Original Research Article

Thyroid Dysfunction in Cirrhosis of Liver and Its Correlation with Severity of Liver Cirrhosis

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Abstract

Background: The liver plays an important role in thyroid hormone metabolism and action. Liver cirrhosis leads to impairment of liver functions, including thyroid hormone metabolism. **Aims and Objectives**: To study thyroid dysfunction in patients with liver cirrhosis and its correlation with the severity of liver disease. **Materials and Methods**: Ninety-six in-hospital patients with liver cirrhosis were studied. Detailed history and physical examination were done as per a pre-fixed proforma. Relevant hematological, biochemical, and radiological investigations were done to assess thyroid function and liver cirrhosis. The severity of liver cirrhosis was judged by the Child Pugh score. **Results**: The prevalence of hypothyroidism in chronic liver disease was found to be 33.3% (32/96), with 27.1% (26/96) of patients having subclinical hypothyroidism, 3.1% (3/96) for primary hypothyroidism and sick euthyroid each. Most of the participants were in the age group of 41-59 years. Out of them, 78.1% were males, while 21.9% were females. There was a significant correlation between hypothyroidism and the severity of liver disease (p-value 0.001). Sixteen cases of subclinical hypothyroidism belonged to Child Pugh C, while ten belonged to B. No thyroid abnormality was seen in Child Pugh A category. Also, levels of serum albumin and T3 were also showing a statistically negative correlation with the severity of liver disease with p-values of 0.005 and <0.001, respectively. **Conclusion**: The prevalence of hypothyroidism in liver cirrhosis was found to be 33.3% with subclinical hypothyroidism being the most common. There was a significant association of hypothyroidism, low serum albumin, and low T3 levels with the severity of liver disease. Therefore, all patients with liver cirrhosis should be evaluated for thyroid function test to prevent the development of overt hypothyroidism and also to use thyroid function tests as a marker of liver disease severity.

Keywords: Cirrhosis of liver, Hypothyroidism, Child Pugh Score

Introduction

Liver diseases are a common cause of morbidity and mortality worldwide, and the burden of liver disease in India is significant.[1] The liver plays an important role in metabolism of hormones and synthesis of carrier proteins and is associated with various endocrinal disturbances.[2-3] In particular, the liver plays an important role in Thyroid hormone metabolism, including deiodination, conjugation, and by synthesizing thyroid binding proteins.[4] Thyroid hormones, T3 and T4, are essential for normal organ growth, development, and function, and they regulate the basal metabolic rate of all cells, including liver cells, and therefore modulate hepatic function. The conversion of T4 to T3 occurs rapidly by D1 and slowly by D2, with D1 mainly found in the liver and kidney, and D2 found in the pituitary, CNS, and skeletal muscles.[5] In addition to metabolism, the liver also synthesizes transport proteins responsible for the transport of thyroid hormones to various tissues like the liver, where they are converted to the free form for their action. Therefore, a normal liver-thyroid relationship is essential for a normal thyroid functioning. Various studies have shown a relationship between thyroid hormone levels and liver disease, with low serum T3 and high TSH concentrations being reported in patients with chronic liver disease, and T3 being a marker of liver disease progression.[6,7] In this study, we aim to investigate the relationship between thyroid hormone levels in patients with chronic liver disease and to determine if S.T3 and. S.TSH levels can be used as a marker of severity of liver disease by correlating it with Child-pugh score and its biochemical parameters.

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Materials and Methods

Study Design
Prospective study

Source of Data
Department of General Medicine, G.R. Medical College, Gwalior (M.P.) from Jan 2021 - Jun 2022.

Sample Size
The sample size was calculated using the formula

$$n = \frac{Z^2_{\alpha/2} \times PQ}{D^2}$$

Where, $Z_{\alpha/2} = 1.96$, P = 62, Q = 38, D = 10
The calculated sample size was 96 patients.

Study Population
The study included 96 patients with symptoms and signs of chronic liver disease who were admitted to the medicine ward of JAH and KRH. The Inclusion Criteria were patients over 18 years of age with chronic liver disease. The Exclusion Criteria were known cases of hypothyroidism on treatment, pregnant females, patients on medications that affect the study like phenytoin, amiodarone, NSAIDS, salicylates, and patients with sepsis.

Data Collection
All patients underwent a detailed clinical examination at admission,

and relevant history and physical examination including symptoms and signs of liver failure, hepatomegaly, splenomegaly, and abdominal vein collaterals were recorded. Ascites were graded as none, mild, moderate, and severe. Hematological and biochemical workup was performed, which included measurement of hemoglobin, total leukocyte count, platelet count, prothrombin time, and serum concentration of bilirubin (both direct and indirect), protein, albumin, alanine aminotransferase, and aspartate aminotransferase.

USG findings suggestive of chronic liver disease were noted, which included nodular irregular surface of the liver, distorted vascular pattern, ascites, and signs of portal hypertension (splenomegaly or dilated portal venous system on ultrasonography).

Hormonal assessment was performed by measuring thyroid hormone levels. Fasting venous sample taken in the vaccutainer in the early morning was used to test thyroid hormones levels.

