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A Study of Thyroid Function Test in Cirrhosis of Liver and Its Correlation with Severity of Liver Disease in A Tertiary Care Centre of Kolkata

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Abstract

Background: Cirrhosis of liver is defined as a stage of progressive hepatic fibrosis characterised by distortion of hepatic architecture and formation of regenerative nodules. Liver plays an important role in thyroid hormone activation and inactivation, transport, and metabolism, as well as the synthesis of thyroid binding globulin. Conversely, thyroid hormones have widespread systemic actions involving all organ systems. A complex relationship exists between thyroid and liver in health and disease.

Aims & objectives of the study: To study the levels of thyroid hormone in Cirrhosis of liver & its possible correlation with the severity of liver cirrhosis.

Methods: 200 patients were included in this study from July 2023 to June 2024. They were classified as per Child-Turcotte-Pugh scoring after clinical assessment and investigations. Serum TSH, FT3, FT4 levels were measured for all the patients.

Results: Out of 200 patients, it was found that 36 (18%) patients belonged to CTP class A, 78 (39%) patients had CTP score of class B, while maximum 86 (43%) patients belonged to CTP class C. There was significant positive correlation between CTP class and TSH values ($p<0.001$) with mean (SD) of CTP class A, B and C were 2.42 (0.76), 3.9 (1.02) and 5.91 (1.08) respectively. There was significant negative correlation between CTP class and FT3 values ($p<0.001$) and between CTP class and FT4 values ($p<0.001$).

Conclusion: Our study found that there was significant positive correlation of serum TSH values with severity of liver cirrhosis as assessed by CTP score, while FT3 and FT4 were having significant negative correlation.

Keywords: Cirrhosis of Liver, Hormones, Thyroid, Toxins.

Introduction

Liver diseases are associated with various endocrinal disturbances, which can be due to the effects of toxins that are not metabolized by liver or by the alteration of

the carrier protein synthesis. The liver plays an important role in metabolism of thyroid hormones, being involved in their conjugation, excretion, peripheral de-iodination and the synthesis of thyroxine binding-globulin. Thyroxine and Tri-iodothyronine regulate the basal metabolic rate of all cells, including hepatocytes and thereby modulate hepatic function. [1,2] Both hormones are bound to plasma proteins, including thyroxine-binding globulin, transthyretin and albumin. [3] A complex relationship exists between thyroid and liver in health and disease. So thyroid dysfunction may result in deterioration of liver functions, & any liver disease may modulate metabolism and serum concentration levels of thyroid hormones. [4] Various scores have been used for the assessment of prognosis in patients of CLD such as Child Turcotte Pugh (CTP) score, model for end stage liver disease (MELD) score, etc. This study is therefore being done to study thyroid function profile in patients of cirrhosis of liver and its correlation with CTP score.

Aims & Objectives of the Study

1. To study the levels of thyroid hormone in Cirrhosis of liver.
2. To study possible correlation between thyroid hormone levels and severity of Cirrhosis of liver.

Materials & Methods

This is a hospital based analytical cross-sectional study which was conducted from July 2023 to June 2024 in ESI-PGIMSR & ESIC Medical College & Hospital, Joka, Kolkata, West Bengal.

Inclusion Criteria

Admitted patients aged more than 18 years of either sex with evidence of cirrhosis of liver who gave positive consent to be a part of study.

Exclusion Criteria

- Known case of thyroid dysfunction.
- Acute hepatitis and fulminant liver failure
- Chronic renal failure
- Congestive heart failure
- Malignancy
- Drugs effecting thyroid function
- Sepsis
- Patients who did not give consent for the study.

