# Evaluate the liver function in hyperthyroidism patients

**Seyed Hamid Madani[1], Zahra Rostami Far[1], Nasrin Jalilian[2], Mohammad Erfan Zare[3], Farhad Shaveisi Zadeh*[4]**

[1] Molecular Pathology Research Center, Emam Reza Hospital, Kermanshah University of Medical sciences, Kermanshah, Iran
[2] Department of Obstetrics and Gynecology, faculty of medicine, Kermanshah University of Medical sciences, Kermanshah, Iran.
[3] Medical Biology Research Center, Kermanshah University of Medical Sciences, Kermanshah, Iran
[4] Department of Medical Genetics, faculty of medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

*Corresponding author: e-mail address: fa.shaveisizadeh@gmail.com (F. Shaveisi Zadeh)

## ABSTRACT

Thyroid hormones regulate the metabolisms of all cells including hepatocytes, and hence, modulate hepatic function. Hyperthyroidism is one of the most common endocrine disorders characterized by increased secretion of thyroid hormones T3 and/or T4. This study investigated frequency of abnormal liver function tests in the patients with hyperthyroidism that referred to Imam Reza Hospital of Kermanshah from 1st October 2009 to 30th April 2012. Patients who had complication disorders such as cardiovascular disease, hypertension, diabetes mellitus, liver disease and using any of drugs effecting liver and thyroid function tests and patients with positive hepatic viral markers were excluded from the study. After excluding patients with complication disorders, fifty patients were remained. Fifty volunteers without history of significant diseases were chosen as matched control group. Mean ALT (Alanine amino transferase) of cases were 52.1±6.97 and of controls were 25.6±3.9. Also, Mean ALP (Alkaline phosphatase) of cases was 259.94±25.83 and of controls were 185.10±33.75. There is significant difference between ALT, ALP in case group in compare the control group ($P<0.05$and $P<0.01$ respectively). Further, there is no significant difference in serum levels of AST (Aspartate amino transferase) and Mean direct bilirubin between case and control group. These findings indicate that ALT and ALP levels are frequently elevated in hyperthyroidism. Hence, they are possibly thyroid dependent enzymes.

**Keywords**: Liver enzymes; direct bilirubin; hyperthyroidism.

## INTRODUCTION

Hyperthyroidism is a relatively common disease in which tissues are stimulated by an increased secretion of thyroid hormones tiroiodothyronin (T3) and/or thyroxin (T4) (1). T3 is the biologically active thyroid hormone. These hormones are required for the normal growth, development and function of nearly all tissues (2).Thyroid hormones are metabolized within the liver and subsequently excreted into the bile. Increased metabolism in response to hyperthyroidism can cause oxidative damage to certain organs including the cardiovascular, nervous, gastrointestinal, and hepatic systems (3).Therefore it is not surprising that hepatic dysfunction is commonly observed in patients with hyperthyroidism. The pathogenesis of hepatic disorders in hyperthyroidism is unknown. Liver function tests (LFT) including Alanine amino transferase (ALT), Aspartate amino transferase (AST), Alkaline phosphatase (ALP) and direct bilirubin (DBIL) are the best way for evaluation of liver function (4). There is no enough study about hepatic dysfunction in hyperthyroidism. Obtaining information about hepatic dysfunction in hyperthyroidism can help to physician for understanding about non-cause and illusory of liver dysfunction.

The aim of this study was to evaluate the liver function in hyperthyroidism patients refer to Imam Reza Hospital of Kermanshah University of Medical Sciences.

