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Original article

Impact of Hyperthyroidism on Liver Function: A Study of Serum Enzyme Variations

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Abstract
Hyperthyroidism is a clinical disorder marked by the excessive production and release of thyroid hormones by an overactive thyroid gland, leading to a hypermetabolic state that affects multiple organ systems, including the liver. This study aims to assess the serum ALT, AST, ALP, and GGT in patients with Hyperthyroidism. This cross-sectional study was conducted between January 1 and July 10, 2025, at Alshams Medical Laboratories in Diyala City. It included 100 participants: 70 patients with Hyperthyroidism and 30 healthy controls. Serum pituitary and thyroid hormone levels were measured using the cobas® e 411 analyzers, while liver enzymes were analyzed with a cobas® c 311 analyzer. Serum ALT, AST, and ALP were significantly higher in hyperthyroid compared to controls (P= 0.001 for all). Although GGT levels were slightly higher in the patient group than in controls, the difference did not reach statistical significance (P=0.274). ALP showed a significant negative correlation with TSH (P=0.038), and significant moderate positive correlations with Free T3 (P=0.003 and Free T4 (P=0.042). Hyperthyroid patients show elevated liver enzymes, with ALP inversely related to TSH and positively to Free T3 and T4. This may signal potential liver dysfunction and calls for further evaluation among these patients.
Keywords. *Hyperthyroidism; Liver enzymes; ALP; Free T3/T4; TSH*

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Introduction

Hyperthyroidism is a disorder characterized by the overproduction of thyroid hormones. It has profound effects on various organ systems, specifically the liver [1,2]. In recent decades, research has increasingly highlighted the complex relationship between thyroid function and hepatic metabolism, confirming the role that thyroid hormones play in regulating key enzymatic processes within the liver. In cases of hyperthyroidism, this imbalance can lead to a range of liver function disorders, which in turn range from a slight increase in serum enzymes to severe liver dysfunction. Physiologically, it is believed that excess thyroid hormones in hyperthyroidism cause direct toxicity to liver cells, disrupt cellular energy balance, and induce oxidative stress through increased metabolic activity. Moreover, hypermetabolism can lead to hepatic hypoxia, with subsequent cellular degeneration and necrosis, especially in cases accompanied by heart failure or pre-existing liver disease [3,4]. Epidemiological studies indicate that liver function abnormalities occur in a large proportion of hyperthyroid patients. This is evidenced by elevated serum liver enzymes such as alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (ALP) in 15% to 76% of cases [5,6]. It is worth noting that these abnormalities often improve with the restoration of normal thyroid function, supporting the existence of a direct pathological link [2].

The mechanisms underlying liver dysfunction in hyperthyroid patients are multifactorial and not fully understood. Direct cellular hepatotoxicity results from hypermetabolism caused by increased thyroid hormones, leading to increased oxygen demand in liver tissue and ultimately to central hypoxia, which damages liver cells and releases intracellular enzymes into the bloodstream. Additionally, autoimmune processes, congestive hepatopathy secondary to thyrotoxic heart failure, and adverse effects of antithyroid drugs contribute to liver impairment. Histologic findings in affected individuals often reveal fatty infiltration, cytoplasmic vacuolization, and mitochondrial alterations within hepatocytes [2–4,7].At the local level, several Iraqi studies have shown a marked increase in liver enzyme levels in patients with hyperthyroidism. For instance, Samir and Hameed [6] confirm that both hyperthyroidism and hypothyroidism patients show a significant increase in AST, ALT, and ALP enzyme levels in their blood serum compared to healthy groups, with hyperthyroidism patients generally showing higher enzyme levels. In addition to enzymatic changes, other Iraqi studies have found that patients with hyperthyroidism suffer from changes in lipid metabolism, reflecting the findings reported in the broader international literature and reinforcing the systemic nature of the interactions between the thyroid gland and liver [8,9]. Generally, the effect of hyperthyroidism on liver function is multifaceted, reflecting both the metabolic burden of thyrotoxicosis and the potential

cardiovascular or immunological factors that accompany it. The assessment of serum enzyme changes provides a valuable window into these interactions, with direct clinical implications for diagnosis and treatment. This study aims to determine the patterns and significance of serum enzyme alterations attributable to hyperthyroidism in the Iraqi population.

