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Original Research

Correlation Of Thyroid Function In Patients Of Chronic Liver Disease With Severity Of Liver Disease

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Abstract:

Introduction: The liver plays a crucial role in thyroid hormone metabolism, converting T4 to active T3 and clearing plasma reverse T3. Thyroid hormones regulate liver cell metabolism and are essential for liver function. Hence, this study aimed to assess the relationship between thyroid function and liver disease severity in CLD patients. **Materials and Method:** This study was conducted among 71 adult patients with chronic liver disease (CLD) and cirrhosis. Participants underwent physical examination, laboratory tests, and ultrasound abdomen, and their data was analyzed using SPSS software. The relationship between thyroid function and liver disease severity using MELD and Child-Pugh scores was assessed. **Results:** The mean age of patients with chronic liver disease was 49.55 years, with 25.4% being elderly. Low FT3 levels were more common in patients with severe liver disease (Child Pugh score C), but the association was statistically insignificant. Similarly, no significant associations were found between thyroid hormone levels (FT3, FT4, TSH) and liver disease severity (Child Pugh score, MELD score). **Conclusion:** The present study found that thyroid abnormalities are common in patients with chronic liver disease (CLD), with free T3 levels being the most affected. Additionally, derangements in TSH and T4 levels were also observed in a significant proportion of patients. However, no significant association was found between the severity of liver disease and thyroid function tests. Further multicentric studies with larger sample sizes are needed to validate and support these findings.

Keywords: Chronic liver disease (CLD); Cirrhosis; Thyroid Function; T3; T4; TSH

Introduction

The thyroid hormones plays an important role in controlling the basal metabolic rate of all the cells, including hepatocytes and fulfilling the needs of the peripheral tissues. Additionally, these hormones are crucial in regulation of the growth of nervous tissues as well as maintenance of metabolic and thermogenic homeostasis in adults.[1,2] One of the important step of metabolism is Deiodination, which helps in converting inactive T4 hormone to active T3 hormone.[3,4] Amongst these Deiodinase enzymes, D1 is secreted by liver whereas D2 is secreted by central nervous tissue.[3] Liver is the main site for peripheral conversion of T4 to active T3 and liver is the major site for clearance of plasma reverse T3 (rT3) as well, which majorly inhibit T3 and T4.[3,5] Thus liver is involved in metabolism, conjugation as well as excretion of thyroid hormones. Both the thyroid hormones are bound to plasma proteins such as albumin, transthyretin (prealbumin), and thyroxine-binding globulin (TBG), which are mainly synthesized in liver.[2] As a result of plasma protein binding with the thyroid hormones, the clearance of these hormones is decreased, which leads to increase in the level of circulating hormones. This is essential for modulating the thyroid hormones delivery to the target tissues.[6,7] Thus, liver has an important role metabolism of thyroid hormones and vice-versa liver function is modulated by thyroid hormones, as these hormones are involved in regulating basal metabolic rate of cells including hepatocytes.[8]

Chronic liver disease (CLD) refers to a condition characterized by continuous and progressive deterioration of functions of liver (such as synthesis of plasma proteins, clotting factors, detoxification of harmful metabolism products as well as excretion of bile) as a result of inflammation, destruction and regeneration of parenchyma of liver for 6 months or more. The continuous and chronic insult to liver leads to fibrosis and cirrhosis of liver, which is described as

an end stage of any chronic liver disease.[9]
Literature suggests that thyroid disorders like hypothyroidism, hyperthyroidism, or thyroiditis are common in patients with cirrhosis and chronic liver disease. Vice-versa, patients with thyroid dysfunction have significant impact on liver function that may lead to abnormal liver functions.[8] It has been found that patients of cirrhosis with low T3 and T4 levels have a particularly severe form of liver disease. Thus, low thyroid hormone levels may be used as prognostic indicators and predictors of mortality in such cases.[10] To determine the severity and outlook of such patients, thyroid function tests should be performed on all patients presenting with chronic liver disease and liver cirrhosis. With the above background, the present study was done to assess the relationship between thyroid function and liver disease severity in patients with chronic liver disease.

