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Original Research Article

Thyroid Function Abnormalities in Chronic Liver Disease

Dr. Mohan B.R.[1*], Dr. N.C. Srinivas Prabhudev[2], Dr. Shantha M.[3]
[1*]Professor & HOD, Department of General Medicine, K.C. General Hospital, Bangalore, Karnataka, India.
[2]Professor, Department of General Medicine, K.C. General Hospital, Bangalore, Karnataka, India.
[3]Postgraduate, Department of General Medicine, K.C. General Hospital, Bangalore, Karnataka, India.
Corresponding Author: Dr. Mohan B.R.
Professor & HOD, Department of General Medicine, K.C. General Hospital, Bangalore, Karnataka, India.
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ABSTRACT

Background: Chronic liver disease alters several endocrine pathways, and the thyroid-liver relationship is clinically relevant because the liver contributes to thyroid hormone binding, conversion, conjugation, and clearance. Mild thyroid dysfunction may remain clinically silent in cirrhosis, yet it may carry information about hepatic reserve.

Objectives: To assess thyroid function abnormalities in subjects with chronic liver disease and to determine their association with severity of liver disease assessed by Child-Pugh class and CLD stage.

Methods: This prospective observational study was conducted in the Department of General Medicine, K.C. General Hospital, Bangalore, Karnataka, for a period of 9 months. A total of 130 subjects aged 18-60 years with chronic liver disease were evaluated. Free triiodothyronine (FT3), free thyroxine (FT4), and thyroid-stimulating hormone (TSH) were assessed using a chemiluminescence assay. Liver disease severity was graded using Child-Pugh class. Categorical associations were tested using the chi-square test, with $p<0.05$ considered statistically significant.

Results: The mean age was 45.24±9.88 years, with a range of 24-59 years. Males constituted 94 (72.3%) subjects. Child-Pugh class A, B, and C accounted for 41 (31.5%), 56 (43.1%), and 33 (25.4%) subjects, respectively; 89 (68.5%) belonged to CLD stage 2. Thyroid function was normal in 85 (65.4%) subjects, whereas 39 (30.0%) showed a hypothyroid biochemical pattern and 6 (4.6%) showed a hyperthyroid biochemical pattern. Hypothyroid-pattern dysfunction was concentrated in advanced disease: 21/39 (53.8%) were in Child-Pugh class C and 36/39 (92.3%) were in CLD stage 2. The association between thyroid functional status and Child-Pugh class, as well as CLD stage, was statistically significant (chi-square test, $p<0.001$). Low FT3 was observed in 35 (26.9%) subjects and showed a significant association with Child-Pugh class and CLD stage ($p<0.001$).

Conclusion: Biochemical thyroid dysfunction was frequent in chronic liver disease despite clinical euthyroidism. Hypothyroid-pattern abnormalities, particularly low FT3, increased with advancing Child-Pugh severity. Routine thyroid profiling may therefore add useful biochemical context while assessing hospitalized patients with chronic liver disease.

Keywords: Chronic Liver Disease; Cirrhosis; Thyroid Dysfunction; FT3; FT4; TSH; Child-Pugh Class.

INTRODUCTION

Chronic liver disease (CLD) sits quietly for a long time, then announces itself through decompensation, portal hypertension, infection, or metabolic failure. Its burden remains substantial worldwide, with cirrhosis and other chronic liver diseases contributing meaningfully to premature mortality and health-system pressure across countries [1,2]. In India, the clinical landscape is complicated by overlapping drivers such as viral hepatitis, alcohol-related liver injury, metabolic risk, late presentation, and variable access to structured follow-up [3]. For physicians working in general medicine wards, CLD is therefore rarely a single-system illness. It is a slow systemic disorder with hepatic, nutritional, hematological, renal, and endocrine shadows.