Methods

Study Design and Setting

This cross-sectional study was carried out at Alshams Medical Laboratories in Diyala City between January 1 and July 10, 2025. The diagnosis of hyperthyroidism among patients was confirmed through serological assessment of thyroid hormone levels.

Exclusion Criteria

Participants with known liver disease, renal impairment, recent infections, or those taking medications that could influence liver function were excluded from the study.

Blood Collection

4 mL of venous blood was drawn from each hyperthyroid patient and control participant under strict aseptic conditions. The samples were collected into gel-activator tubes and allowed to clot at room temperature. Following clot formation, the samples were centrifuged at 2000 rpm for 15 minutes. The separated serum was then aliquoted into two sterile Eppendorf tubes and stored at -20 °C until further analysis for thyroid hormone levels and liver enzyme activity.

Laboratory Analysis

Detection of Pituitary and Thyroid Hormones

Serum levels of TSH, free T3, and free T4 were measured using the cobas® e 411 analyzers (Roche Diagnostics, Mannheim, Germany), following the manufacturer's standardized protocols and instructions.

Assessment of Serum Liver Enzyme Levels

Serum levels of ALT, AST, ALP, and GGT were determined utilizing the cobas® c 311 analyzers (Roche Diagnostics, Germany), in agreement with the manufacturer's procedures.

Ethical Considerations

Written informed consent was obtained from all participants before their enrollment in the study. The research adhered to the ethical standards outlined in the Declaration of Helsinki and received approval from the Institutional Review Board at the University of Diyala.

Statistical Analysis

Data were analyzed using SPSS version 26. Descriptive statistics were expressed as mean ± standard error for continuous variables with normal distribution, while categorical data were presented as frequencies and percentages. Group differences in continuous variables were examined using the independent samples t-test. Pearson's correlation coefficient was employed to assess the relationships between continuous and categorized variables, where applicable. A p-value less than 0.05 was considered statistically significant.

Results

Demographic and clinical features of CKD patients

This study included 70 patients diagnosed with hyperthyroidism and 30 healthy controls. The mean age of the patient group was 34.01 ±1.12 years, while the control group had a mean age of 33.27 ±1.28 years (P=0.695). Gender distribution was similar between the groups, with 31.4% males and 68.6% females in the patient group, compared to 30.0% males and 70.0% females in the control group. No statistically significant difference was observed in body mass index (BMI) between patients (24.81 ± 0.44 kg/m²) and controls (25.65 ±0.89 kg/m²) (P=0.398). Thyroid hormone levels showed highly significant differences between the two groups. Patients with hyperthyroidism had markedly reduced thyroid-stimulating hormone (TSH) levels (0.162 ±0.008 mIU/L) compared to controls (1.91 ±0.16 mIU/L) (P = 0.001). Conversely, both free triiodothyronine (Free T3) and free thyroxine (Free T4) were significantly elevated in the patient group (7.23 ± 0.20 and 28.10 ±0.61 pmol/L, respectively) versus controls (3.26 ± 0.12 and 14.93 ± 0.53 pmol/L, respectively) (both P=0.001) (Table 1). Analysis of liver enzymes revealed significant elevations in patients with hyperthyroidism. Serum alanine aminotransferase (ALT) was significantly higher in patients (46.23 ± 1.51 U/L) compared to controls (27.27 ± 10.51 U/L) (P=0.001) (Figure 1A). Similarly, aspartate aminotransferase (AST) was elevated in patients (39.62 ± 1.44 U/L) versus controls (27.83 ± 1.53 U/L) (p =

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0.001) (Figure 1B). Alkaline phosphatase (ALP) levels were also significantly higher among patients (121.01 ± 3.76 U/L) compared to controls (96.96 ± 3.09 U/L) (P = 0.001) (Figure 1C). Although gamma-glutamyl transferase (GGT) levels were slightly higher in the patient group (32.12 ± 1.16 U/L) than in controls (29.20 ± 2.36 U/L), the difference did not reach statistical significance (P = 0.274) (Figure 1D).

Table 1: Demographic Profile and Clinical Parameters of Participants.

