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Original Research Article

Prevalence of subclinical hypothyroidism in patients of chronic liver disease

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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. Thyroid function profile was measured for all the patients.
Results: Among 103 patients, 8 (7.76%) patients were having overt hypothyroidism and 28 (27.18%) patients had subclinical hypothyroidism, while 67 (65.04%) patients had normal thyroid profile levels. There was significant correlation between CTP class and hypothyroidism status of patient (p value <0.001) with 25 (56.81%) patients of CTP class C having subclinical hypothyroidism, while 3 (7.5%) patients of CTP class B had subclinical hypothyroidism and none patient of CTP class A had subclinical hypothyroidism.
Conclusions: Our study found that there was increased prevalence of subclinical hypothyroidism in CLD patients which increased with severity of CLD as assessed with CTP class.

Keywords: Chronic liver disease, 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. Chronic liver disease is a frequently encountered disease clinically.[1]

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 a 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. Liver is 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. 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 the prevalence of subclinical hypothyroidism in CLD patients and to find out its correlation with CTP class.

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 chronic liver disease 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, and 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. The normal values of the thyroid function test were taken as the following according to department of biochemistry, GSVM Medical College Kanpur, where the evaluation was carried out (S. TSH) (0.5-5.5 uIU/ml), FT3 (1.8-4.2 pg/ml), FT4 (0.7-2.0 ng/dl)].

Statistical analysis

Analysis of data was performed using statistical package for the social sciences (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 chronic liver disease (CLD), maximum 64 (62.13%) patients where 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).

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

Aetiology of liver disease	Number of cases (%)
Alcohol	64 (62.13)
Hepatitis B	15 (14.56)
Hepatitis C	13 (12.62)
Others	11 (10.67)

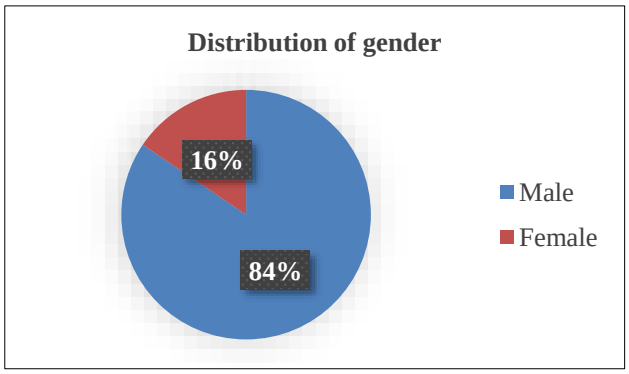

Figure 1: Gender distribution of study subjects' distribution of patients according to Child Pugh classification.

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 mg/dl. Mean S. albumin was found to be 3.02 gm/dl with SD of 0.57. The range of S. albumin was 1.6-4.2 gm/dl. 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.

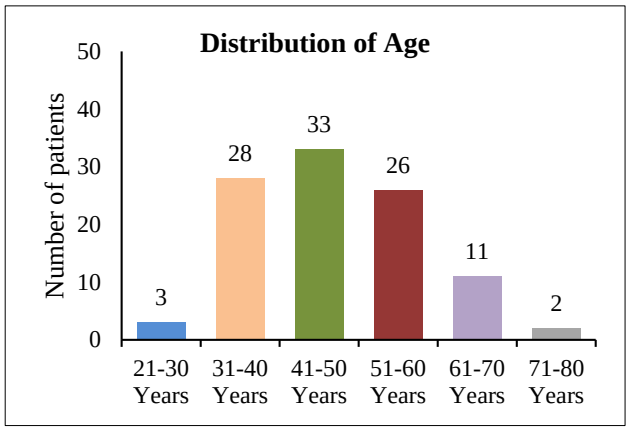

Figure 2: Age distribution of study subjects.

Among 103 patients, 8 (7.76%) patients were having overt hypothyroidism and 28 (27.18%) patients had subclinical hypothyroidism, while 67 (65.04%) patients had normal thyroid profile levels (Figure 3). There was significant correlation between CTP class and thyroid status of patient (p value <0.001). Out of 44 patients with CTP class C, 25 (56.81%) patients were having subclinical hypothyroidism and 8 (18.18%) patients were having overt hypothyroidism. While 3 (7.5%) patients out of total 40 patients of CTP class B had subclinical hypothyroidism. All of 19 patients with CTP class A were having normal thyroid function profile (Figure 4). There was significant correlation between grade of ascites and hypothyroidism status of patient (p value <0.001). Out of total 18 patients with severe ascites 11 (61.11%) were having subclinical hypothyroidism while 1 (5.55%) patient was having overt hypothyroidism.

In 64 patients with alcohol related CLD 19 patients were having subclinical hypothyroidism and 5 patients were having overt hypothyroidism. Among 15 patients with hepatitis B related CLD 6 patients were having subclinical hypothyroidism and 1 patient was having overt hypothyroidism. While in 13 patients with hepatitis C related CLD 2 patients were having subclinical hypothyroidism and 2 patients were having overt hypothyroidism. There was no significant association between aetiology of CLD and hypothyroidism status with p value of 0.376.