The thyroid-liver axis is one such shadow. Thyroid hormones influence basal metabolic rate and hepatocyte function, while the liver participates in thyroid hormone transport, peripheral conversion, conjugation, and biliary excretion [4,5]. A damaged liver may alter the serum concentrations of FT3, FT4, TSH, thyroid-binding globulin, albumin-bound fractions, and peripheral deiodination patterns. This is why patients with cirrhosis can show abnormal thyroid function tests while remaining clinically euthyroid. Borzio et al. described

multiple thyroid-test abnormalities in chronic liver disease despite the absence of overt thyroid symptoms, giving an early biochemical explanation for what clinicians still observe at the bedside [6].

The most consistent abnormality reported in cirrhosis is a fall in T3 or FT3, often interpreted as part of non-thyroidal illness physiology, reduced hepatic type 1 deiodinase activity, altered binding-protein availability, and impaired peripheral conversion of T4 to T3. Thyroid gland size and function may also vary in cirrhosis, and not every abnormal value indicates primary thyroid disease requiring replacement therapy [7]. This distinction matters. Fatigue, weakness, edema, altered mentation, weight change, constipation, cold intolerance, and menstrual irregularity may be attributed casually to liver disease, yet several of these symptoms overlap with hypothyroid states. Without biochemical testing, subtle thyroid-axis disturbance is easy to miss.

Severity assessment in cirrhosis still commonly relies on Child-Pugh classification, which incorporates bilirubin, albumin, prothrombin time or INR, ascites, and hepatic encephalopathy [8]. If thyroid function shifts in parallel with Child-Pugh severity, the finding may not simply be an incidental laboratory association. It may reflect declining hepatic reserve, altered protein synthesis, impaired hormone metabolism, and the broader catabolic state of advanced CLD. Here, the clinical question becomes simple but important: are thyroid function abnormalities more frequent or more severe as CLD advances?

The present study was undertaken to assess thyroid hormone abnormalities in subjects with chronic liver disease and to evaluate their association with disease severity. The working emphasis was deliberately pragmatic. Instead of treating thyroid tests as isolated endocrine values, the study examined FT3, FT4, TSH, Child-Pugh class, and CLD staging together, in a hospitalized Indian cohort where liver disease is often advanced by the time formal evaluation occurs.

MATERIALS AND METHODS

Study Design and Setting

A prospective observational study was conducted in the Department of General Medicine, K.C. General Hospital, Bangalore, Karnataka, for a period of 9 months.

Study Population

Subjects with chronic liver disease admitted under General Medicine were recruited after applying the eligibility criteria.

Sample Size

A minimum sample size of 113 was calculated using 95% confidence level, 90% power, 41% expected prevalence, and 15% desired precision. After allowing an additional margin, the final sample size was 130 subjects.

Inclusion Criteria

Subjects aged 18-60 years with liver disease for at least 6 months or ultrasound evidence suggestive of chronic liver disease were included. Written informed consent was obtained before enrolment.

Exclusion Criteria

Subjects who had received thyroid hormone therapy, thyroid medications, or thyroid surgery before thyroid dysfunction assessment were excluded. Pregnant and lactating women, known diabetic subjects, and known cases of autoimmune disease were also excluded.

Clinical Assessment

A detailed history and clinical examination were performed. Demographic variables, duration of CLD, symptoms and signs of decompensation, ascites, hepatic encephalopathy, and other relevant clinical findings were recorded.

Laboratory and Imaging Assessment

All subjects underwent complete blood count, fasting and post-prandial blood sugar, HbA1c, renal function tests, liver function tests, prothrombin time/INR, FT3, FT4, TSH, and ultrasound abdomen. Other investigations were performed when clinically indicated.

Thyroid Hormone Estimation

FT3, FT4, and TSH were measured by chemiluminescence assay. Approximately 2 ml of blood was collected, centrifuged, and serum was processed using the COBAS 600 platform. The reference ranges used were FT3 2.3-4.2 pg/ml, FT4 0.89-1.76 ng/dl, and TSH 0.42-4.5 microIU/ml.

