RESEARCH

THYROID PROFILE IN ALCOHOLIC LIVER DISEASE PATIENTS- A HOSPITAL BASED CROSS-SECTIONAL STUDY IN NORTH-EASTERN PART OF INDIA

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Abstract

Background: Liver plays a vital role in thyroid hormone metabolism and circulation of thyroid hormones by producing thyroid binding globulin. Hence, thyroid dysfunction has been reported in various liver diseases and is dependent on the severity of liver disease. We wanted to study thyroid dysfunction in patients with alcoholic liver disease and it's correlation with Child Pugh (CTP) score. **Objectives:** To evaluate the thyroid hormone profile in alcoholic liver disease and correlate it with the severity of alcoholic liver disease. **Materials and Methods:** This cross-sectional study was conducted at medicine ward with the biochemistry department, Regional Institute of Medical Sciences, Imphal, Manipur, from August 1, 2018 to August 31, 2020. After giving informed consent, 100 medicine ward patients aged 30 or older with alcoholic liver disease were randomly recruited for the study. Child-Turcotte-Pugh grading determined liver disease severity. We tested thyroid function (FT3, FT4, TSH). Excel recorded data and SPSS for Windows, version 25, analyzed it. **Result:** 98 (98%) of the 100 study participants were male and 2 (2%) were female. The patients ranged in age from 40 to 73, with a mean of 55.90±6 years. The patient age distribution was: 50% of the patients were 51–60 years old, whereas 26—including 2 females—were 40–50. Additionally, 23 patients were 61–70 years old. The study group of 71-80-year-olds includes one 73-year-old man. Nine (9%) of the 100 patients were Child-Pugh Class B and 91 (91%) were Class C. None were in Child-Pugh Class A. There were 53 Child-Pugh class C patients and 1 Child-Pugh class B patient with hypothyroidism among 100 alcoholic liver disease patients. Seven patients exhibited hyperthyroidism, while 39 (39%) had normal thyroid function scans. This shows that many people had hypothyroidism. **Conclusion:** This study found that most patients had severe alcoholic liver disease, with 91 having Child-Pugh Class C and 9 Class B. Thyroid function tests showed 54 hypothyroidism, 7 hyperthyroidism, and 39 normal values. Hypothyroidism was seen in most patients and correlated with liver disease severity.

INTRODUCTION

Alcoholism is a major public health problem and alcoholic liver disease is responsible for significant morbidity and mortality.[1] Liver damage due to chronic alcohol intoxication initially leads to accumulation of lipids within the liver and with ongoing exposure this condition of steatosis may first progress to an inflammatory stage which leads the way for fibrogenesis and finally cirrhosis of the liver.[2] Chronic intake of large quantities of alcohol causes damage to many organs, the liver being the most affected one.[3] Alcoholic liver disease is a major healthcare problem worldwide.[4] Alcoholic liver disease still represents an important cause for death and disability in well-developed countries and is becoming a leading cause of disease in developing countries.[5] Liver disease due to alcohol is devastating in terms of medical care, cost, loss of productive years and poorer prognosis than that of many cancers, yet it is attracting much less concern, both amongst the public and the medical profession.[6]

At present, except for the control of alcohol abuse, there is no effective modality of either prevention or treatment.[7] Two thirds of individuals who drink alcohol do not suffer from alcoholic hepatitis or cirrhosis but one third may develop alcoholic liver disease.[8] Joeimon et al.[9] reported the prevalence of hypothyroidism was 21.6% (similar to our study), but this prevalence was contradicts to Patira et al.,[10] in which prevalence of subclinical hypothyroidism

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was 62%. This difference may be due to sample size, age, sex, and regional variation in thyroid disease.The spectrum of alcoholic liver injury is currently grouped into three clinical forms: fatty liver, alcoholic hepatitis and cirrhosis.[11]

Previously, unsuspected hepatomegaly is often the only clinical findings in fatty liver. Occasionally patients with fatty liver will present with right upper quadrant discomfort, tender hepatomegaly, nausea and jaundice. Alcoholic hepatitis is associated with a wide gamut of clinical features. The typical laboratory abnormalities seen in fatty liver are non-specific and include modest elevations of the aspartate aminotransferase (AST), alanine aminotransferase (ALT) and gamma glutamyltranspeptidase accompanied by hypertriglyceridemia, hypercholesterolemia and occasionally hyperbilirubinemia. In alcoholic hepatitis and in contrast to other causes of fatty liver, the aspartate aminotransferase and alanine aminotransferase was usually elevated two to seven fold. They are rarely > 400 IU, and the AST/ALT ratio >1. Hyperbilirubinemia is common and is accompanied by modest increase in the alkaline phosphatase level.[12]

Liver plays a major role in modifying the total circulating hormone concentration of thyroxine and tri-iodothyronine by secretion and degradation of carrier proteins. It is also a major site of peripheral conversion, degradation and excretion of thyroid hormones.[13]

Thyroxine and tri-iodothyronine are essential for normal organ growth, development and function. These hormones regulate the basal metabolite rate of all cells including hepatocytes, and thereby modulate hepatic function; the liver in turn metabolizes the thyroid hormone and regulates their systematic endocrine effects. Thyroid dysfunction may perturb liver function; liver disease modulates thyroid hormone also.[14]

Szilagyi A[15] found that ethanol can affect directly on the thyroid gland and may also directly interfere with thyroid hormone metabolism. With this background, this study is aimed to assess the thyroid function in patients with cirrhosis of liver and correlate the levels of thyroid hormone with the severity of the disease

Aims and Objects

1. To evaluate the thyroid hormone profile in alcoholic liver disease.
2. To correlate thyroid hormone levels with Child-Pugh Score in alcoholic liver disease.