N	Variables		Patients (No. 70)	Controls (No. 30)	*P- value*
1.	Age		34.01 ± 1.118	33.27± 1.275	0.695
2.	Gender	Male	22 (31.4%)	9 (30.0%)	–
		Female	48 (68.6)	21 (70.0%)	
3.	BMI		24.81± .438	25.65± 0.887	0.398
4.	TSH		0.162± .008	1.91± 0.158	0.001
5.	Free_T3		7.23± .199	3.26± 0.119	0.001
6.	Free_T4		28.10± . 610	14.93± 0.534	0.001

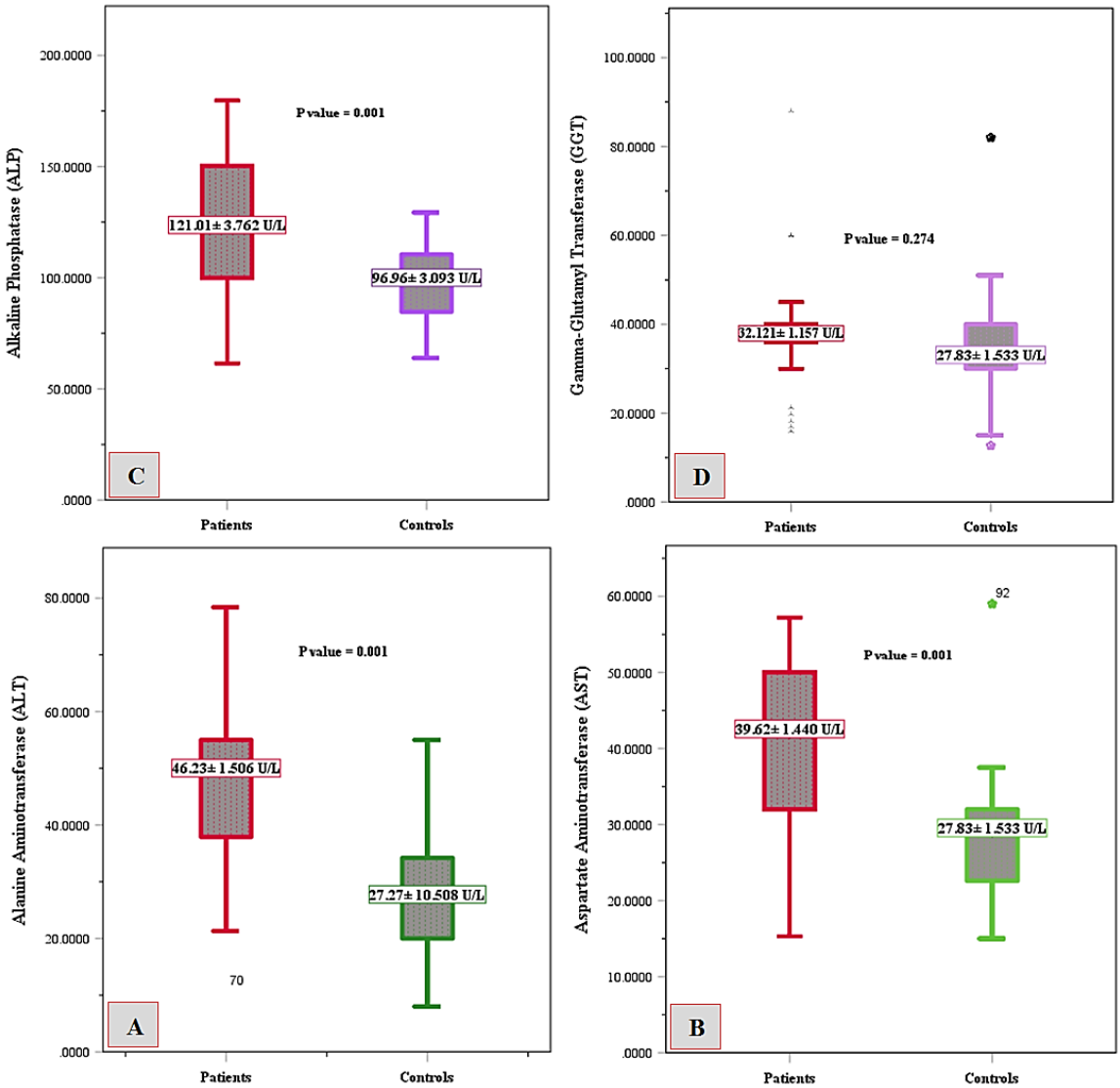

Figure 1: Multi-panel representation of liver enzymes in hyperthyroid and control groups: (A) ALT, (B) AST, (C) ALP, (D) GGT.