Operational Classification

Child-Pugh class A was defined by a score of 5-6, class B by 7-9, and class C by a score of 10 or more. CLD stage 1 corresponded to Child-Pugh class A, while CLD stage 2 included Child-Pugh classes B and C. Thyroid functional status was categorized as normal, hypothyroid biochemical pattern, or hyperthyroid

biochemical pattern according to FT3, FT4, and TSH values in relation to the stated reference ranges.

Statistical Analysis

Data were entered in Microsoft Excel 2007 and analyzed using SPSS version 22.0. Continuous variables were summarized using mean and standard deviation. Categorical variables were described using frequencies and percentages. Associations between categorical variables were tested using the chi-square test. A p-value <0.05 was considered statistically significant.

RESULTS

A total of 130 subjects with chronic liver disease were included. The mean age was 45.24±9.88 years, and the observed age range was 24-59 years. The largest age group was >50 years, comprising 47 (36.3%) subjects, followed by 41-50 years with 40 (30.8%) subjects. Males were predominant, accounting for 94 (72.3%) subjects, while females constituted 36 (27.7%). Duration of CLD was 6 months to 1 year in 51 (39.2%), 1-2 years in 26 (20.0%), more than 2 years in 21 (16.2%), and incidentally detected in 32 (24.6%) subjects. The commonest clinical features were abdominal distension in 75 (57.7%) and pedal edema in 72 (55.4%) subjects; icterus was present in 26 (20.0%), while 40 (30.8%) were asymptomatic at the time of assessment (Table 1, Figure 1).

Variable	Category	N (%)
Age group	≤30 years	14 (10.8)
Age group	31-40 years	29 (22.3)
Age group	41-50 years	40 (30.8)
Age group	>50 years	47 (36.3)
Age	Mean±SD, range	45.24±9.88 years, 24-59 years
Sex	Male	94 (72.3)
Sex	Female	36 (27.7)
Duration of CLD	6 months-1 year	51 (39.2)
Duration of CLD	1-2 years	26 (20.0)
Duration of CLD	>2 years	21 (16.2)
Duration of CLD	Incidentally detected	32 (24.6)
Clinical feature	Icterus	26 (20.0)
Clinical feature	Pedal edema	72 (55.4)
Clinical feature	Abdominal distension	75 (57.7)
Clinical feature	Asymptomatic	40 (30.8)

Table 1. Baseline Demographic and Clinical Profile of the Study Population (N=130)

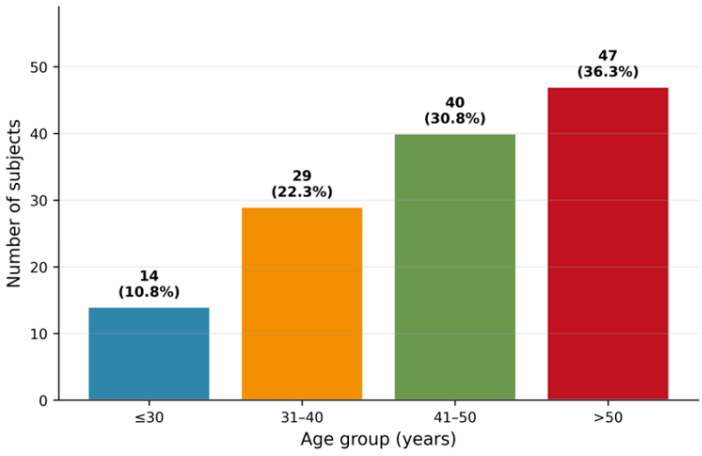

Figure 1. Age distribution of the study population

Bars show counts; percentages are calculated using N=130 as denominator.

Child-Pugh classification showed that 41 (31.5%) subjects were in class A, 56 (43.1%) in class B, and 33 (25.4%) in class C. Based on the study staging definition, 41 (31.5%) belonged to CLD stage 1 and 89 (68.5%) to CLD stage 2. Easily controlled ascites was seen

across the three classes but was most frequent in class B. Poorly controlled ascites was restricted to classes B and C, and advanced hepatic encephalopathy occurred only in class C. A total of 26 (20.0%) subjects did not have either ascites or hepatic encephalopathy recorded in this severity table (Table 2, Figure 2).

