# Influence of Thyroid Disorders on Liver Function Tests in – Diyala Governorate

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## Abstract

**Background:** Thyroid diseases may disturb liver function; liver disease modulates thyroid hormone metabolism, and a range of systemic diseases disturb both organs. There are clinical and laboratory relations between thyroid and liver diseases. Patients with chronic liver disease may have thyroiditis, hyperthyroidism, or hypothyroidism.aPatients with subacute thyroiditis or hyperthyroidism may have abnormalities in liver function tests, which return to normal as the thyroid disorder improves.

**Objective:** The present study is designed to investigate the effects of thyroid disorders on liver function tests.

**Patients and Methods:** In this study sixty patients were employed and categorized into two groups, thirty patients with hyperthyroidism (13 male and 17female) with age range of 25-45years, (mean 33.38) and thirty patients with hypothyroidism (11male and 19 female) with age range 25-45 years (mean 36.78),while 30 normal healthy individuals were chosen as a control group (15male and 15 female) in the same age range (mean 34.44) were taken for comparison. Blood samples were collected from the patients at Baqubah Teaching Hospital , between April 2020 to July 2020. Basic serum biochemical parameters including, thyroid stimulation hormone (TSH), triiodothyronine(T3) and thyroxin (T4)were assayed for patients and control groups by Cobas e 411 autoanalyzer within eight weeks. Serum normal values for alanine aminotransferase (ALT). ALT (Alanine Aminotransferase), Aspartate aminotransferase (AST), alkaline phosphatase test (ALP), direct bilirubin (DB) and total bilirubin( TSB) were assayed within four days by Cobas integra 400 plus autoanalyzer.

**Results:** The mean value of ALT, AST, ALP,TSB, and DB in patients with hyperthyroidism, and hypothyroidism was significantly increased when compared with their mean values of healthy control ($p < 0.05$).A significant difference was also found in mean values of T3,T4,TSH in hyperthyroidism and hypothyroidism when compared with their mean values of healthy control($p < 0.05$). Results of this work revealed a significant negative correlation of TSH with ALP and TSB ($p<0.05$). Further, T4 showed a significant positive correlation with ALP ($P<0.05$).The same results revealed that there was a significant positive correlation between T3 and ALP with ($p<0.05$).There was no significant correlations between ALT,AST,DB with TSH,T3,T4.Further,no significant correlations between TSB and T3,T4 ($p >0.05$).

**Conclusion:** The current study shows that thyroid disorder might cause significant effect on the metabolism of hepatocytes reflected by an increase in biochemical parameters of liver function test AST, ALT ALP,TSB and DB in both hyperthyroidism and hypothyroidism subjects.

**Keywords:** Thyroid diseases ,Alanine aminotransferase , hyperthyroidism, Tetraiodothyronin ,Thyroid stimulating hormone,hypothyroidism

## Introduction

Thyroid hormones are important for normal organ growth and development. Thyroid hormones control the basal metabolic rate of all cells, so change in their levels can affects the whole metabolism [1]. Thyroid hormones regulate calorigenesis in tissues, with hepatocytes and thereby modulating the hepatic function. The liver, in turn, metabolizes the thyroid hormones and adjust their endocrine effects [2].A complex association happens between thyroid and liver in health and disease. The liver works an important physiological role in thyroid hormones activation and inactivation, transport, and metabolism. In opposition, thyroid hormones affect the actions of hepatocytes and hepatic metabolism. Serum liver enzymes abnormalities detected in hypothyroidism may be linked to impaired lipid metabolism, hepatic steatosis or hypothyroidism stimulated myopathy[3].Severe hypothyroidism may have biochemical and clinical features, such as hyperammonemia and ascites, mimicking those of liver failure. Liver function tests are often abnormal also in hyperthyroidism, triggered by oxidative stress, cholestasis, or enhanced osteoblastic activity [4]. A cross-sectional study of the hepatic response to thyroxine replacement submitted that patients with spontaneous primary hypothyroidism are more susceptible to hepatocellular damage than patients who have radioiodine-induced hypothyroidism [5]. In patients with hypothyroidism and abnormal liver function tests, once primary thyroid pathology is recognized and treated, the liver function abnormalities return to normal [6].