MATERIALS AND METHODS

The study was conducted in medicine ward in collaboration with the department of biochemistry, Regional Institute of Medical Sciences, Imphal, Manipur, during the period 1st August, 2018 to 31st July 2020.

A total of 100 cases(98 male and 2 female) diagnosed as alcoholic liver disease, admitted in medicine ward, Regional Institute of Medical Sciences, Imphal, were randomly selected for the study after taking full inform consent.

Inclusion criteria: Patients above the age of 30 years with a history of alcohol consumption for more than five years.

Exclusion criteria: Those patients with non alcoholic liver disease, hepatitis B, hepatitis C, human immunodeficiency virus infections, hepatocellular carcinoma, diabetes mellitus, chronic heart disease, and chronic pulmonary disease and on medication for thyroid disease were excluded. Approval from the Institutional Ethical Committee, Regional Institute of Medical Sciences, Imphal, Manipur, was sought.

After obtaining clearance and approval from the institutional ethical committee and written informed consent, patients with cirrhosis of liver fulfilling inclusion and exclusion criteria were enrolled in the study. Demographic data, history, clinical examination and details of investigations were recorded in the study proforma. Investigations: Complete Hemogram, Liver function tests, renal function tests, Serum electrolytes, Ultra-Sonography of Abdomen, Prothrombin time, International Normalized Ratio, Thyroid function tests. After all investigations, alcoholic liver cirrhosis were divided according to Child Pugh score child into A, B, C groups. Thyroid function tests (TFT)[16] was done by electrochemiluminescence immunoassay. The normal range of thyroid profile as a following: FT3 is (2.1–4.4 pg/ml), FT4 is (0.8–2.7 ng/dl), and TSH is (0.35–5.5 μIU/ml).

Statistical Analysis

The data obtained were analyzed using describtive statistics (mean,and standard deviation), chi-square and percentage analysis. SPSS program for Windows, version 25 was used to analyze the data. A $p<0.05$ was considered statistically significant.

RESULTS

Out of the 100 subjects in the study, 98 cases (98%) were male and 2 (2%) were female. The age of the patients ranged from 40-73years with a mean of 55..90± 6 years. Majority (50%) of the patients were between 51 and 60 years, 26 patients including 2 female patients were in the age group of 40 to 50 years, followed by 23 patients between 61 to 70 years. There was only 1 male patient aged 73 years in the study group of 71-80years.

Table 1: Child-Pugh Class to assess severity of liver disease

Class	No. of patients	Percent (%)
A	0	0
B	9	9

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C	91	91

Out of 100 patients included in the study, there were 91 (91%) patients in the Child –Pugh Class C which indicates that the patients in this group had a 1 year survival rate of 45% and 2 year survival rate of 35%. 9 (9%) patients were in Child-Pugh Class B which indicates that they had 1 year survival rate of 81% and 2 year survival rate of 57%. There were none in the Child –Pugh Class A. This shows that the maximum numbers of patients included in the study were having severe alcoholic liver disease.

Table 2. Thyroid status of patients in alcoholic liver disease

Groups	Normal	Hypothyroidism	Hyperthyroidism
No. of patients (%)	39	54	7

Out of the 100 patients of alcoholic liver disease, 54(54%) patients were in Child–Pugh class C, 1(1%) patients in Child-Pugh class B had hypothyroidism , 7 patients had hyperthyroidism and 39 (39%) patients had normal thyroid function test reports. This shows that majority of the patients were suffering from hypothyroidism. The average levels of serum total T3 and total T4 were 0.75±.48ng/dl and 5.46±3.71µg/dl respectively and that of serum free T3 and serum free T4 were 1.26 ±0.53pg/ml and 1.25l±1.11ng/dl respectively. The maximum levels of serum TSH were 9.57µIU/ml .

There is no significant correlation between Child –Pugh Class and Thyroid status. Patients with more severe alcoholic liver disease were suffering more from hypothyroidism.

DISCUSSION

Thyroid dysfunction is one of the endocrine changes encountered in alcoholic liver disease. This is due to the facts that liver is a main organ of the conversion from T4 to T3; that the binding protein of thyroid hormones in blood is synthesized in liver. In this study, the changes of serum thyroid parameters, in alcoholic liver disease was investigated and studied the usefulness of thyroid hormones as liver function tests. The average level of serum total T3 was 0.75±.48ng/dl and serum total T4 was 5.46 ± 3.71µg/dl .The average level of serum TSH was 3.75l± 2.31µIU/ml. The maximum and minimum levels of serum TSH were 9.57µIU/ml and 0.29µIU/ml respectively. The average levels of serum free T3 and serum free T4 were 1.26 0.53pg/ml and 1.25l± 1.11ng/dl respectively.