CLD Stage	Child-Pugh Class	Score	Subjects N (%)	Ascites Easily Controlled	Ascites Poorly Controlled	HE Minimal	HE Advanced
Stage 1	A	5-6	41 (31.5)	2 (1.5)	0	0	0
Stage 2	B	7-9	56 (43.1)	17 (13.1)	24 (18.5)	5 (3.9)	0
Stage 2	C	≥10	33 (25.4)	2 (1.5)	29 (22.3)	15 (11.5)	10 (7.7)

Table 2. Child-Pugh Class, CLD Stage, Ascites, and Hepatic Encephalopathy (N=130)

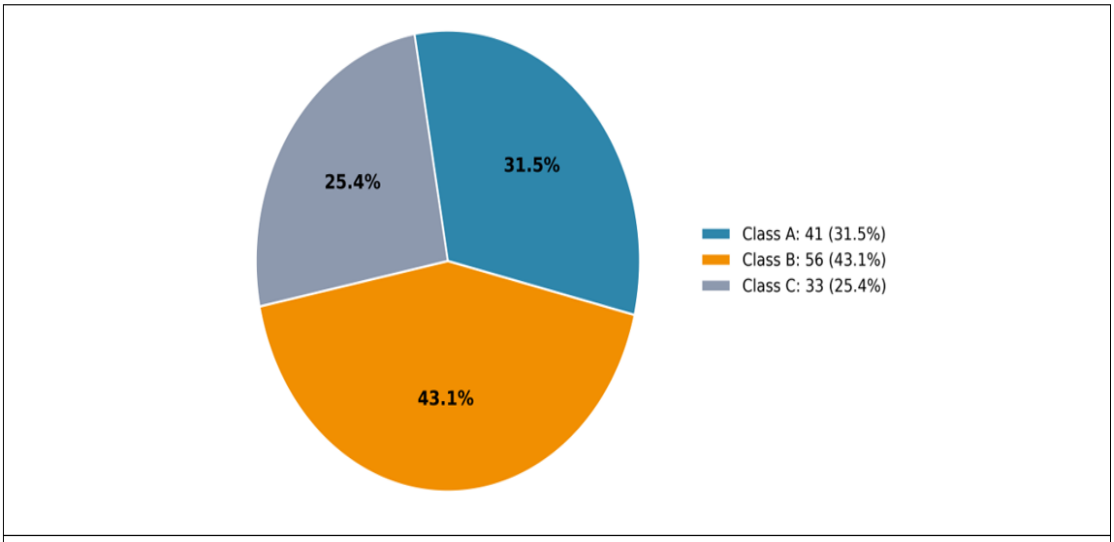

Figure 2. Distribution of Child-Pugh classes among subjects with chronic liver disease

Pie segments show percentage distribution of classes A, B, and C.

Thyroid function was normal in 85 (65.4%) subjects. A hypothyroid biochemical pattern was present in 39 (30.0%) subjects and a hyperthyroid biochemical pattern in 6 (4.6%). Although all subjects were clinically euthyroid, 45 (34.6%) had biochemical thyroid dysfunction. Hypothyroid-pattern dysfunction increased with liver disease severity: 21/39 (53.8%) hypothyroid-pattern subjects were in Child-Pugh class C, and 36/39 (92.3%) were in CLD stage 2. The association between thyroid functional status and Child-Pugh class was statistically significant (chi-square test, $p<0.001$), as was the association with CLD stage (chi-square test, $p<0.001$) (Table 3, Figures 3 and 4).