Patents were enrolled in the study as per inclusion and exclusion criteria. All subjects were explained about the procedure, valid informed written consent was taken, detailed clinical, biochemical (TFT, LFT and other routine investigations) and ultrasonographical evaluations were done. The Child Pugh Turcotte score was calculated and the subjects were categorized based on severity of liver disease. Serum TSH, FT3, FT4 levels were measured for all the patients. TSH was measured by Sandwich chemiluminescent immunoassay (CLIA), while FT3 and FT4 were measured by competitive CLIA. CTP score is a prognostic scoring system used to predict mortality in patients with cirrhosis. It is based on 5 parameters – Ascites, Total Bilirubin, Albumin, INR, Encephalopathy. The CTP score categorizes patients into three classes:

A: 5–6 points, indicating compensated cirrhosis

B: 7–9 points, indicating early decompensation

C: 10–15 points, indicating late or further decompensation.

Statistical analysis

Analysis of data was performed using SPSS version 20.0. Continuous variables were expressed as means and standard deviation. Categorical variables were expressed as percentages. Comparison between variables was done by using appropriate statistical tests of significance. Association between variables was considered statistically significant if p value was less than 0.05.

Results

Among 200 patients, 168 (84%) patients were male while 32(16%) patients were female. Gender distribution is shown in Figure 1.

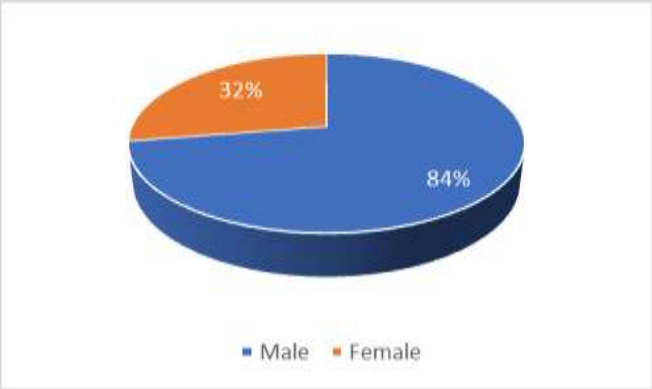

Figure 1: Gender distribution of study subjects

Out of total 200 patients having cirrhosis, maximum 124 (62%) patients were having alcoholic liver disease as etiology while 30 (15%) had hepatitis B, 26 (13%) had hepatitis C and 20 (10%) had other aetiologies (Figure 2).

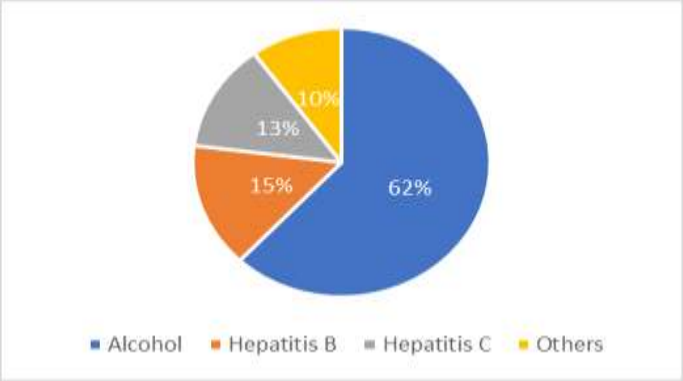

Figure 2: Distribution of patients as per etiology of liver cirrhosis.

CTP score was calculated for all of 200 patients and it was found that 36 (18%) patients belonged CTP class A, 78 (39%) patients had CTP score of class B, while maximum 86 (43%) patients belonged CTP class C (as mentioned in Table 1).

CTP Class	Frequency	Percentage
A	36	18
B	78	39
C	86	43

Table 1: Severity of Cirrhosis of liver based on CTP Score

Significant positive association was found between CTP class and TSH (μIU/mL) values ($p<0.001$) with mean (SD) of CTP class A, B and C were 2.42 (0.76), 3.9 (1.02) and 5.91 (1.08) respectively. There was significant negative association between CTP class and FT3 (pg/ml) values ($p<0.001$) with mean (SD) of CTP class A, B and C were 3.4 (0.57), 2.59 (0.57) and 2.22 (0.76) respectively. There was significant negative association between CTP class and FT4 (ng/ml) values ($p<0.001$) with mean (SD) of CTP class A, B and C were 1.4 (0.21), 1.01 (0.32) and 0.84 (0.47) respectively.

