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Assessment of Liver Function Tests in Primary Hypothyroidism: A Case Control Study

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ABSTRACT

Patients with subacute thyroiditis or hyperthyroidism may have abnormalities in liver function tests; and higher prevalence of hypothyroidism is found in patients with liver diseases. With this background, liver function tests, international normalized ratio and TSH were assayed in 136 primary hypothyroid cases and controls. SGOT and SGPT levels were highly significantly increased and total protein and albumin levels were significantly increased, in cases compared to controls. Hepatic function may be partly impaired in hypothyroidism. The present findings need to be corroborated by further research with larger number of subjects and with more parameters.

Keywords: Liver function tests, primary hypothyroidism

INTRODUCTION

Hypothyroidism is the most common functional disorder of the thyroid gland. [(1)] Primary hypothyroidism is an insidious condition with a significant morbidity and often subtle and nonspecific symptoms and clinical signs. [(2,3)] The common clinical features associated with hypothyroidism are tiredness, weight gain, dry skin, cold intolerance, constipation, muscle weakness and hoarse voice. [(4)] Though hypothyroidism is a clinical disorder commonly encountered by the primary care physician, clinical symptoms of hypothyroidism are nonspecific and may be subtle, especially in older persons. Untreated hypothyroidism can contribute to hypertension, dyslipidemia, infertility, cognitive impairment, and neuromuscular dysfunction. [(5)] In persons living in iodine-replete areas, hypothyroidism may be caused by congenital, spontaneous because of chronic autoimmune disease (atrophic autoimmune thyroiditis or goitrous autoimmune thyroiditis [Hashimoto's thyroiditis]), or iatrogenic because of goitrogens, drugs, or destructive treatment for thyrotoxicosis. [(6)] The term 'subclinical hypothyroidism' is used to define that grade of primary hypothyroidism in which there is an elevated thyroid-stimulating hormone (TSH) concentration in the presence of normal serum free thyroxine and triiodothyronine concentrations. [(7)]

In addition to these common manifestations, however, there are many additional manifestations of hypothyroidism that are less commonly acknowledged and include involvement of other systems because thyroid hormone exerts direct effects on essentially all of the organ systems of the body. It is important to recognize that these other organ systems may be involved and that the resulting disease states can dominate the clinical picture. As with the classic manifestations of hypothyroidism, these unusual manifestations respond to thyroid hormone replacement therapy. Thus, the importance of recognizing these signs and symptoms, as a result of hypothyroidism, is evident. [(8)] Patients with subacute thyroiditis or hyperthyroidism may have abnormalities in liver function tests which return to normal

as the thyroid condition improves. [9] On the other hand, higher prevalence of hypothyroidism was demonstrated in patients with nonalcoholic fatty liver disease compared to controls. [10] With this background, the present study was undertaken to evaluate the blood levels of some parameters to estimate whether liver function in hypothyroidism is altered.

MATERIALS AND METHODS

This study was a hospital-based, case-control study conducted in a tertiary care centre of West Bengal. The study was approved by the local ethical committee and all patients and control subjects gave their informed consent to take part in this investigation.

The duration of the present study was 7 months and included 136 primary hypothyroid adult patients (group 1) attending the outpatient department (OPD). In addition, 152 patients who were age- and sex-matched with the subjects served as controls (group 2). The controls had attended the OPD with minor unrelated ailments. Complete history and physical examination of all cases and controls were undertaken. Exclusion criteria included subjects who had preexisting or past history of hepatic diseases, alcoholics, those taking hepatotoxic drugs, other concomitant infections affecting the liver such as malaria, typhoid, hepatitis A and B, etc.

Venous blood sample was collected from each case and control after 12 hours of fasting. All samples were coded and assayed for liver function tests, INR (international normalized ratio) and TSH in a blind fashion by an investigator who was unaware of the subjects' clinical status.

Statistical analysis of the data was performed by using Statistical Package for Social Sciences (SPSS version 16), and inferences were drawn. $p < 0.05$ was considered to be significant and $p < 0.001$ highly significant.

RESULTS

Table 1. Liver function tests, INR and TSH levels in cases and controls, expressed as mean ± SD

Parameter	Group 1	Group 2
TSH (Mu/L)	14.2±1.7	2.6±0.3
Total bilirubin (mg)	0.76±0.21	0.72±0.13
SGPT (IU/L)	81.4±7.2	29.1±2.6
SGOT (IU/L)	107.9±12.5	32.6±2.0
Alkaline phosphatase (IU/L)	316.2±64.1	303.8±51.6
Total protein (gm/dl)	6.2±0.67	6.4±0.71
Albumin (gm/dl)	4.8±0.33	4.9±0.46
INR	1.0±0.2	1.0±0.1

t test for TSH:
p value and statistical significance:
The two-tailed p value is less than 0.0001
By conventional criteria, this difference is considered to be extremely statistically significant.
Confidence interval:
The mean of Group 1 minus Group 2 equals 11.600
95% confidence interval of this difference: From 11.324 to 11.876
Intermediate values used in calculations:
t = 82.7152
df = 286
standard error of difference = 0.140
SEM values for groups 1 and 2 are respectively 0.146 and 0.024

t test for bilirubin:
p value and statistical significance:
The two-tailed p value equals 0.0504
By conventional criteria, this difference is considered to be not quite statistically significant.
Confidence interval:
The mean of Group 1 minus Group 2 equals 0.0400
95% confidence interval of this difference: From -0.0001 to 0.0801
Intermediate values used in calculations:
t = 1.9651
df = 286
standard error of difference = 0.02
SEM values for groups 1 and 2 are respectively 0.018 and 0.0105

t test for SGPT:
p value and statistical significance:
The two-tailed p value is less than 0.0001

