journal of Molecular Sciences*. 2018; 19(9):p2792.
- Tahs YH, Hussein HKA, Ali EA. Estimation of Serum Copper, Manganese, Selenium, and Zinc in Hypothyroid Patients, *Journal of the Faculty of Medicine*. 2008; 50(2):255-260.
- Manjula KS, Priyadarshini KSHV, Shetty, Usha SMR, Reena R. Study of serum transaminases in hypothyroidism. *Journal of Evolution of Medical and Dental Sciences*. 2013; 2:230-234.
- Hasan B, Ibrahim N. Estimation of thyroid hormones and liver enzymes levels in hypo and hyperthyroidism in iraqi women. *Int j pharm bio sci*. 2016; 7:707-713.

10. Larsen PR. Thyroidal triiodothyronine and thyroxine in Graves' disease: Correlation with presurgical treatment, thyroid status, and iodine content. *J Clin Endocrinol Metab.* 1975; 41:1098-1104.
11. Delitala AP, Pilia MG, Ferreli L, Loi F, Curreli N, Balaci L, *et al.* Prevalence of unknown thyroid disorders in a Sardinian cohort. *Eur. J. Endocrinol.* 2014; 171:143-149.
12. Mushtaq S, Ishaq S, Rashid T, Rasool S, Bhat AA, Majid S. Dyslipidemia in Thyroid Disorders. *Indo Amer J Pharm Res.* 2015; 5(11):3439-3443.
13. Seely EW, Williams GH. The heart in Endocrine Disorder In: Eugene Braunwald, Douglas P. Zipes. *Heart Disease* 6th edition. W. B. Saunders Company, Philadelphia, 2001, 2151-2171.
14. Rizos CV, Elisaf MS, Liberopoulos EN. Effects of Thyroid Dysfunction on Lipid Profile. *Open Cardiovasc Med J.* 2011; 5:76-84.
15. Galesanu C, Lisnic N, Teslaru R, Apostu L, Zbranca E. Lipid profile in a group of hypothyroid patients Vs treated hypothyroid patients. *Rev Med Chir Soc Med Nat Iasi.* 2004; 108(3):554-560.
16. Pucci E, Chiovato L, Pinchera A. Thyroid and lipid metabolism. *Inter J Obesity.* 2000; 24(2):109-112.
17. Zhang G, Berardi LV. An investigation of neural networks in thyroid function diagnosis, *Health Care Manag Sci.* 1998; 1(1):29-37.
18. Valeix P, Dos Santos C, Castetbon K, Bertrais S, Cousty C, Herberg S. Thyroid hormone levels and thyroid dysfunction of French adults participating in the SU.VI.MAX study. *Annal Endocrinol.* 2004; 65(6):477-486.
19. Danes MD, Ladenson PW, Meinert CL, Powe NR. Effect of thyroxine therapy on serum lipoproteins in patients with mild thyroid failure: A quantitative review of literature. *Clin Endocrinol Meta.* 2000; 85:2993-3001.
20. Luboshitzky R, Aviv A, Herer P, Lavie L. Risk factors for cardiovascular disease in women with sub-clinical hypothyroidism. *Thyroid.* 2002; 12:421-425.
21. Liberopoulos EN, Elisaf MS. Dyslipidemia in patients with thyroid disorders. *Hormones.* 2002; 1(4):218-223.
22. Mittal A, Sathian B, Kumar A, Chandrasekharan N, Dwedi S. The Clinical Implications of Thyroid Hormones and its Association with Lipid Profile. *Nepal Journal of Epidemiology.* 2010; 1:11-16.
23. Delitala AP, Pilia MG, Ferreli L, Loi F, Curreli N, Balaci L, *et al.* Prevalence of unknown thyroid disorders in a Sardinian cohort. *Eur. J. Endocrinol.* 2014; 171:143-149.
24. Fleisher GA, Mcconaheyw M, Pankow M. Serum creatine kinase, lactic dehydrogenase, and glutamic-oxalacetic transaminase in thyroid diseases and pregnancy. *Mayo Clin Proc.* 1965; 40:300-311.
25. Griffiths PD, Hodgson H. Serum enzymes in diseases of thyroid gland. *J Clin Pathol.* 1965; 18:600-663.
26. Finstrer J, Stellberger C, Grossege, Koroiss CA. Hypothyroid myopathy with unusually high serum creatine kinase. *Hormone Res.* 1999; 52(2):205-208.
27. Cinamon U. Exceptionally elevated creatine kinase levels in a laryngectomized patient: Hypothyroid myopathy. *J Laryngol otol.* 2004; 118(8):651-652.
28. Hennemann G, Docter R, Friesema EC, *et al.* Plasma membrane transport of thyroid hormones and its role in thyroid hormone metabolism and bioavailability. *Endocr Rev.* 2001; 22:451-476.
29. Bianco AC, Salvatore D, Gereben B, *et al.* Biochemistry, cellular and molecular biology, and physiological roles of the iodothyronine selenodeiodinases. *Endocr Rev.* 2002; 23:38-89.
30. Hasan BF, Ibrahim NA, ABD DA. Estimation of thyroid hormones and liver enzymes levels in hypo and hyperthyroidism in Iraqi women, *Int J Pharm Bio Sci.* 2016; 7(4):707-713.
31. Malik R, Hodgson H. The relationship between the thyroid gland and the liver. *Q J Med.* 2002; 95:559-569.
32. Targher G, Montagnana M, Salvagno G, Moghetti P, Zoppini G, Muggeo M. Association between serum TSH, free T4 and serum liver enzyme activities in a large cohort of unselected outpatients, *Clinical endocrinology.* 2008; 68(3):481-484.
33. Pandey R, Jaiswal S, Bastola JPSK, Dulal S. Assessment of Serum Enzymes Level in Patients with Thyroid Alteration Attending Manipal Teaching Hospital, Pokhara, *Research & Reviews: A Journal of Life Sciences.* 2018; 3(1):1-9.