Functional Thyroid Status	Total N (%)	Class A N (%)	Class B N (%)	Class C N (%)	Stage 1 N (%)	Stage 2 N (%)
Hyperthyroid pattern	6 (4.6)	4 (66.7)	2 (33.3)	0	4 (66.7)	2 (33.3)
Hypothyroid pattern	39 (30.0)	3 (7.7)	15 (38.5)	21 (53.8)	3 (7.7)	36 (92.3)
Normal	85 (65.4)	34 (40.0)	39 (45.9)	12 (14.1)	34 (40.0)	51 (60.0)

Table 3. Functional Thyroid Status According To Child-Pugh Class and CLD Stage (N=130)

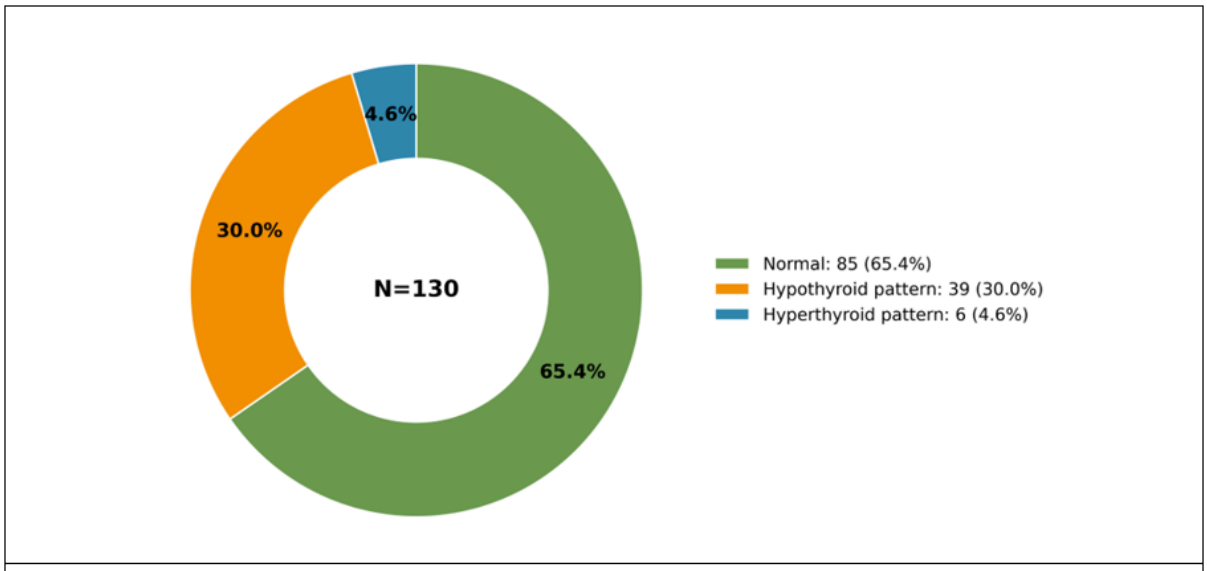

Figure 3. Functional thyroid status distribution in the study population

Donut chart shows normal thyroid function, hypothyroid biochemical pattern, and hyperthyroid biochemical pattern