Materials and Method

The present cross-sectional study was conducted among patients diagnosed with chronic liver disease (CLD) admitted to the Department of Medicine and Endocrinology at People's Hospital in Bhopal, India.
The study included adult patients with established chronic liver disease (CLD) and cirrhosis confirmed through clinical, radiological, and biochemical tests. Participants had to be willing to take part in the study and provide written consent, which was obtained after explaining the study's purpose and ensuring confidentiality. Exclusion criteria consisted of known thyroid disorders, organ failure, cancer, chemotherapy, active infections, and use of medications that interfere with thyroid metabolism. After obtaining ethical clearance, patients fulfilling the inclusion criteria were enrolled and their information was collected using a predesigned proforma. The proforma gathered socio-demographic data, clinical history, mode of presentation, duration of liver disease, etiology, and addiction history. A detailed physical and systemic examination was conducted, including vital signs, abdominal examination, and routine investigations such as CBC, liver function tests, and thyroid function tests (T3, T4, TSH). Additionally, an ultrasound abdomen was performed and findings were documented.

MELD Score and Child Turcotte Pugh Score were used to assess the severity of CLD. MELD score was calculated using serum bilirubin, serum creatinine,and International Normalized Ratio (INR).

Based upon this score, the severity of Cirrhosis was graded as

- Child-Pugh A- 5 to 6 points
- Child-Pugh B- 7 to 9 points
- Child-Pugh C- 10 to 15 points

Data was compiled using MsExcel and analysed using IBM SPSS software version 20. Categorical data was grouped and expressed as frequency and proportions whereas continuous data was expressed as mean and SD. Association of severity of CLD with thyroid function test was done using chi square test. P value less than 0.05 was considered statistically significant.

Results

Mean age of patients with chronic liver disease enrolled in our study was 49.55±16.21years and majority i.e. approximately one fourth(25.4%)cases belonged to elderly age group, followed by 22.5% cases belonging to 4th and fifth decade. Only 15.5% and14.1%casesbelonged to less than 30and 31to 40 years of age.
In present study, higher proportions of cases with Child Pugh score C had low FT3levels as compared to patients with Child Pugh score B and A (79.1% vs. 65.4% vs 50% respectively) the observed association of severity of CLD with FT3 was statistically insignificant (p>0.05). Similarly, 7.7% cases with Child Pugh B class and4.7% cases with Child Pugh C class had low serum FT4 levels, we observed nosignificant association of FT4 levels with severity of CLD (p>0.05). As with FT3 andFt4 values, we observed no significant association of Child Pugh score with TSH(p>0.05). In present study,though higher proportions of cases with normal MELD score had low FT3 and FT4 levels and high TSH levels as compared to patients with low MELD score,we found no significant association between MELD score and FT3, FT4 and TSH as observed from above table (p>0.05).
About 87.3% cases with low TSH and 66.7% cases with high TSH had low MELD score and the observed association of MELD with TSH levels was statistically significant (p>0.05), about 61.8% cases with TSH level below 4.5 and 66.7% cases with TSH above 10 had severe liver disease (belonged to Child Pugh category C).The observed association of Child Pugh score with TSH in cases with CLD was statistically insignificant (p>0.05).,we found nosignificant association of MELD score with thyroid status (p>0.05). **Discussion**
The present study aimed to explore the correlation between thyroid function and the severity of chronic liver disease (CLD) in a cohort of 71 patients. The findings reveal that the mean age of patients with CLD was 49.55±16.21 years, with 25.4% being elderly. This age distribution is consistent with other studies that highlight the increasing prevalence of CLD with advancing age. Notably, a considerable number of patients were in their fourth and fifth decades of life (22.5%), while younger age groups, particularly those under 30 years, constituted a smaller fraction (15.5%). Similarly in a study by **Punekar P et al (2018)** for cases, the mean age was 43 ± 14 years, while for controls, it was 42 ± 15 years.[11] **Raj A et al (2023)** documented that all the 100 patients were aged

between 30 and 80years.[12] Additionally, in a study by **Chaudhary S et al (2019)** it was documented that the patients ranged in age from 32 to 94 years old, with a mean age of 51.1±12.13 years. The majority of our patients were adults in their fifth and sixth decade of life, making up 63% (n=69) of the study population as a whole.[13] In the present study, the mean Child-Pugh score among CLD patients was 9.89±1.55, indicating moderate to severe liver disease. The distribution of Child-Pugh classes in the study population highlights the predominance of severe liver disease. Specifically, 60.6% of patients were classified as Child-Pugh class C, reflecting advanced

Table: 1-Distributionofcasesaccordingtoage

Age(years)	Frequency (n=71)	Percentage
≤30	11	15.5
31-40	10	14.1
41-50	16	22.5
51-60	16	22.5
>60	18	25.4
Mean	49.55±16.21	

Table: 2- Association of thyroid functions tests with severity of CLD using Child Pugh score

