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**Original Research Article**

# A study of thyroid function profile in patients of chronic liver disease and its correlation with child Pugh score

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## ABSTRACT

**Background:** Chronic liver disease (CLD) is a continuous process of inflammation, destruction, and regeneration of liver parenchyma, which leads to fibrosis and cirrhosis. Liver plays an essential physiological role in thyroid hormone activation and inactivation, transport, and metabolism, as well as the synthesis of thyroid binding globulin. A complex relationship exists between thyroid and liver in health and disease.
**Methods:** 103 patients of CLD were included in this study from December 2020 to September 2022. They were classified as per child Pugh scoring after clinical assessment and investigations. Serum TSH, FT3, FT4 levels were measured for all the patients.
**Results:** Out of 103 patients and it was found that 19 (18.44%) patients belonged CTP class A, 40 (38.83%) patients had CTP score of class B, while maximum 44 (42.71%) patients belonged 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 ($p<0.001$).
**Conclusions:** Our study found that there was significant positive correlation of S.TSH values with severity of CLD as assessed by CTP score, while FT3 and FT4 were having significant negative correlation.

**Keywords:** CLD, Thyroid function, TSH, FT3

## INTRODUCTION

Chronic liver disease (CLD) is a spectrum of disorders characterised by deterioration of liver functions for six months or more, including removal of harmful products of metabolism, synthesis of clotting factors, other proteins and bile excretion. Its pathogenesis includes inflammation of hepatic tissue, destruction, and regeneration of liver parenchyma, which ultimately leads to fibrosis and cirrhosis and in few cases can progress to Hepatocellular carcinoma (HCC). The aetiological spectrum for CLD consists of various factors such as toxins, alcohol abuse for a chronic duration of time, infections such has hepatitis viruses, autoimmune diseases, genetic and metabolic disorders. CLD is a frequently encountered disease clinically.[1]

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. Child and Turcotte initially gave Child-Pugh score in patients undergoing portosystemic shunt surgery for variceal bleeding to predict the operative risk. That score included following parameters, ascites, nutritional status, total bilirubin, hepatic encephalopathy (HE) and albumin. Pugh et al provided a modification by substituting clinical nutrition status with prothrombin time. CTP class A: 5-6 points, CTP class B: 7-9 points, CTP class C: 10-15 points).[2-4]

The thyroid gland in human body is responsible for production of two tyrosine-based hormones, thyroxine (T4) and triiodothyronine (T3). These hormones bind to

the thyroid hormone receptors α and β, and in turn have an critical role in overall growth and cell differentiation during development of human body and also help in maintaining the homeostasis in the adult by regulating various thermogenic, autonomic and metabolic parameters.[5] The liver contains type 1 deiodinase which is responsible for production of about 30%-40% of extrathyroidal T3 present in circulation. Type 1 deiodinase have ability to do both 5-deiodinisation and 5'-deiodinisation of thyroxine hormone. Also, the liver plays a critical role in conjugation and excretion of thyroid hormones. It is also responsible for synthesising the thyroid binding globulin (TBG). Thyroid hormones are involved in regulation of basal metabolic rate (BMR) of all cells including that of hepatocytes, thus modifying hepatic functions. The hepatocytes in turn are responsible for metabolism and excretion of the thyroid hormones, thus modulating their overall endocrine effects.[6,7]

Thyroid dysfunction may perturb liver function, liver disease modulates thyroid hormone metabolism. A complex relationship exists between thyroid and liver in health and disease. Liver plays an essential physiological role in thyroid hormone activation and inactivation, transport, and metabolism. Thus any thyroid dysfunction may result in deterioration of liver functions, while any liver disease may modulate metabolism and serum concentration levels of thyroid hormones.[8] Since the liver and to some extent kidneys have a primary impact on the levels of thyroid hormones and their metabolites in the circulation, the normal and healthy functioning of these organs is an important and under-recognized factor of thyroid hormone functions.[9] This study is therefore being done to study thyroid function profile in patients of CLD and its correlation with child Pugh score.

## METHODS

This hospital based analytical cross-sectional study was conducted from December 2020 to September 2022 in K.P.S. post graduate institute of medicine, GSVM medical college Kanpur, Uttar Pradesh.

### *Inclusion and exclusion criteria*

The study group consisted of the patients with age of more than 18 years of either sex with evidence of CLD who gave positive consent to be a part of study while excluding any pregnant females, any known case of thyroid illness, patients with previous history of thyroid surgery, major neck surgery, patients on drugs affecting thyroid function (e.g. dopamine, levodopa, bromocriptine, steroids, amiodarone.), patients with sepsis and patients who gave negative consent for participation in the study.