There were 91 patients with Child-Pugh Class C and 9 patients with Child-Pugh Class B. There were none in Child-Pugh Class A. Out of 100 patients of alcoholic liver disease, 54 patients(54 from Child-Pugh class C and 1 from Child-Pugh Class B) had hypothyroidism. This study showed that majority of the patients was suffering from hypothyroidism.

In the present study, majority of the patients was found to have lower levels of serum total T4, serum total T3, free T4 and free T3, whereas TSH level remained elevated or normal. It is reported that serum T4 and FT4 decreased in liver diseases, and low T4 state is considered a more serious condition than low T3 state, and therefore decreased T4 and or FT4 in liver cirrhosis is considered significant in terms of poor prognosis but in a study conducted by Custro N et al[17] on thyroid hormone picture of alcoholics in connection with their liver status, they found that serum T3 levels were significantly lower among alcoholics compared to control group. Serum T4 levels were not significantly different in the comparison between alcoholics and control.

In a similar study conducted by Takahashi et al[18] in 26 patients of alcoholic liver cirrhosis, they found that there was no significant change in serum T4 levels. Serum total T3 levels, serum FT3 levels and serum FT4 levels were low, but serum TSH level was elevated. They found that seum FT3 decreased according to the degree of liver dysfunction and so they considered serum FT3 a sensitive index of liver dysfunction; serum FT4 decreased only in liver cirrhosis, decrease of serum FT4 was noted under critical condition of liver diseases. Therefore serum FT4 is assumed to be an useful index for prognosis and has a different significance from serum FT3, whereas in the present study serum total T3, total T4, FT4 and FT3 were low in most of the cases and TSH was elevated or normal. So most of the patients in the present study had severe liver dysfunction and poor prognosis as compared to the study of Takahashi et al.

Burra P et al[19] reported a reduction in circulating free tri-iodothyronine (fT3) in patients of alcoholic hepatitis and cirrhosis with normal or reduced thyrotrophin. There was no abnormality in patients with fatty liver despite similar ethanol intake to the other groups, and correlation between free tri-iodothyronine and liver function test suggested that changes in free tri-iodothyronine reflect the severity of underlying liver disease.

In a study conducted by Becker U et al[20] in 73 euthyroid male patients with histologically verified alcoholic cirrhosis, they found that serum concentrations of tri-iodothyronine decreased significantly and TSH increased with progressing liver dysfunction which is in consonance with our findings.

Bandyopadhyay S K et al[21] studied 72 adult males with liver cirrhosis of different etiologies in terms of clinical and biochemical evidence of endocrine dysfunctions related to hypothalamic-pituitary-gonadal axis and the thyroid status, they reported that with more advanced disease, there is a

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progressive fall in triiodothyronine .Severity of the liver disease determined by Child –Turcotte-Pugh class ,rather than aetiology (alcoholic or postviral), was the chief determinant of such dysfunction which tallies with our finding.

In another study done by Sheridan P[22] on thyroid hormones and the liver, he reported that there exists a close relationship between the liver and the thyroid. Liver disease alters thyroid function tests at all levels of the hypothalamic-pituitary-peripheral axis. Since thyroid disorders occur more frequently than expected in certain kinds of liver disease, awareness of the limitations of thyroid function tests in this situation are necessary. Likewise in our study, we found that there was reduction in the level of serum thyroid hormones.

In conclusion, our study also showed that most of the patients were having significantly lower level of thyroid hormones which shows that majority of them were suffering from severe alcoholic liver disease and a poor prognosis. The present study was almost similar to a study conducted by Hitomi Takahashi and Shoji Yamada in Japan.

CONCLUSION

The current study analyzed 100 cases of alcoholic liver disorders and conducted thyroid function tests to compare the findings among the patients. Out of the total of 100 instances, 98 were men and 2 were females. The ages of the two females were 48 and 49 years, while the remaining patients were between the ages of 51 and 60 years.All patients had a history of alcohol consumption exceeding 10 years, with the majority consuming 750ml of alcohol per day. A total of 91 individuals presented with severe alcoholic liver disease, whereas 9 patients had mild alcoholic liver disease. This indicated that the majority of the patients were experiencing chronic alcoholic liver damage.Among the 100 cases, 54 patients had a substantial deficiency in thyroid hormones, 7 patients had an elevated level of thyroid hormones, and 39 patients had a normal level of thyroid hormones. Our investigation revealed alterations in thyroid hormone levels among individuals with alcoholic liver disease, with the majority exhibiting decreased levels of thyroid hormones. Therefore, thyroid levels in cirrhotic patients may be used as a prognostic marker. Low FT3 might be used as a predictor of patients for underlying HE, These findings are consistent with previous studies undertaken on this topic.

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