## Patients and Methods

Thirty patients with hyperthyroidism,13 male and 17 female with age range 25–45years (mean 33.38) and thirty patients with hypothyroidism (11male and 19 female with age range 25–45 years (mean 36.78) were studied. Blood samples were collected from

the patients at Baqubah Teaching Hospital in Baquba, Diyala-Iraq from April 2020 to July 2020. The Ethical Committee of the Hospital approved this study. Thirty subjects (15male and 15 female) in the same age range (mean 34.44) who constituted the control group were taken for comparison. The diagnosis of hyperthyroidism and hypothyroidism was made by specialized consultants, through considering the results of laboratory tests and clinical features of the patients.

These patients were recently diagnosed with hyperthyroidism and hypothyroidism. The liver function tests which were done within 6 months of the diagnosis were reviewed. For evaluation of hypothyroidism subjects with a thyroid-stimulating hormone (TSH) level equal or greater than 10 µIU/mL were classified as having hypothyroidism, and subjects with (TSH) level lower than 0.27µIU/mL were classified as having hyperthyroidism. The data for patients and control included information about sex, age, take medication affect liver function, date of diagnosis, medication and chronic illness history.

**Sample collection**

About 5 milliliters venous blood were obtained from all subjects (patients and controls) in the morning before taking medication. The blood samples were centrifuged at 3000 rpm for 10 minutes and the samples were kept in two places, freezed at about -20°C for hormonal assay and in 2 - 8°C for ALT, AST,.ALP, DB and TSB assay.

**Exclusion criteria**

Patients diagnosed withhyperthyroidism and hypothyroidism who taking medications more than six months were excluded. History of liver diseases, individuals with an active infection or a recent infection including liver disease, chronic alcoholism, bone and muscle disease, cardiac disease Hepatobillary disease, diabetes, malignancy, and hypertension were excluded.

**Serum investigation**

Basic serum biochemical parameters including, thyroid stimulation hormone (TSH), triiodothyronine (T3) and thyroxin (T4) were assayed for patients and control groups within eight weeks. Serum ALT, AST, ALP, DB and TSB were assayed within four days.

Cobas Integra 400 plus analyzer and Cobas E411(Roche, Germany) are automatically applicable for serum and plasma, Pipetting reagents -working solution and steps of calculates the analyte activity of each sample.

## Statistical analysis

Data of current study were analyzed by using Chi-square ($\chi^2$) test to compare between percentages. Measured sensitivity and specificity of diagnostic tests (detection the best test for diagnosis). Continuous data were described by (Mean ± SD). Student's t-test used to compare between two continuous variables, while F-test (ANOVA) used to compared between three continuous variables or more. Pearson correlation (r) accounted to explain type and strength of relationship between variables. A level of significance of ≤0.05 was applied to test. (SPSS version .22 and Excel 2013) programs used to analyze current data.

## Results

The registered cases for both sexes were located within the age range (33.38) for patients with hyperthyroidism, (36.78) for

hypothyroidism, and (34.44) for control group. Data illustrated in Table(1) revealed that the mean value of ALT, AST, ALP, TSB, DB (23.92, 22.11, 115.24, 14.06, 4.04) in patients with hyperthyroidism, and ALT ,AST,ALP,TSB,DB (28.19 , 27.09, 82.00, 10.38, 3.30) in hypothyroidism were significantly increased when compared with their mean values of healthy control (15.39, 16.83, 76.53, 9.80, 2.87), ($p < 0.05$). The same table showed that a significant difference was found in mean values of T3, T4, TSH(3.48, 145, 0.01) in hyperthyroidism, and (1.54 , 66.61, 19.02) in hypothyroidism when compared with their mean values of healthy control(1.76, 99.00, 1.78), ($p < 0.05$).