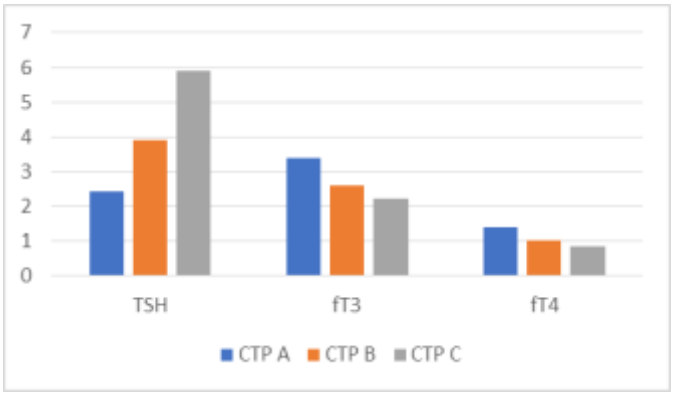

Figure 3: Comparison of mean thyroid profile markers according to CTP class.

Correlation between thyroid profile (TSH, FT3, FT4) and child Pugh score was analysed and Pearson correlation score was calculated and found to be 0.706, -0.453 and -0.371 for TSH, FT3 and FT4 respectively with $p<0.001$ for all of them (as mentioned in Figure 4 & 5).

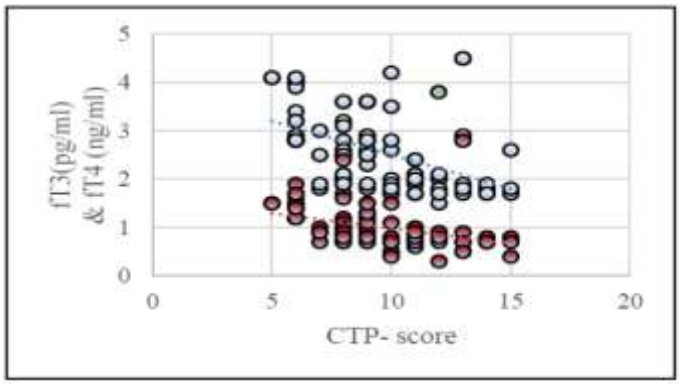

Figure 4: Scatter-plot of correlation between FT3 and FT4 (y-axis) with CTP score (x-axis)

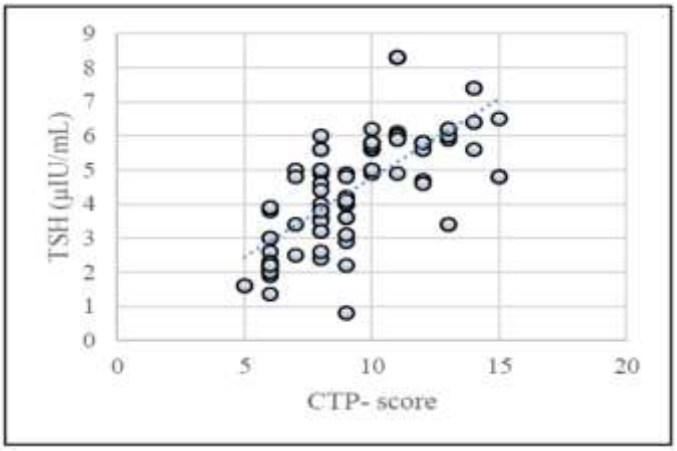

Figure 5: Scatter-plot of correlation between TSH (y-axis) and CTP score (x-axis)

Discussion

In the present cross-sectional study, liver cirrhosis patients were studied to assess thyroid hormone status and to establish possible correlation between thyroid hormone levels and the severity of liver disease.