Correlation Analysis of Variables Among Patients with Hyperthyroidism

Correlation analysis was performed to assess the relationship between ALP and thyroid hormones (TSH, Free T3, and Free T4) in the hyperthyroid patient group (n = 70). ALP showed a significant negative

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correlation with TSH (r = -0.248, P = 0.038) (Figure 2), indicating that lower TSH levels were associated with higher ALP levels. Additionally, ALP demonstrated significant positive correlations with Free T3 (r = 0.349, P = 0.003) and Free T4 (r = 0.243, p = 0.042) (Figure 3), suggesting that increased thyroid hormone levels corresponded to elevated ALP values. All correlations were significant at either the 0.05 or 0.01 level.

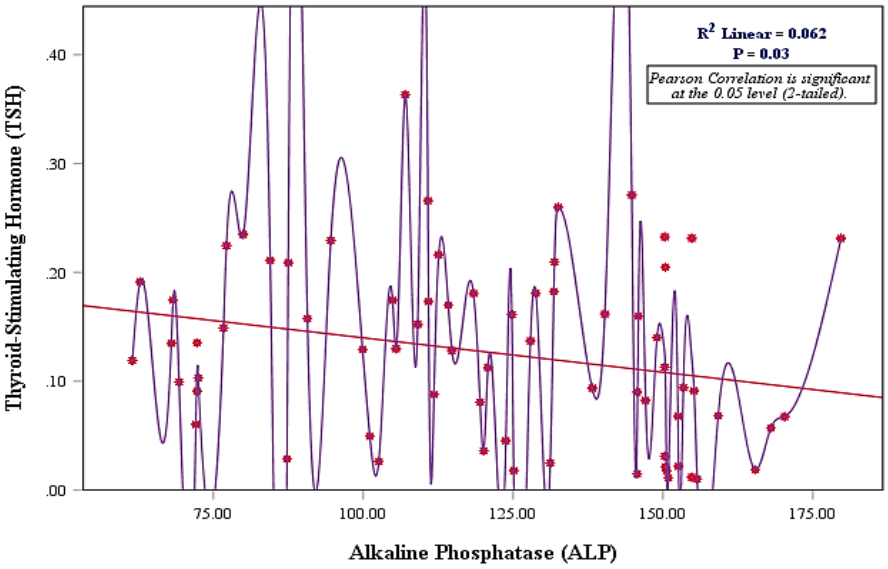

Figure 2: Pearson correlation between ALP and TSH among patients diagnosed with hyperthyroidism.

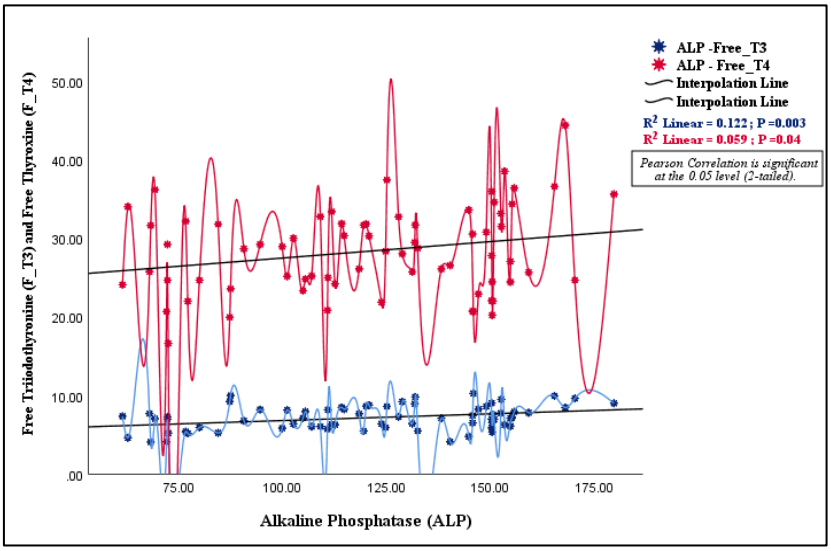

Figure 3. Pearson correlation between ALP and Free T3 and T4 among patients diagnosed with hyperthyroidism.