**Table (1):** comparison between biochemical parameters within study groups by using (ANOVA)

| | | Mean | SD | Statistics |
|---|---|---|---|---|
| ALT | Hyperthyroidism | 23.92 [a b] | 11.98 | P= 0.005** LSD=11.55 |
| | Hypothyroidism | 28.19 [a] | 16.03 | |
| | Control | 15.39 [b] | 4.78 | |
| AST | Hyperthyroidism | 22.11 [a b] | 7.95 | P=0.006** LSD=7.77 |
| | Hypothyroidism | 27.09 [a] | 9.69 | |
| | Control | 16.83 [b] | 3.62 | |
| ALP | Hyperthyroidism | 115.24 [a] | 37.43 | P=0.002** LSD=25 |
| | Hypothyroidism | 82.00 [b] | 18.06 | |
| | Control | 76.53 [b] | 13.02 | |
| TSB | Hyperthyroidism | 14.06 [a] | 6.19 | P=0.001*** LSD=4.44 |
| | Hypothyroidism | 10.38 [a b] | 4.07 | |
| | Control | 9.80 [b] | 2.40 | |
| DB | Hyperthyroidism | 4.04 [a] | 2.11 | P=0.03* LSD=1.02 |
| | Hypothyroidism | 3.30 [a b] | 1.49 | |
| | Control | 2.87 [a] | 1.37 | |
| T3 | Hyperthyroidism | 3.48 [a] | 1.68 | P=0.002** LSD= 1.08 |
| | Hypothyroidism | 1.54 [b] | 0.58 | |
| | Control | 1.76 [b] | 0.34 | |
| T4 | Hyperthyroidism | 145.77 [a] | 48.91 | P=0.003** LSD= 31.22 |
| | Hypothyroidism | 66.61 [c] | 26.23 | |
| | Control | 99.00 [b] | 15.06 | |
| TSH | Hyperthyroidism | 0.01 [b] | 0.00 | P=0.001*** LSD= 3.92 |
| | Hypothyroidism | 19.02 [a] | 6.42 | |
| | Control | 1.78 [b] | 0.76 | |
| NOTE: The difference symbols refers to significant difference | | | | |

**Table (2):** Correlations between biochemical parameters

| | | ALT | AST | ALP | TSB | DB | T3 | T4 | TSH |
|---|---|---|---|---|---|---|---|---|---|
| ALT | R | 1 | .791** | -.008 | .082 | .156 | .129 | .031 | .092 |
| | sig | | .000 | .955 | .531 | .235 | .327 | .814 | .486 |
| AST | R | .791** | 1 | .020 | .054 | .073 | .045 | -.089 | .204 |
| | sig | .000 | | .882 | .681 | .581 | .731 | .497 | .117 |
| ALP | R | -.008 | .020 | 1 | .121 | -.070 | .416** | .429** | -.468** |
| | sig | .955 | .882 | | .355 | .594 | .001 | .001 | .000 |
| TSB | R | .082 | .054 | .121 | 1 | .655** | .216 | .123 | -.346** |
| | sig | .531 | .681 | .355 | | .000 | .098 | .350 | .007 |
| DB | R | .156 | .073 | -.070 | .655** | 1 | .130 | .055 | -.224 |
| | sig | .235 | .581 | .594 | .000 | | .323 | .674 | .085 |
| T3 | R | .129 | .045 | .416** | .216 | .130 | 1 | .872** | -.594** |
| | sig | .327 | .731 | .001 | .098 | .323 | | .000 | .000 |
| T4 | R | .031 | -.089 | .429** | .123 | .055 | .872** | 1 | -.697** |
| | sig | .814 | .497 | .001 | .350 | .674 | .000 | | .000 |
| TSH | R | .092 | .204 | -.468** | -.346** | -.224 | -.594** | -.697** | 1 |
| | sig | .486 | .117 | .000 | .007 | .085 | .000 | .000 | |

Data illustrated in Table (2) showed significant negative correlations of TSH with ALP and TSB (R= -0.468, -0.346) ($p<0.05$). Further, T4 showed significant positive correlation with ALP (R= 0.429) ($p<0.05$).The same table showed that there was significant positive correlation between T3 and ALP with (R= 0.416) and ($p<0.05$).

## Discussion

In spite of the differences in percentage and number of males and females in study groups, there was no significant difference ($p = 0.581$). These results were in agreement with a study carried out by Sudha Ambiger *et al* 2019 [7], who found that there was no significant differences in mean level of age ($p=0.726$) and sex ratio ($p=0.648$) between control group and the test groups in the setting of hyperthyroidism.