The study was conducted after due approval from institutional ethics committee. After assessment of eligible patients as per inclusion and exclusion criteria, we had sample size of 103 patients, who underwent detailed history and thorough clinical examination after written informed consent. They were classified as per child Pugh scoring after clinical assessment and investigations as per pre-set working proforma. 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.

### *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 103 patients, 87 (84.46%) patients were male while 16 (15.53%) patients were female. Gender distribution is shown in Figure 1. Age distribution is shown in Figure 2. Mean (SD) age of all patients was 45.67 years (10.50) with range of 28-75 years. Out of total 103 patients having CLD, maximum 64 (62.13%) patients were having alcoholic liver disease as aetiology while 15(14.56%) had hepatitis B, 13 (12.62%) had hepatitis C and 11 (10.67%) had other aetiologies (Table 1).

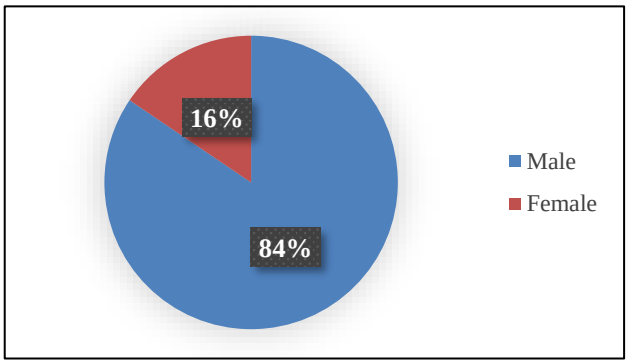


**Figure 1: Gender distribution of study subjects distribution of patients according to child Pugh classification.**

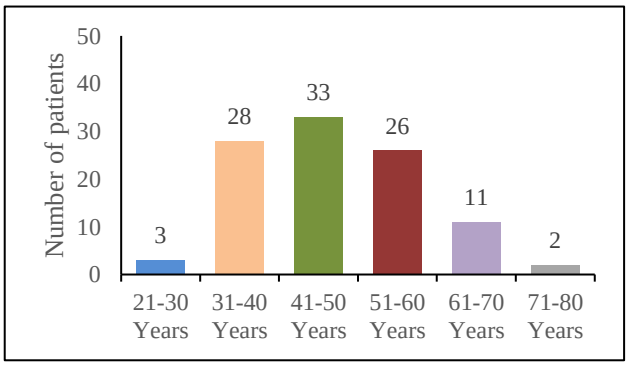


**Figure 2: Age distribution of study subjects.**

**Table 1: Distribution of patients as per aetiology of liver disease.**

| Aetiology of liver disease | N (%) |
|---|---|
| **Alcohol** | 64 (62.13) |
| **Hepatitis B** | 15 (14.56) |
| **Hepatitis C** | 13 (12.62) |
| **Others** | 11 (10.67) |

The 55 (53.39%) patients had no (grade 0) hepatic encephalopathy, while 8 (7.76%) patients had grade I HE, 24 (23.3%) patients had grade II HE, 9 (8.73%) patients had grade III HE and 7 (6.79%) patients had grade IV HE. Out of total 103 patients, 36 (34.95%) patients had no ascites, 21 (20.38%) had mild ascites, while 28 (27.18%) patients had moderate ascites and 18 (17.47%) patients had severe ascites. Mean International normalized ratio of prothrombin time (INR) was found to be 2.23 with SD of 0.93. The range of INR was 1.1-5.1. Mean S. bilirubin was found to be 3.38 mg/dl with SD of 3.82. The range of S. bilirubin was 0.4-20.7. Mean S. albumin was found to be 3.02 gm/dl with SD of 0.57. The range of S. bilirubin was 1.6-4.2

CTP score was calculated for all of 103 patients and it was found that 19 (18.44%) patients belonged CTP class A, 40 (38.83%) patients had CTP score of class B, while maximum 44 (42.71%) patients belonged CTP class C. Mean CTP score was calculated and found to be 9.4 with SD of 2.55.

There was significant positive association 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).

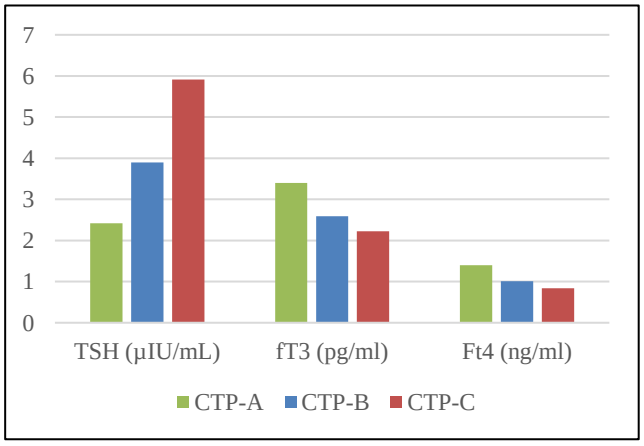


**Figure 3: Comparison of mean thyroid profile markers according to CTP class.**

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 (Figure 4 and 5).