Due permission of Ethics committee was taken regarding the study participants and all ethical practices were followed.

Statistical Analysis

All data were entered into an Excel format and analyzed using SPSS Software. Numerical values were reported using mean and standard deviation or median. Categorical values were reported using number and percentages. A probability value (p) less than 0.05 was considered statistically significant.

Results

The observations and results show the demographic profile, etiology, biochemical parameters, thyroid function test and severity of liver disease.

In terms of the demographic profile, the study included 96 participants, out of which 75(78.1%) were male, and 21(21.9%) were female. The majority of participants were aged between 41-49 years (34) and 50-59 years (30), while only 5 cases were ≤ 30 years.

Regarding etiology, alcohol was the most common cause of CLD (53 cases), followed by HBsAg (12) and HCV (9). Other causes were responsible for 21 cases of CLD.

The biochemical parameters of cases were also studied, Almost half of the CLD cases had bilirubin levels below 2mg/dl, and the other half had bilirubin levels above 2mg/dl. About 41 cases of CLD had below-normal albumin levels, and 26 patients had raised serum creatinine levels. Around 51 cases of CLD had hyponatremia.

The thyroid function test showed that 88 participants had normal T3 levels, while 8 of them had low T3 levels. 88 patients had normal T4 levels, while 7 had low T4 levels. 68 participants had TSH levels within the normal range, while 28 had elevated TSH levels. None of the patient had TSH below normal range. 26 of participants had subclinical hypothyroidism. 3 cases had primary hypothyroidism and 3 had subclinical hypothyroidism.

Regarding the severity of ascites and hepatic encephalopathy, 61 of participants had severe ascites, and 5 had grade 4 hepatic encephalopathy. The majority of participants with total 57 cases belonged to the Child Pugh B category, while 33 belonged to the Child Pugh C score category.

Table 1: Demographic profile of study participants

Demographic profile		Frequency	Percent
Age Groups	≤30 Year	5	5.2
	31-40 Year	16	16.7
	41-49 Year	34	35.4
	50-59 Year	30	31.3
	≥60 Year	11	11.5

Table 2: Distribution of cases according to etiology

		Frequency	Percentage
Etiology of CLD	Ethanol	53	55.2
	HBsAg	12	12.5
	HCV	9	9.4
	Congestive	1	1
	Others	21	21.9

Table 3: Biochemical parameters of Cases

		Frequency	Percent
INR	<1.7	77	80.2
	1.7-2.5	15	15.6
	>2.5	4	4.2
Total Bilirubin	<2 mg/dl	47	49.0
	>2 mg/dl	49	51.0
Serum Albumin	<2.5 g/dl	41	42.7
	2.5-3.5 g/dl	40	41.7
	>3.5 g/dl	15	15.6
Serum Creatinine	<1.4 mg/dl	70	72.9
	>1.4 mg/dl	26	27.1
Serum Sodium	<136 mEq/l	51	53.1
	136-145 mEq/l	42	43.8
	>145 mEq/l	3	3.1

Table 4: Thyroid Function Test

		Frequency	Percent
T3	<0.69 ng/ml	8	8.3
	0.69-2.15 ng/ml	88	91.7
	>2.15 ng/ml	0	0
T4	<52 ng/ml	7	7.3
	52-127 ng/ml	88	91.7

	>127 ng/ml	1	1.0
TSH	<0.3 mIU/ml	0	0
	0.3-4.5 mIU/ml	68	70.8
	>4.5 mIU/ml	28	29.2
Thyroid Function	Hypothyroid	3	3.1
	Normal	64	66.7
	Sick Euthyroid	3	3.1
	Subclinical Hypothyroidism	26	27.1

Table 4: Association between Child Pugh Score and Thyroid Function of study participants

Child Pugh Score	Thyroid Function				Total	P value
	Hypo-thyroid	Normal	Sick Euthyroid	Subclinical Hypothyroidism		
	N (%)	N (%)	N (%)	N (%)		
A	0 (0%)	6 (9.4%)	0 (0%)	0 (0%)	6 (6.3%)	0.001
B	1 (33.3%)	46 (71.9%)	0 (0%)	10 (38.5%)	57 (59.4%)	
C	2 (66.7%)	12 (18.8%)	3 (100%)	16 (61.5%)	33 (33.4%)	
Total	3 (100%)	64 (100%	3 (100%)	26 (100%)	96 (100%)	

Child Pugh Score was found statistically associated with thyroid function, C category of child pugh score shows higher proportions of hypothyroid, sick euthyroid and subclinical

Figure 1: Association between Child Pugh Score and Thyroid Function of study participants