Discussion

The observed findings of significantly elevated Free T3 and T4 levels, alongside suppressed TSH in hyperthyroid patients compared to controls, are well-established markers of hyperthyroidism and align with current clinical standards for diagnosis. Elevated thyroid hormones (Free T3 and T4) directly reflect increased thyroid gland activity, while the low TSH results from the negative feedback imposed by circulating thyroid hormones on the pituitary gland. Furthermore, in conditions such as Graves' disease or toxic nodular goiter, autoantibodies stimulate excessive hormone production. The relatively high mean values of these hormones indicate a robust thyroid response to regulatory signals that are dysfunctional in hyperthyroid states. This hormonal profile is critical for distinguishing overt hyperthyroidism from other thyroid disorders, as noted in authoritative recent reviews and clinical guidelines [1,10–13].

In addition to the thyroid profile, this study revealed significantly higher levels of ALT, AST, and ALP in hyperthyroid patients compared to controls. GGT was slightly elevated in patients, but the difference was not statistically significant. Multiple contemporary studies have observed a high rate of abnormal liver

function tests in untreated hyperthyroidism [5,7,14,15]. For instance, a recent study in Iraq by Hasan et al.[16] reported an increase in ALT, AST, and ALP levels in hyperthyroid patients compared to healthy controls. Similarly, a meta-analysis by Campos et al [17] highlights that hyperthyroidism can cause liver enzyme abnormalities, particularly elevated ALT. Liver dysfunction may worsen with antithyroid drugs like carbimazole, showing a hepatitic pattern rather than the usual cholestatic one. Liver enzymes improved after stopping the drug, emphasizing the need to monitor liver function in hyperthyroid patients, especially during medication. However, the prevalence rates of liver enzyme abnormalities in hyperthyroid cohorts range from 15% to 76% depending on the specific enzyme and population studied [2,18]. Additionally, the results of this study revealed that ALP had a significant inverse correlation with TSH and positive correlations with Free T3 and Free T4 among hyperthyroid patients. Several recent clinical studies confirm that ALP levels are typically elevated in hyperthyroid patients and inversely related to TSH. TSH, which is suppressed in hyperthyroidism, shows a weak negative correlation with ALP, as reported in a 2024 multicenter analysis, where ALP and TSH correlation coefficients were notably negative (r = -0.06), though not always reaching statistical significance [19]. The drop in TSH is accompanied by a rise in ALP, reflecting thyroid-driven metabolic changes impacting liver and bone tissue. Multiple studies suggest that as free T3 and T4 levels increase, so do ALP levels. In a 2021 cross-sectional study, hyperthyroid patients showed significantly higher levels of ALP and free ALP compared to euthyroid controls, corresponding to the severity of thyroid dysfunction [20]. Another robust clinical study from 2019 supports this view: a multivariate analysis found that elevated free T3 and T4 levels independently predicted the presence of abnormal liver enzymes, particularly ALP [18].

The liver plays a crucial role in thyroid hormone metabolism, and hyperthyroidism has been associated with various hepatic abnormalities, including elevated liver enzymes. The pathophysiology of these changes is multifactorial. Excess thyroid hormones, particularly T3 and T4, increase hepatic oxygen consumption and metabolic activity, which may lead to relative hepatic hypoxia and oxidative stress, resulting in hepatocellular injury and subsequent elevation of transaminases (ALT and AST) [2–4,21]. In addition, increased bone turnover under thyrotoxic conditions contributes to elevated ALP, particularly its bone isoenzyme, with GGT sometimes rising in parallel when cholestasis or biliary dysfunction occurs [22,23]. Autoimmune mechanisms, especially in Graves' disease, may further exacerbate hepatocyte injury, because thyroid-stimulating immunoglobulins can bind hepatocyte receptors and induce inflammation [2,17]. Existing conditions, such as heart failure from thyrotoxicosis, may lead to congestive hepatopathy, compounding liver dysfunction [4]. Most liver enzyme abnormalities resolve following treatment and normalization of thyroid hormone levels, underscoring the reversible nature of thyrotoxicosis-induced liver injury.

Conclusion

This study demonstrates that patients with hyperthyroidism exhibit significantly elevated levels of liver enzymes compared to These findings suggest that persistently elevated liver enzymes in hyperthyroid patients may indicate a future risk for liver dysfunction and warrant comprehensive evaluation.

Conflict of interest. Nil

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