In this study, 168 (84%) patients were male while 32(16%) patients were female which is comparable to the study conducted by Punekar et al. [5] where males (71%) were involved more than female. Ashish Kumar et al. [6] studied 50 patients with liver cirrhosis, where 21 patients had alcoholic liver disease, 20 had Hepatitis C, 5 had hepatitis B and 4 patients had cryptogenic cirrhosis. Whereas in our study, 124 (62%) patients were having alcoholic liver disease while 30 (15%) had hepatitis B, 26 (13%) had hepatitis C and 20 (10%) had other aetiologies.

Chaudhary S et al. [7] in their study conducted in Nepal, has mentioned that most of their patients (56.36%) were in Child-Pugh class C followed by 31.82 % in Child-Pugh class B and remaining 11.82% were in Child-Pugh class A, which is similar to our study where 36 (18%) patients belonged CTP class A, 78 (39%) patients had CTP score of class B, while maximum 86 (43%) patients belonged CTP class C. This may be due to the fact that patient comes late to health facilities in developing country may be because of poor socio-economic condition.

Punekar P et al.[8] noted that, the mean FT3 and FT4 levels were significantly decreased and mean TSH levels were significantly increased in liver cirrhosis patients and also correlated with the severity of liver disease. Mansour-Ghanaei et al.[9] found in their study that there was a negative correlation between child-Pugh scores and total serum T3 level ($r=-0.453$, $p<0.001$). Vincken et al.[10] found that fT3 and fT4 levels were significantly lower in patients with cirrhosis than in healthy subjects ($p=0.001$ and 0.002, respectively). Liu et al.[11] found that free triiodothyronine (FT3) and free thyroxine (FT4) levels in the liver cirrhosis group were lower than the control group ($p<0.001$), thyroid-stimulating hormone (TSH) levels in liver cirrhosis group were higher than the control group ($p<0.001$).

Most of the past studies showed that there was decreased serum FT3 and FT4 levels, while serum TSH levels were increased in patients with cirrhosis of liver. Few studies also suggested that FT3 levels decreased while serum TSH levels increased with severity of liver dysfunction.

Our study showed similar results with significant positive correlation between serum TSH values and CTP score ($r=0.706$, $p<0.001$) while there was significant negative

correlation between serum FT3 levels and CTP scores (r=-0.453, p<0.001) and between serum FT4 levels and CTP scores (r=-0.371, p<0.001).

There was significant positive association between CTP class and TSH values (p<0.001) with mean (SD) of CTP class A, B and C were 2.42 (0.76), 3.9 (1.02) and 5.91 (1.08) respectively while there was significant negative association between CTP class and FT3 values (p<0.001) with mean (SD) of CTP class A, B and C were 3.4 (0.57), 2.59 (0.57) and 2.22 (0.76) respectively. There was significant negative association between CTP class and FT4 values (p<0.001) with mean (SD) of CTP class A, B and C were 1.4 (0.21), 1.01 (0.32) and 0.84 (0.47) respectively.

Our study showed that there was increase in S.TSH values with increasing severity of liver dysfunction as assessed by CTP scores, while serum FT3 and FT4 values decreased with increasing severity of CLD.

Limitation

The present study was a single-centred hospital based study with small sample size so results obtained in this study cannot be generalised. There is a potential for referral bias as the study was performed at a tertiary care centre. In future, we need multi-centric study with larger sample size. Follow-up of patients can be done to see variation of thyroid hormone levels as liver function and CTP score changes in cirrhotic patients over time.

Conclusion

The severity of thyroid dysfunction increased with increasing severity of liver dysfunction in patients of Cirrhosis of liver. It was found that serum TSH values increased with severity of cirrhosis, while FT3 and FT4 values decreased with severity of liver disease as assessed by CTP score. Thus, thyroid hormone levels can be considered as a marker of severity of liver dysfunction and prognosis in patients of liver cirrhosis. The presence of any thyroid dysfunction should be treated promptly as thyroid hormones play an important role in the normal functioning of various systems.

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