## MATERIALS AND METHODS

The study was conducted on 50 subjects of age group 23 to 65 years old who had been diagnosed with hyperthyroidism between October 2009 to April 2012. Patients who had complications such as cardiovascular disease, hypertension and diabetes mellitus were excluded from the study. The patients who have the history of liver disease and using any of drugs effecting liver and thyroid function tests and patients with positive hepatic viral markers were excluded from the study. 50 healthy subjects free from hyperthyroidism aged 25 to 65 years were used as control. In all subjects, after 12h fasting period, 5ml venous blood sample was collected. The samples were spun in a Centrifuge at 1000g for 5 minutes. Serum obtained after centrifugation was divided into2 aliquots, one for liver function tests and second for thyroid function tests. Sample for ALT, AST, ALP and DBIL was analyzed immediately. Aliquots for thyroid function tests were stored at -70oC until batch analysis. Liver Function Tests (DBIL, ALT, AST and ALP) were assayed by the calorimetric method using standard reagent kits (pars azmoom,iran).Serum T3, T4and TSH measurements were performed by using Enzyme linked immunosorbent assay(ELISA) kits (monobind,USA). Results are expressed as the mean ± standard deviation. The statistical evaluation of data was performed by student t-test. $P < 0.05$ was considered statistically significant. Statistical analysis was carried out using SPSS for windows 16.0 software. Age group 23 to 65 years old who had been diagnosed with hyperthyroidism between October 2009 to April 2012. Patients who had complications such as cardiovascular disease, hypertension and diabetes mellitus were excluded from the study. The patients who have the history of liver disease and using any of drugs effecting liver and thyroid function tests and patients with positive hepatic viral markers were excluded from the study. 50 healthy subjects free from hyperthyroidism aged 25 to 65 years were used as control. In all subjects, after 12h fasting period, 5ml venous blood sample was collected. The samples were spun in a Centrifuge at 1000g for 5 minutes. Serum obtained after centrifugation was divided into2 aliquots, one for liver function tests and second for thyroid function tests. Sample for ALT, AST, ALP and DBIL was analyzed immediately. Aliquots for thyroid function tests were stored at -70oC until batch analysis. Liver Function Tests (DBIL, ALT, AST and ALP) were assayed by the calorimetric method using standard reagent kits (pars azmoom,iran).Serum T3, T4and TSH measurements were performed by using Enzyme linked immunosorbent assay(ELISA) kits(monobind,USA). Results are expressed as the mean ± standard deviation. The statistical evaluation of data was performed by student t-test. $P<0.05$ was considered statistically significant. Statistical analysis was carried out using SPSS for windows 16.0 software.

## RESULTS

The mean age of 50 hyperthyroid cases and 50 controls were 45.08±17.38 and 46.11±16.83 years, respectively. Mean age of males and females in hyperthyroid cases were 43.1±5.42 and 43±5.89 years respectively. And of controls were 42.32±7.81 and 43.03±6.35 years respectively. The cases and controls did not differ significantly with respect to age and gender. Table 1 shows mean thyroid hormone concentration in cases and controls. Table 2 shows the mean serum concentration of DBIL, ALP, AST and ALT of the controls and hyperthyroid cases. The serum levels of AST and ALP in hyperthyroid cases were significantly increased when compared with controls ($P< 0.05$). The levels of ALT and DBIL in hyperthyroid cases were not significantly differ from controls ($P>0.05$).

**Table 1.** mean thyroid hormone and TSH concentration in cases and controls.

| Test | Cases n=50 | Controls n=50 |
|---|---|---|
| $T_3$ | 3.80±0.71 | 1.13±0.33 |
| $T_4$ | 18.66±2.20 | 7.89±1.93 |
| TSH | 0.075±0.02 | 2.16±0.46 |

**Table 2**. mean serum concentration of liver function test in cases and controls.

| Parameters | Cases n=50 | Controls n=50 | P |
|---|---|---|---|
| **DBIL** | 0.59±0.10 | 0.23±0.07 | NS |
| **ALP** | 259.94±25.83 | 185.10±33.75 | P<0.01 |
| **ALT** | 52.1±6.97 | 25.6±3.9 | P<0.05 |
| **AST** | 38.12±7.2 | 23.78±4.67 | NS |