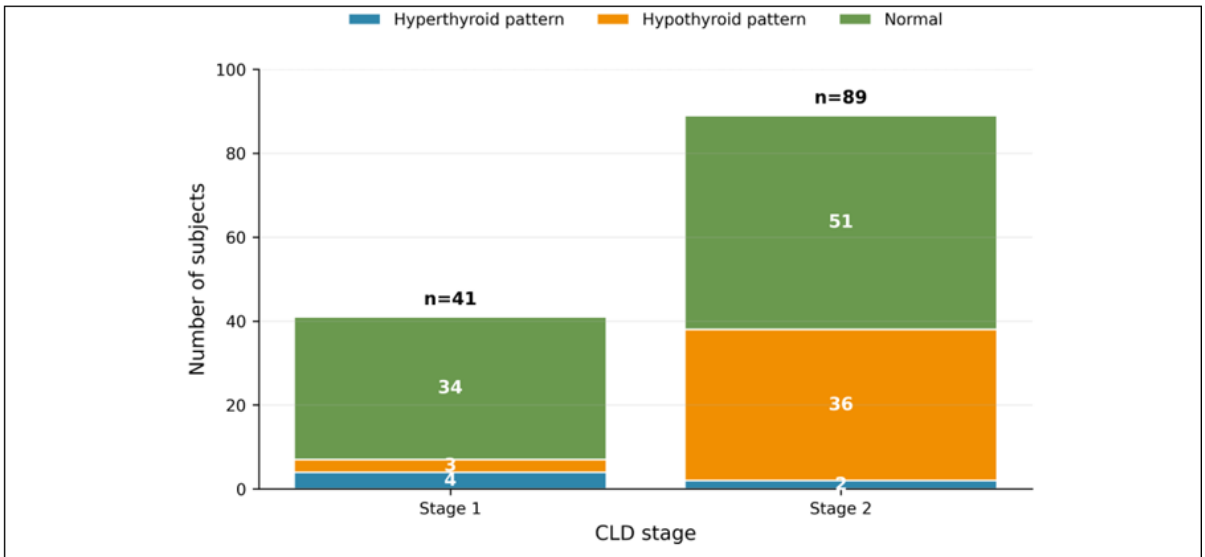

Figure 4. Functional thyroid status across CLD stages

Stacked bars show counts within each CLD stage; stage 1 corresponds to Child-Pugh class A and stage 2 corresponds to classes B and C.

FT3 showed the clearest severity-related pattern. Low FT3 was documented in 35 (26.9%) subjects, of whom 19 (54.28%) were in Child-Pugh class C; only 3 (8.6%) were in class A. The association of FT3 category with Child-Pugh class and CLD stage was statistically significant (chi-square test, $p<0.001$ for both comparisons). Low FT4 was documented in 10 (7.7%) subjects, with 8/10 (80.0%) in class C. FT4 category differed significantly across Child-Pugh class (chi-square test, $p=0.001$), although the CLD-stage comparison for FT4 categories did not reach statistical significance in the analysis ($p=0.141$). TSH was normal in 108 (83.1%) subjects, high in 21 (16.2%), and low in 1 (0.8%); high TSH was most frequent in class C, where 11/21 (52.4%) high-TSH subjects were located. TSH category was significantly associated with Child-Pugh class (chi-square test, $p=0.014$) and CLD stage (chi-square test, $p=0.045$) (Table 4, Figure 5).

Parameter	Category	Class A N (%)	Class B N (%)	Class C N (%)	P-Value By Child-Pugh Class	P-Value By CLD Stage
FT3	Low (n=35)	3 (8.6)	13 (37.14)	19 (54.28)	<0.001	<0.001
FT3	Normal (n=93)	36 (38.7)	43 (46.2)	14 (15.0)		
FT3	High (n=2)	2 (100.0)	0	0		
FT4	Low (n=10)	1 (10.0)	1 (10.0)	8 (80.0)	0.001	0.141
FT4	Normal (n=117)	38 (32.5)	54 (46.2)	25 (21.4)		
FT4	High (n=3)	2 (66.7)	1 (33.3)	0		
TSH	Low (n=1)	0	1 (100.0)	0	0.014	0.045
TSH	Normal (n=108)	39 (36.1)	47 (43.5)	22 (20.4)		
TSH	High (n=21)	2 (9.5)	8 (38.1)	11 (52.4)		