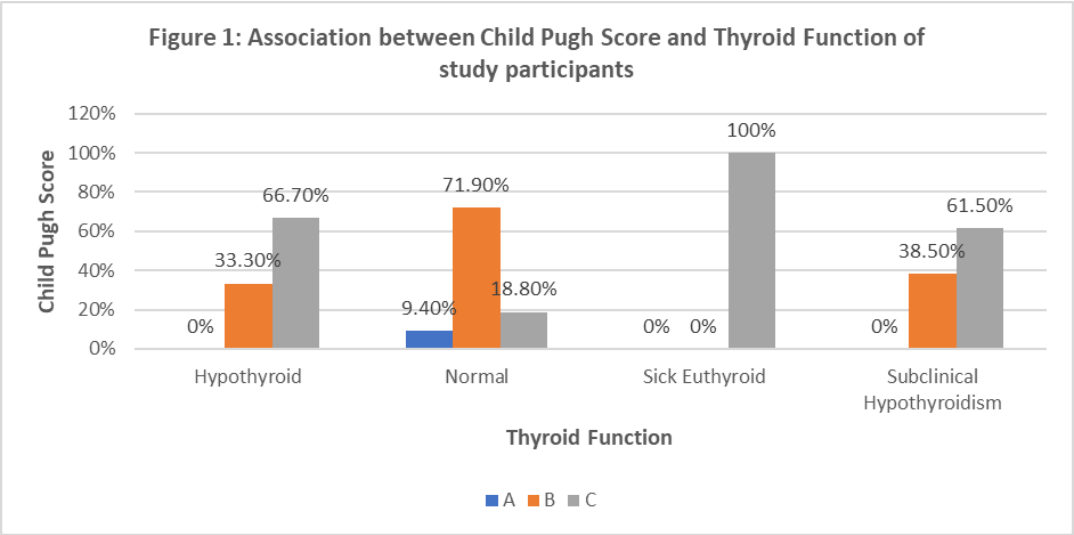

Table 5: Association between T3 and Child Pugh Score of study participants

T3 (mEq/L)	Child Pugh Score			Total	P value
	A	B	C		
	N (%)	N (%)	N (%)		
<0.69 mg/ml	0 (0%)	2 (3.5%)	6 (18.2%)	8 (8.3%)	0.039
0.69-2.15 mg/ml	6 (100%)	55 (96.5%)	27 (81.8%)	88 (91.7%)	
Total	6 (100%)	57 (100%	33 (100%)	96 (100%)	

Table 6: Association between Serum Albumin and Thyroid Function of study participants

Serum Albumin (g/dl)	Thyroid Function				Total	P value
	Hypo-thyroid	Normal	Sick Euthyroid	Subclinical Hypothyroidism		
	N (%)	N (%)	N (%)	N (%)		
<2.5	2 (66.7%)	18 (28.1%)	3 (100%)	18 (69.2%)	29 (42.7%)	0.005
2.5-3.5	1 (33.3%)	32 (50%)	0 (0%)	7 (26.9%)	67 (41.7%)	
>3.5	0 (0%)	14 (21.9%)	0 (0%)	1 (3.8%)	15 (15.6%)	
Total	3 (100%)	64 (100%	3 (100%)	26 (100%)	96 (100%)	

Hypothyroid, Sick Euthyroid and subclinical euthyroid condition was found statistically associated with low serum albumin level among chronic liver diseases patients.

Discussion

In this study, 96 patients with chronic liver disease were examined to investigate the correlation between thyroid function tests and the severity of liver disease, as measured by the Child Pugh score. The study found a high prevalence of hypothyroidism in the patient

population, with subclinical hypothyroidism being the most common type observed. Alcohol was identified as the most common cause of chronic liver disease in this patient population, followed by hepatitis B and C.

Comparing these findings to those of other studies, the results are largely consistent with previous research on chronic liver disease. For instance, Mukherjee et al.[8] (2010-2020) found that alcohol was the most common cause of cirrhosis, followed by hepatitis B, which aligns with the results of this study. However, Choudhuri et al.[9] (2015) reported nonalcoholic fatty liver disease as the most common cause of chronic liver disease, suggesting that the etiology of chronic liver disease may differ depending on the patient population.

Regarding hypothyroidism, the prevalence rates reported in this study are within the range reported by other studies. Kharab et al.[10] (2019) reported a prevalence of 16% for thyroid dysfunction in patients with liver disease, while Harikumar et al. (2018) found subclinical hypothyroidism in 10% of their patient population. Patira et al.[11] (2017) reported a much higher prevalence rate of 62% for subclinical hypothyroidism in patients with cirrhosis.

Interestingly, the results of this study and those of Sayal et al.[12] (2014) suggest that there may not be a statistically significant correlation between serum bilirubin levels and the severity of liver disease. This contrasts with the common clinical practice of using serum bilirubin levels as a marker of liver disease severity.

In conclusion, there is a significant association between thyroid disease and liver disease. Both the thyroid gland and the liver play essential roles in regulating the body's metabolic processes, and abnormalities in either organ can have adverse effects on the other. Patients with thyroid disease are at increased risk of developing liver disease, and vice versa. Thyroid hormones are crucial for maintaining liver function, and a deficiency in these hormones can lead to impaired liver function. Additionally, liver disease can affect thyroid hormone metabolism and lead to hypothyroidism. Therefore, clinicians should be aware of the potential association between thyroid and liver disease and carefully monitor patients with one condition for the development of the other. Early detection and treatment of both thyroid and liver disease can help to prevent serious complications and improve patient outcomes.

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