By conventional criteria, this difference is considered to be extremely statistically significant.
Confidence interval:
The mean of Group 1 minus Group 2 equals 52.300
95% confidence interval of this difference: From 51.070 to 53.530
Intermediate values used in calculations:
t = 83.6788
df = 286
standard error of difference = 0.625
SEM values for groups 1 and 2 are respectively 0.617 and 0.211

t test for SG0T:
p value and statistical significance:
The two-tailed p value is less than 0.0001
By conventional criteria, this difference is considered to be extremely statistically significant.
Confidence interval:
The mean of Group 1 minus Group 2 equals 75.300
95% confidence interval of this difference: From 73.276 to 77.324
Intermediate values used in calculations:
t = 73.2429
df = 286
standard error of difference = 1.028
SEM values for groups 1 and 2 are respectively 1.072 and 0.162

t test for alkaline phosphatase:
p value and statistical significance:
The two-tailed p value equals 0.0704
By conventional criteria, this difference is considered to be not quite statistically significant.
Confidence interval:
The mean of Group 1 minus Group 2 equals 12.400
95% confidence interval of this difference: From -1.037 to 25.837
Intermediate values used in calculations:
t = 1.8164
df = 286
standard error of difference = 6.827
SEM values for groups 1 and 2 are respectively 5.497 and 4.185

t test for total protein:
p value and statistical significance:
The two-tailed p value equals 0.0149
By conventional criteria, this difference is considered to be statistically significant.
Confidence interval:
The mean of Group One minus Group Two equals -0.2000
95% confidence interval of this difference: From -0.3606 to -0.0394
Intermediate values used in calculations:
t = 2.4507
df = 286
standard error of difference = 0.082
SEM values for groups 1 and 2 are respectively 0.0575 and 0.0576

t test for albumin:
p value and statistical significance:
The two-tailed P value equals 0.0368
By conventional criteria, this difference is considered to be statistically significant.
Confidence interval:
The mean of Group One minus Group Two equals -0.1000
95% confidence interval of this difference: From -0.1938 to -0.0062
Intermediate values used in calculations:
t = 2.0977
df = 286
standard error of difference = 0.048
SEM values for groups 1 and 2 are respectively 0.0283 and 0.0373

t test for INR:
p value and statistical significance:
The two-tailed p value equals 1.0000
By conventional criteria, this difference is considered to be not statistically significant.
Confidence interval:
The mean of Group 1 minus Group 2 equals 0.000
95% confidence interval of this difference: From -0.036 to 0.036
Intermediate values used in calculations:
t = 0.0000
df = 286
standard error of difference = 0.018
SEM values for groups 1 and 2 are respectively 0.017 and 0.008

DISCUSSION

In the present study SGOT and SGPT levels were highly significantly increased in cases compared to controls (table 1). It is our opinion that the findings of the present study may be due to hepatocellular injury, which is also the probable mechanism stated by Loria et al, who pointed that the downstream mechanisms by which endocrine disturbances cause liver disease might be similar to those involved in the development of primary liver disease. Hypothyroidism, for example, might lead to nonalcoholic steatohepatitis, cirrhosis and potentially liver cancer via the development of hyperlipidemia and obesity. [(11)] Thyroid hormones regulate the basal metabolic rate of all cells, including hepatocytes, and thereby modulate hepatic function. This may be the mechanism of elevation of SGPT and SGOT. But in contrast to our findings, Bruck et al found decreased levels of SGPT and SGOT in hypothyroid rats. [(12)] In another study, in the hypothyroid versus the euthyroid state, a significant negative correlation was found by Oren et al between thyroid-stimulating hormone blood levels and both functional and synthetic liver function tests (p <0.001). A significant negative correlation was also found between thyroid-stimulating hormone blood levels and clinical deterioration manifested as bleeding varices, the development of ascites, and episodes of encephalopathy. He concluded that in patients with liver cirrhosis, the liver function in the hypothyroid state tend to be better than in the euthyroid state. [(13)] Again, significant improvement in alanine aminotransferase (p < 0.001), alkaline phosphatase (p < 0.0001), albumin (p < 0.001), and bilirubin (p < 0.01) levels was found in subjects with increased TSH and Prothrombin time was also found to be significantly improved (p < 0.001) in those subjects, by a group of researchers. The authors concluded that euthyroid patients with liver cirrhosis might benefit from a controlled hypothyroidism. [(14)]

In the present study total protein and albumin levels also were significantly increased in cases compared to controls (table 1). We think that this finding is because of chronic impairment in hepatic function, which causes decreased synthetic function such as production of albumin in liver, leading to lower levels of serum total protein.

In this study we also found nonsignificant increases in levels of alkaline phosphatase and bilirubin in cases compared to controls (table 1). These findings are in accordance with those of Ajayi et al who reported no significant increases in levels of alkaline phosphatase in hypothyroid rats. [(15)] These data might indicate that hypothyroidism causes mild or no obstructive pathology. As table 1 shows, there was no significant increase in INR in cases compared to controls, which might imply that the hepatic pathology is probably not significant as far as prognosis is concerned.

The present study has limitations. The sample size should have been bigger; more studies are required with larger samples. Study was selection biased as it was conducted in a hospital; due to limited resources and time constraint a bigger population based study was not possible. So, the study data cannot be extrapolated on the general population.

Despite these shortcomings, we believe that results of this study will be helpful for further investigations in this line. It is thus recommended that liver function should be monitored in conditions associated with hypothyroidism to avoid hepatic complications of thyroid dysfunction.

CONCLUSION

Hepatic function may be partly impaired in hypothyroidism. Data from the present study need to be corroborated by further research with larger number of subjects and with more parameters.

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