The mechanism of the elevation of liver enzymes seems to be due to a relative hypoxia in periventricular regions of the liver [8]. Upadhyay *et al* 2004 [4] showed that raised levels of T3 induce apoptosis of hepatocytes and the reasons hepatic dysfunction through the activation of the mitochondrial-dependent pathway. There was no significant correlations between ALT,

AST,DB with TSH,T3,T4. Further, no significant correlation between TSB and T3,T4 .The present study was not agreed with Sudha Ambiger et al 2019 [10] who found that TSHshowed a significant positive correlation with ALP (P<0.001) in both subclinical and overt hypothyroidism. A study done by Seyed Hamid et al 2014[9] reported thatalthough liver enzymes levels were elevated in many hyperthyroid cases, there was no significant correlations emerged between the thyroid hormones and AST and DB, either in patients or controls probably because of small sample size. In patients with hyperthyroidism who have never been treated, changes in liver biochemistry are frequent, happening in 45%–90% of this people [10,11] and being frequently mild and asymptomatic [12]. Raises in serum alkaline phosphatase, frequently attributed to its bone fraction, followed in regularity by increases in levels of aminotransferases and bilirubin are also detected [13].

## Conclusions

The present study shows that thyroid disorder might cause a significant impact on the metabolism of hepatocytes reflected by an increase in the biochemical measurements of liver function tests, including AST, ALT ALP,TSB and DB in both hyperthyroidism and hypothyroidism patients. This recommends that patients should be frequently checked for biochemical measurements of liver function tests.

## Recommendation

We propose more studies with more cases to determine clearly results about liver dysfunction in hyperthyroidism and hypothyroidism patients.

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**Conflict of interest:** Nill

## References

[1]Pandey R, Jaiswal S, Sah J, Bastola K, Dulal S. Assessment of Serum Enzymes Level in Patients with Thyroid Alteration Attending Manipal TeachingHospital, Pokhara. A Journal of Life Sciences(2014).,3:2249-8656.

[2]Manjula K. S, Priyadarshini K. S, H. V. Shetty, UshaS.M.R, Reena. RStudy of serum transaminases in hypothyroidism. Journal of Evolution of Medical and Dental Sciences.( 2013).,2:230-234.

[3]E. Piantanida, S. Ippolito, D. Gallo, E. Masiello, *et al*.The interplay between thyroid and liver: implications for clinical practice. Journal of Endocrinological Investigation.(2020). , 43:885–899.

[4]Upadhyay G, Singh R, Kumar A, et al. Severe hyperthyroidism induces mitochondria mediated apoptosis in rat liver. Hepatolog(2004).,39(11):1120-30.

[5]Gow SM, Caldwell G, Toft AD, *et al*.Different hepatic responses to thyroxine replacement in spontaneous and I 131-induced primary hypothyroidism. Clin Endocrinol.( 1990). ,30:505-512.

[6]Bayrakter M, Thiel DHV.. Abnormalities in measures in liver function and injury in thyroid disorders. Hepatogastroenterology. (1997), 44:1614 -1618.

[7]Sudha A, Shrikanth P. .Study of liver function tests in patients of hypothyroidism. J International Journal of Contemporary Medical Research(2019). ,6(8): 5-8.

[8]Biscoveanu M and Hasinski S.Abnormal results of liver function test in patients with Grave's disease. Endocr Pract. ( 2000). ; 6:367-369.

[9]Seyed H, Zahra R, Nasrin J, Mohammad E, Farhad S.Evaluate the liver function in hyperthyroidism patients.J Paramedical Sciences; .( 2014). , 5, (2):75-78.

[10]Youssef WI, Mullen KD.The liver in other (nondiabetic) endocrine disorders. Clin Liver Dis. ( 2002)., 6:879–889.

[11]KubotaS, Amino N, Matsumoto Y, *et al*.Serial changes in liver function tests in patients with thyrotoxicosis induced by Graves' disease and painless thyroiditis. Thyroid. .( 2008)., 18:283–287.

[12]Fong TL, McHutchinson JG, Reynolds TB.Hyperthyroidism and hepatic dysfunction. A case series analysis. J Clin Gastroenterol. .( 1992). ;14:240–244.

[13]Huang MJ, Li KL, Wei JS, Wu SS, Fan KD, Liaw YF.Sequential liver and bone biochemical changes in hyperthyroidism: prospective controlled follow-up study. Am J Gastroenterol(1994).,89:1071–1076.