Thyroid functiontest		Child Pughscore						χ^2	P value
		A(n=2)		B (n=26)		C (n=43)			
		n	%	n	%	n	%		
FT3	Low	1	50	17	65.4	34	79.1	2.12	0.347
	Normal	1	50	9	34.6	9	20.9		
	Mean±SD	3.0±1.41		2.5±1.27		2.42±1.14			
FT4	Low	0	0	2	7.7	2	4.7	2.206	0.698
	Normal	2	100	23	88.5	41	95.3		
	High	0	0	1	3.8	0	0		
	Mean±SD	15.5±4.95		15.92±6.83		17.67±8.69			
TSH	Low	0	0	2	7.7	1	2.3	2.275	0.685
	Normal	2	100	20	76.9	32	74.4		
	High	0	0	4	15.4	10	23.3		
	Mean±SD	5.0±2.66		3.38±1.09		3.72±1.10			

Table: 3-AssociationofthyroidfunctiontestswithMELDscore

Thyroid function test		MELD				χ^2	P value
		Low		Normal			
		n	%	n	%		
FT3	Low	44	71	8	88.9	1.28	0.256
	Normal	18	29	1	11.1		
	Mean±SD	2.51±1.23		1.54±0.06			
FT4	Low	2	3.2	2	22.2	5.43	0.066
	Normal	59	95.2	7	77.8		
	High	1	1.6	0	0		
	Mean±SD	17.56±9.54		12.14±6.24			
TSH	Low	3	4.8	0	0	0.47	0.790
	Normal	47	75.8	7	77.8		
	High	12	19.4	2	22.2		
	Mean±SD	3.47±1.94		4.31±2.53			

Table:4-AssociationbetweenMELDscoreandTSHinpatientswithCLD

MELD score	TSH			
	<4.5 (n=55)		>10(n=3)	
	n	%	n	%
Low	48	87.3	2	66.7
Normal	7	12.7	1	33.3
χ^2	1.448			
P value	0.485			

Table 5-Association between Child Pugh score and TSH in patients with CLD

Child Pugh score	TSH			
	<4.5 (n=55)		>10 (n=3)	
	n	%	n	%
A	1	1.8	0	0
B	20	36.4	1	33.3
C	34	61.8	2	66.7
χ^2	1.528			
P value	0.822			

Table: 6-AssociationofMELDScorewiththyroidstatus

Thyroid status	MELD score			
	<11		>11	
	n	%	n	%
Normal	15	24.2	1	11.1
Hypothyroidism	12	19.4	2	22.2
Hyperthyroidism	3	4.8	0	0
Sickeuthyroid syndrome	32	51.6	6	66.7
χ^2	1.39			
P value	0.71			

Table: 7-Association of Child Pugh score with thyroid status

Thyroidstatus	Child Pugh score					
	A		B		C	
	n	%	n	%	n	%
Normal	1	50	7	26.9	8	18.6
Hypothyroidism	0	0	4	15.4	10	23.3
Hyperthyroidism	0	0	2	7.7	1	2.3
Sick euthyroid syndrome	1	50	13	50	24	55.8
χ^2	3.40					
P value	0.757					