NS, not significant

## DISSCUSSION

Thyroid hormones modulate the functions of body organs, tissues and cells (5). The liver is generally affected in thyroid function (6). Assessment of thyroid in liver disease should be accompanied with laboratory measurement of thyroid hormones (7). The laboratory procedure based on the measurement of T3, T4 and thyroid stimulating hormone (TSH) and others related thyroid parameters at the first step of laboratory investigations. In fact, laboratory measurements are suggested not only for hepatic dysfunction but also in other various abnormalities (8). Many liver function test elevation, have been reported in hyperthyroidism. These could be listed as increase in DBIL, ALT, AST and ALP (9, 10). The mechanism of this elevation appears to be relative hypoxia in periventricular regions of the liver (11). Upadhyay *et al.* (12) show that elevated levels of T3 induces apoptosis of hepatocytes and causes hepatic dysfunction through the activation of the mitochondrial dependent pathway. In the present study 50 hyperthyroid cases and 50 matched controls were selected and examined for their serum levels of enzymes AST, ALT, ALP and DBIL. The results of this study showed that ALP and ALT level was elevated in cases when compared with the control. In hepatic injury an increase in levels of AST and ALT was reported in 27% and 37% of the patients respectively (13). Out of the 50 cases, 19 (38%) had at least one abnormal result of a liver function test and ALP is the most commonly elevated enzyme among them (16, 32%). These findings indicate that abnormal results of liver function tests are common in patients with hyperthyroidism. Biscoveanu *et al.* (6) reports of the 30 study patients, 11 (37%) had at least one abnormal result of a liver function test. All 30 patients in his study had determinations of AP (not fractionated), of which 10 values (33%) were above normal (range, 124 to 283 U/L). Of the 30 patients who had determinations of AST, 5 (17%) had increased values that ranged from 36 to 71 U/L. Six of the 23 patients (26%) with determinations of ALT had increased values that ranged from 45 to 157 U/L. In addition, 2 of the 24 patients (8%) with determinations of total bilirubin had increased levels. Further, our results are in according to Nobakht and Aydemirstudies studies (2, 14). The increased osteoblastic activity is pointed out as a cause of elevated ALP in patients with hyperthyroidism (15). Although liver enzymes levels were elevated in many hyperthyroid cases, no significant correlation emerged between the thyroid hormones and AST and DBIL, either in cases or controls probably because of small sample size. The study showed that prevalence of hyperthyroidism is higher in females than in males, but its etiology is unknown. With respect to it was mentioned in this present study, for preventing any mistreatment it is recommended that thyroid laboratory investigation for the thyroid gland should be done before any liver treatment.

## CONCLUSION

In summary, Based on the results obtained from this study, suggest that hyperthyroidism is often associated with abnormal hepatocellular enzymes particularly ALT and ALP elevation and thus can be used as a diagnostic tool for predicting the presence of clinically significant hepatic changes in patients with hyperthyroidism. Also, our results show that make the diagnosis of concomitant, unrelated liver disease difficult until the euthyroid state has been established. Our results can help to physician for understanding about non-cause and illusory of liver dysfunction. We propose more study with more cases to determine clearly results about liver dysfunction in hyperthyroidism.

## REFERENCES

1. Huang MI, Li KL, Wei JS, Wu SS, Fan KD and Liaw YF.Sequential liver and bone biochemical changes in hyperthyroidism. Am. J. Gastroenterol.1994; 89(7):1071-6 .

2. Nobakht H, mousavi S, Rashidy Pour A. Abnormalities of liver function test in hyperthyroidism. JSUM Sciences.2000;1:25-29.

3. Khemichian S, Ling Fong T. Hepatic Dysfunction in Hyperthyroidism. Gastro enterol Hepatol. 2011;7(5): 337–339.

4. Ajayi AF, Akhigbe RE. implication of altered thyroid state on liver function. Thyroid Res Pract.2012;9:84-7.

5. Huang MJ, Liaw YF. Clinical associations between thyroid and liver diseases. J GastroenterolHepatol.1995; 10: 344-50.

6. Biscoveanu M, Helsinki S. Abnormal results of liver function tests in patients with Grave's disease. Endocr Pract. 2000;6(5):367–9.

7. Malik R, Hodgson H. The relationship between the thyroid gland and the liver.QJM. 2002;95:559–69.

8. Mansourian AR. A Review of Literatures on the Adverse Effects of Thyroid Abnormalities and Liver Disorders: An Overview on Liver Dysfunction and Hyperthyroidism. P J Biologic Scenc. 2013;16(23):1641-1652.

9. Hull K, Horenstein R, Naglieri R, Munir K, Ghany M, Celi FS. Two cases of thyroid storm associated cholestatic jaundice.EndocrPract.2007;13:476-480.

10. Giannini EG, Testa R and Savarino V. Liver enzyme alteration:A guide to clinicians. MAJ. 2005; 172(3): 367-79 .

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

12. Upadhyay G, Singh R, Kumar A, Kumar S, Kapoor A, Godbole MM. Severe hyperthyroidism induces mitochondria mediated apoptosis in rat liver. Hepatolog 2004;39(11):1120-30.

13. Mehmood Khan T,Malik S, Diju IU. Correlation between plasma thyroid hormones and liver enzymes level in thyrotoxic cases and controls in Hazara Division.J Ayub Med Coll Abbottabad. 2010;22(2):176-179.

14. Aydemir S, Bayraktaroglu T, Demircan N, Sert M, Açikgoz S, Tekin IO, et al . Effect of hyperthyroidism and propylthiouracil treatment on liver biochemical tests.Int J ClinPract .2005;59(11):1304-8.

15. Johnkennedy N, Adamma E, Ndubueze H. Evaluation of Serum Hepatocellular Enzymes In Nigerian with Goitre. AJMed Sciences. 2011; 2:79-81.