Table 4. FT3, FT4, and TSH Categories by Child-Pugh Class and CLD Stage

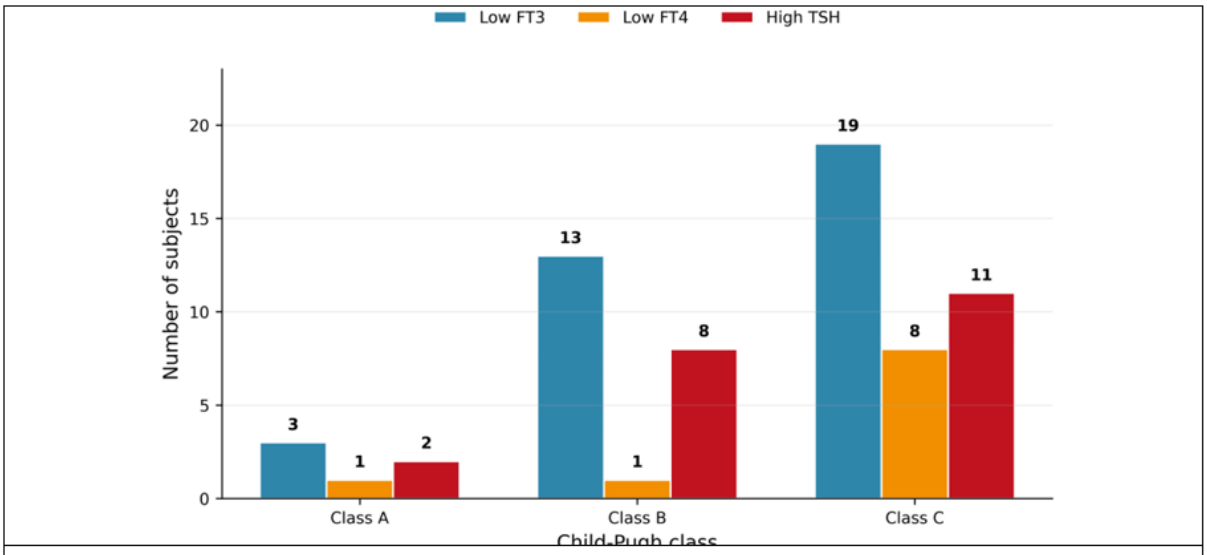

Figure 5. Selected biochemical thyroid abnormalities by Child-Pugh class

Grouped bars show the number of subjects with low FT3, low FT4, and high TSH across Child-Pugh classes.

DISCUSSION

This prospective observational study found that more than one-third of hospitalized subjects with chronic liver disease had biochemical thyroid dysfunction, even though the cohort was clinically euthyroid. The dominant pattern was not overt hyperthyroidism. It was a hypothyroid biochemical pattern, with low FT3 emerging as the most severity-sensitive abnormality. The finding is clinically credible. The liver is central to thyroid hormone handling, and advanced liver dysfunction reduces synthetic capacity, disturbs binding proteins, modifies deiodinase activity, and shifts peripheral conversion away from normal T3 generation [4,5]. What appears as a thyroid report, therefore, may partly be a biochemical mirror of hepatic reserve.

The demographic profile also fits the usual hospital picture of CLD in India. The cohort was predominantly male, with a male-to-female ratio of approximately 2.6:1, and most subjects were in the fifth and sixth decades. Kharb et al. and Papineni et al. similarly reported male-predominant CLD cohorts while examining endocrine or thyroid hormone abnormalities in liver disease [9,10]. This pattern is not only biological; it is social. Alcohol exposure, late help-seeking, occupational migration, irregular follow-up, and delayed recognition of metabolic and viral liver injury all shape who reaches a medicine ward with advanced disease.

In the present study, 68.5% of subjects were in CLD stage 2, combining Child-Pugh classes B and C. Abdominal distension and pedal edema were the commonest clinical features, and severe signs such as poorly controlled ascites and advanced hepatic encephalopathy were concentrated in higher Child-Pugh classes. This matters because thyroid abnormalities were not scattered randomly across the cohort. Hypothyroid-pattern dysfunction was far more frequent in advanced CLD: 92.3% of subjects with this pattern were in stage 2, and more

than half were in Child-Pugh class C. The statistical association was strong ($p<0.001$).