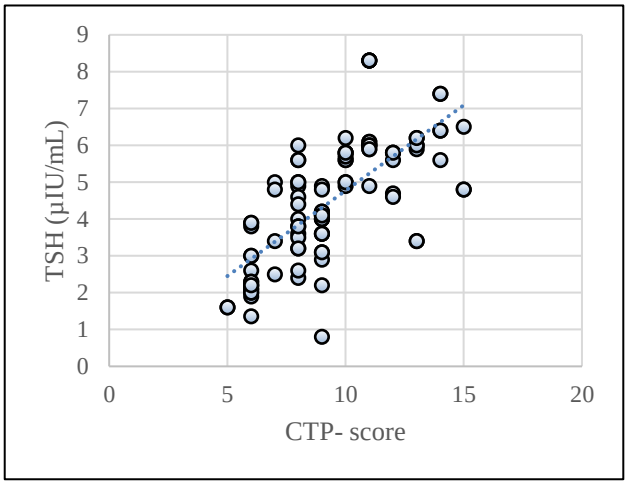


**Figure 4: Scatter-plot of correlation between TSH (y-axis) and CTP score (x-axis).**

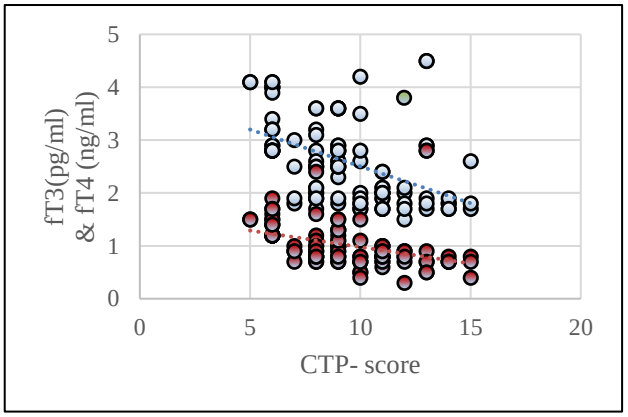


**Figure 5: Scatter-plot of correlation between FT3 and FT4 (y-axis) with CTP score (x-axis).**

Subgroup analysis was also done in all CTP classes, between different aetiology (Alcohol, Hepatitis B, Hepatitis C, unknown) of CLD patients and serum TSH, FT3, FT4 values. There was found to be no significant association between any aetiology of CLD and S.TSH, FT3, FT4 level.

## DISCUSSION

Several studies have been done to study thyroid hormone levels in patients of CLD and cirrhosis

Agha et al found that the mean serum concentration of T3, FT3 and FT4 were significantly decreased in cirrhotic, while no significant change was noted in serum T4 and TSH levels.[10] Sanul et al showed that the mean serum concentration of T3 and T3 / T4 ratio was significantly

decreased in cirrhotic (p<0.01), while no significant change was noted in serum T4 and TSH levels.[11] Mansour-Ghanaei et al 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).[12]

Vincken et al found that fT3 and fT4 levels were significantly lower in patients with cirrhosis than in healthy subjects (p=0.001 and 0.002, respectively). TSH levels were not statistically significantly different in the two groups.[13] Hong-Ling et al found that the chronic hepatitis group had significantly lower FT3 (2.79±0.71 vs. 4.43±0.75 pmol/L, p<0.001) and TSH [0.618 (0.186-1.185) vs. 1.800 (1.570-2.590) mIU/L, p<0.001], and higher FT4 (19.51±6.26 vs. 14.47±2.19 pmol/L, p<0.001) than the control group.[14] Liu et al 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).[15]

Most of the past studies showed that there was decreased serum FT3 and FT4 levels, while serum TSH levels were increased in patients with chronic hepatitis and cirrhosis. 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.

### *Limitations*

The limitation of the present study was that it was conducted at a single tertiary health centre. Future studies can be multi-centred 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 CLD patients over time.

## CONCLUSION

Our study found that the severity of thyroid dysfunction increased with increasing severity of liver dysfunction in patients of CLD. We found that S. TSH values increased with severity of CLD as assessed by CTP score, 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 CLD.

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*Ethical approval: The study was approved by the Institutional Ethics Committee*

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