liver dysfunction and poor prognosis. Child-Pugh class B, comprising 36.6% of cases in this study, signifies moderate liver disease with variable degrees of decompensation and intermediate prognosis. Only 2.8% of patients fell into Child-Pugh class A, indicating well-compensated liver disease with the best prognosis among the Child-Pugh categories. These patients typically exhibit minimal ascites and encephalopathy, along with relatively preserved liver function tests. In another study by **Chaudhary S et al (2019)** it was noted that the patients were grouped according to CPS for the severity of liver cirrhosis, in which 62 patients (56.36%) were in Class C, 35 patients (31.82 %) were in Class B and remaining 13 patients (11.82%) were in Class A Majority of their patients were in class C which shows that they were in advance stage of liver disease.[13] Additionally, **Khalid A et al (2017)** in their study documented that around 68% CLD patients were in class C of CPS. Class A & class C was 11% and 21% respectively.[14] Furthermore, in a retrospective study by **Puentes JCP et al (2018)** it was noted that based on their Child-Pugh score, patients were categorized into three groups: Class A (17%), Class B (48.9%), and Class C (34%). Class A had the highest survival rate (87.5%), followed by Class B (30.4%) and Class C (31.25%).[15] In the present study, the mean MELD score among CLD patients was 7.82±4.18, indicating predominantly mild to moderate disease severity. The distribution of MELD scores in the study population revealed that 87.3% of patients had scores below 11. Conversely, 12.7% of patients had MELD scores above 11, indicating more advanced liver disease and higher risk of mortality. Similarly, in a retrospective study by **Puentes JCP et al (2018)** it was noted that the MELD score intervals were >9 (2.15%), score 10–19 (46.8%), score 20–29 (27.7%), score 30–40 (19.1%), and score >40 (4.3%). Nearly 51.1% had a score >20 and 48.9% <20.[15] In a study by **Singh S et al (2020)** it was noted that 45, 77.6% had a MELD score greater than 12, and only 13 (22.4%) had a score less than 12. P<0.001 indicated that this difference was statistically significant.[16] Additionally, **Havens J et al (2016)** in their studies stated that a decrease in MELD score of more than 3 in the 48 hours following ICU admission was associated with a 2.2-fold decrease in 90-day mortality (odds ratio = 0.46; 95% CI, 0.22-0.98).[17] The MELD score serves as a valuable tool for risk stratification and prognosis assessment in patients with chronic liver disease. Regarding Free T3 (FT3) levels, a higher percentage of patients classified under Child-Pugh score C exhibited low FT3 levels compared to those in Child-Pugh score B and A categories (79.1% vs. 65.4% vs. 50%, respectively). However, despite this trend, the association between FT3 levels and the severity of CLD, as indicated by Child-Pugh score, did not reach statistical significance ($p > 0.05$). Similarly, low serum Free T4 (FT4) levels were observed in 7.7% of patients in Child-Pugh class B and 4.7% in class C. However, like FT3, the association between FT4 levels and Child-Pugh score did not demonstrate statistical significance ($p > 0.05$). Thyroid Stimulating Hormone (TSH) levels also showed no significant association with Child-Pugh score categories ($p > 0.05$). Additionally, study by **Raj A et al** (2023) focused that the correlation analysis of TSH and Child-Pugh score ($r = 0.404$) shows that there is a statistically significant positive correlation between TSH and Child-Pugh score with a p-value < 0.001. The correlation analysis of fT3, fT4 levels, and Child-Pugh score shows that there is a statistically significant negative correlation between fT3 ($r = -0.404$), fT4 ($r = -0.528$) and Child- Pugh Score with p-value < 0. 001.This finding was in contrast to our study finding.[12] In another study by **Chaudhary S et al (2019)** they compared mean score of FT3, FT4 and TSH with CPS score by using ANOVA test. It was seen that mean score of T3 with different CPS categories was found to be statistically significant. Similarly mean score of fT4 with different CPS categories was found to be statistically significant and meanscore of TSH with different CPS category was found to be statistically insignificant.[13] The association between Thyroid Stimulating Hormone (TSH) levels and the Model for End-Stage Liver Disease (MELD) score was investigated in patients with chronic liver disease (CLD) in the present study. Despite observing different proportions of TSH abnormalities across MELD score categories, no significant association was found between TSH levels and MELD score. In a research by **Punekar P et al. (2018)** discussed that the Low levels of FT3 also correlated with the severity of liver disease in the form of CPS or MELD. Level of FT4 decreases as CPS Class (A–C) increases. Level of TSH increases with MELD score. Therefore, thyroid levels in cirrhotic patientsmay be used as a prognostic marker.[11] To best of our knowledge, literature is scarce regarding association of MELD and TSH levels. The present study had two main limitations. Firstly, it was a tertiary hospital based cross-sectional study conducted at a single facility, which restricts the generalizability of the findings to the broader

population. Secondly, the study had a small sample size, with only 71 cases enrolled, which may not be representative of the larger population of patients with chronic liver disease. These limitations highlight the need for further research with a larger sample size and multiple facilities to validate the findings and increase their generalizability.

Conclusion

In conclusion, the present study found that thyroid abnormalities are common in patients with chronic liver disease (CLD), with free T3 levels being the most affected, the association did not reach statistical significance. Additionally, derangements in TSH and T4 levels were also observed in a significant proportion of patients. The majority of patients were adults in their fifth and sixth decade of life, with a mean age of 49.55±16.21 years. The study revealed a predominance of severe liver disease, with 60.6% of patients classified as Child-Pugh class C. The mean MELD score indicated mild to moderate disease severity. These findings are consistent with previous studies, highlighting the importance of considering thyroid function in the management of CLD patients. Further research is needed to fully understand the relationship between thyroid function and CLD severity.

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