Punekar et al. reported that low FT3, low FT4, and raised TSH were significantly more common in cirrhosis than in controls, with low FT3 showing a meaningful relationship with Child-Pugh and MELD-based severity [11]. Patira et al. also described an increasing prevalence of hypothyroidism with worsening cirrhosis and emphasized the correlation between thyroid function tests and liver dysfunction severity [12]. The current findings sit close to that pattern. FT3 was low in 35 subjects, and 54.28% of those with low FT3 were in Child-Pugh class C. The association of FT3 category with both Child-Pugh class and CLD stage was significant ($p<0.001$). The low-FT3 signal is probably not a simple diagnosis of primary thyroid failure; rather, in many patients it may represent non-thyroidal illness physiology superimposed on hepatic failure.

The behavior of FT4 was more restrained. Only 10 subjects had low FT4, but 80.0% of them were in Child-Pugh class C. FT4 category differed significantly across Child-Pugh classes ($p=0.001$), while the broader stage-based comparison was not significant ($p=0.141$). This divergence is not surprising. Combining classes B and C into a single stage improves simplicity, but it may flatten differences that are biologically visible only at the more advanced end of the Child-Pugh spectrum. In other words, class C may carry the endocrine-metabolic signal more sharply than stage 2 as a combined category.

TSH was high in 21 subjects and low in 1 subject. High TSH clustered toward class C, and TSH category was significantly associated with Child-Pugh class ($p=0.014$) and CLD stage ($p=0.045$). Chaudhary et al. found thyroid function test abnormalities in 39.1% of cirrhotic patients, with hypothyroidism more common than hyperthyroidism, while other regional studies have repeatedly reported low T3 or hypothyroid-pattern dysfunction in advanced liver disease [13]. Mansour-Ghanaei et al. observed that serum T3 declined as liver damage became more severe in hepatitis B and C-related cirrhosis, supporting the view that declining T3 may act as a severity-linked biochemical marker [14].

One practical implication is screening. CLD and hypothyroid states share tiredness, edema, constipation, weight change, and slowed mentation. In a busy ward, those symptoms can easily be absorbed into the liver diagnosis. The present findings suggest that this assumption can miss biochemical thyroid dysfunction. Still, screening should not be followed by reflex treatment in every abnormal result. Low FT3 in advanced CLD may reflect illness physiology rather than primary thyroid disease. The more defensible approach is contextual interpretation: assess FT3, FT4, and TSH together, relate them to Child-Pugh severity, look for persistent TSH elevation when the patient is clinically stable, and avoid treating a single isolated abnormality without endocrine reasoning.

There are limitations. This was a single-center hospital-based study, so selection bias is likely. The sample represents admitted CLD patients and may over-represent advanced disease compared with community or outpatient cohorts. Follow-up thyroid function after stabilization was not performed, so reversibility could not be assessed. Total T3 and total T4 were not measured, and reverse T3, thyroid antibodies, thyroid ultrasound, and thyroid-binding globulin were not included. Etiological subgroup analysis of CLD was also not available in the source record. These gaps limit causal interpretation. The study can show association, not prove that liver severity directly causes thyroid dysfunction in each individual patient.

Even with these limitations, the clinical message is consistent. In chronic liver disease, thyroid function testing is not merely an endocrine add-on. It may help identify a biochemical pattern that travels with severity, especially through FT3. In Indian inpatient settings, where CLD often presents late and symptoms overlap, adding thyroid profiling to severity assessment can support a more complete view of the patient.

CONCLUSION

Biochemical thyroid dysfunction was observed in 34.6% of subjects with chronic liver disease, despite clinical euthyroidism. Hypothyroid-pattern abnormalities were more common than hyperthyroid-pattern abnormalities and were strongly associated with advancing Child-Pugh class and CLD stage. Low FT3 showed the clearest inverse relationship with severity of liver disease, while FT4 and TSH abnormalities also clustered toward more advanced Child-Pugh classes. Routine interpretation of FT3, FT4, and TSH alongside Child-Pugh severity may help clinicians recognize endocrine-metabolic disruption in hospitalized CLD patients, particularly when symptoms of liver disease and hypothyroidism overlap.

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