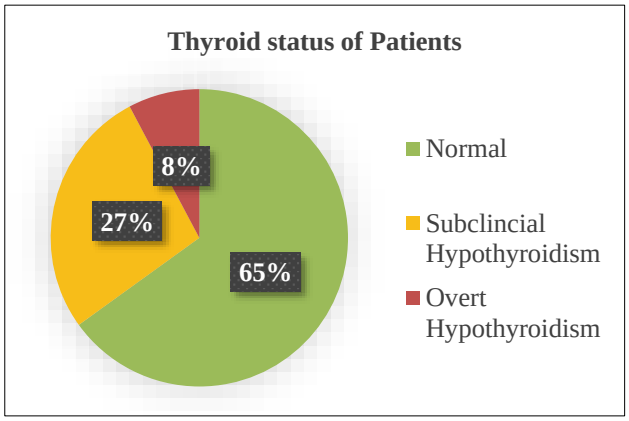

Figure 3: Distribution of patients according to thyroid status of patients.

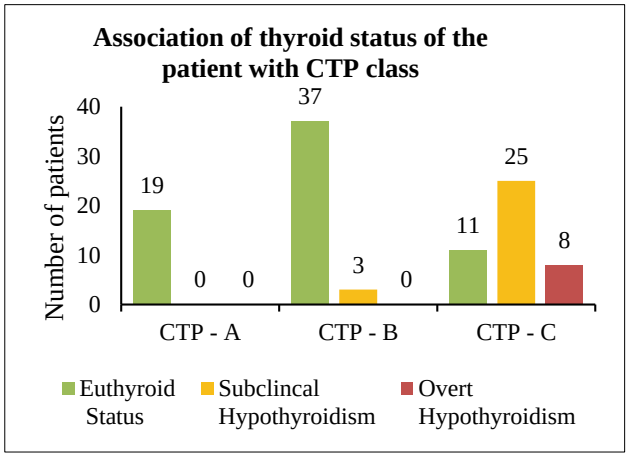

Figure 4: Association of thyroid status of the patient with CTP class.

DISCUSSION

Studies have been conducted in past to assess thyroid function in patients of chronic liver disease and to find out whether there is any association between subclinical hypothyroidism and chronic liver disease.

Maribel Rodríguez-Torres et al found that there was increased incidence of thyroid dysfunction (TD) among chronic hepatitis C patients with severe hepatic fibrosis compared with mild fibrosis. Patients with more hepatic fibrosis require careful attention to diagnose and manage TD.[10] Bandyopadhyay et al conducted a study on endocrine dysfunction in adult males with liver cirrhosis. They found that with more advanced disease, a progressive fall in testosterone, luteinizing hormone and triiodothyronine and a rise in oestradiol was observed.

Severity of the liver disease determined by Child-Turcotte-Pugh class, rather than aetiology (alcoholic or post viral), was the chief determinant of such dysfunctions.[11]

Patira et al found that the prevalence of subclinical hypothyroidism with cirrhosis was 62%. 31 out of 50 patients had subclinical hypothyroidism. The study showed that prevalence of hypothyroidism in cirrhosis patients increases as the severity of cirrhosis increases and findings were statistically significant (p value=0.002).[12]

Punekar et al in their study observed that hypothyroidism (high TSH level) was observed in 20% (20 out of 100) of decompensated liver cirrhosis patients, 26.3% (10 out of 38) in decompensated liver cirrhosis with HE, and 50% (8 out 16) in non-survivor cases. Non-thyroidal illness with low T4 was observed in 15% (15 out of 100) of decompensated liver cirrhosis patients, 16% (6 out of 38) in decompensated liver cirrhosis with HE, and 12% (2 out 16) in non-survivor group.[13]

Feng et al collected the clinical data of patients with liver failure retrospectively, 73 of them were randomly selected for an observational study and to establish prognostic models, and 14 for model validation. They found that patients with liver failure often develop non-thyroidal illness syndrome (NTIS). NTIS was diagnosed in 49 of the patients with liver failure (67.12%).[14]

Most of the data from past studies suggested that the incidence of thyroid dysfunction was higher in patients of chronic liver disease. Results of these studies showed that there was increased prevalence of subclinical hypothyroidism in patients of chronic liver disease. Some studies also suggested that it was associated with severity of liver dysfunction.

Results of our study were in concordance with the recent studies. We found that among 103 patients with CLD in our study, 8 (7.76%) patients were having overt hypothyroidism and 28 (27.18%) patients had subclinical hypothyroidism. And this prevalence was significantly associated with severity of liver dysfunction as determined by CTP class.

We found statistically significant correlation between presence of hypothyroidism and CTP class of CLD patient (p value <0.001). Out of 44 patients with CTP class C, 25 (56.81%) patients were having subclinical hypothyroidism and 8 (18.18%) patients were having overt hypothyroidism. While 3 (7.5%) patients out of total 40 patients of CTP class B had subclinical hypothyroidism. All of 19 patients with CTP class A were having normal thyroid function profile.

We also found that there was no significant association between any specific aetiology of chronic liver disease and occurrence of hypothyroidism (subclinical or overt) (p value=0.376).

Limitations

The limitation of our present study was its small sample size. It was conducted at a single tertiary centre. Further multi-centric studies with larger sample size should be done. Follow-up of patients can be done to see variation of thyroid status from euthyroid to hypothyroid or vice-versa as liver function and CTP score changes in CLD patients over time.

CONCLUSION

Our study showed that there is increased prevalence of subclinical hypothyroidism in patients of chronic liver disease. We also found that this prevalence had statistically significant positive correlation with the increase in severity of liver dysfunction of the CLD patients as determined by CTP class. Thus, we should recommend regular screening of thyroid function in patients of chronic liver disease. Further, more studies are required as of now to know whether the treatment of this subclinical hypothyroidism have any benefit in decreasing morbidity or mortality of CLD patients.

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

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