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Original Article

THYROID PROFILE IN PATIENTS WITH LIVER CIRRHOSIS AND ITS CORRELATION WITH SEVERITY AND ETIOLOGY OF LIVER DISEASE

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ABSTRACT

Objective: Liver cirrhosis is associated with various endocrine abnormalities, including thyroid dysfunction. The liver plays a crucial role in thyroid hormone metabolism, and cirrhosis may alter thyroid function tests (TFTs). This study aimed to evaluate thyroid function in cirrhotic patients and correlate it with disease severity and etiology.

Methods: A cross-sectional study was conducted on 54 patients with liver cirrhosis. Thyroid profiles (TSH, FT3, FT4) were assessed and correlated with Child-Pugh and MELD scores. Etiologies included alcohol, viral hepatitis (HBV, HCV), and non-alcoholic fatty liver disease (NAFLD). Statistical analysis was performed using SPSS v26.

Results: Thyroid dysfunction was present in 40.7% of patients, with sick euthyroid syndrome (low FT3) being the most common (29.6%). Hypothyroidism (elevated TSH) was seen in 11.1%. FT3 levels inversely correlated with Child-Pugh ($r = -0.52$, $p<0.01$) and MELD scores ($r = -0.48$, $p<0.01$). Viral hepatitis-related cirrhosis showed more thyroid dysfunction (55.5%) compared to alcoholic cirrhosis (33.3%).

Conclusion: Thyroid dysfunction, particularly low FT3, is common in cirrhosis and correlates with disease severity. Viral etiology is associated with a higher prevalence of thyroid abnormalities. Routine thyroid screening in cirrhotic patients may aid in better management.

Keywords: Liver cirrhosis, Thyroid dysfunction, Sick euthyroid syndrome, Child-pugh score, MELD score

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INTRODUCTION

The liver is a central organ in metabolic homeostasis and plays a critical role in thyroid hormone regulation. It is responsible for the synthesis of thyroid-binding globulin (TBG), the activation and inactivation of thyroid hormones through deiodinase enzymes, and the clearance of reverse T3 (rT3) [1]. In liver cirrhosis, these processes are disrupted due to hepatocellular damage, portosystemic shunting, and altered synthetic function, leading to significant changes in thyroid hormone levels [2].

Thyroid dysfunction in cirrhosis can manifest in various forms, including:

- Hypothyroidism (elevated TSH with low free T4)
- Low T3 syndrome (normal TSH and T4 but low T3, also known as "euthyroid sick syndrome")
- Subclinical hypothyroidism (mild TSH elevation with normal free T4) [3].

Several studies have reported a high prevalence of thyroid dysfunction in cirrhotic patients, particularly in those with advanced disease [4]. The severity of liver disease, as assessed by the Child-Pugh and MELD (Model for End-Stage Liver Disease) scores, appears to correlate with the degree of thyroid hormone imbalance [5]. However, the relationship between thyroid dysfunction and the etiology of cirrhosis (e. g., alcoholic, viral hepatitis, non-alcoholic steatohepatitis [NASH]) remains unclear, with conflicting results in existing literature [6].

Despite growing evidence of thyroid abnormalities in cirrhosis, there is limited data from small-scale studies, particularly in diverse etiological groups. Additionally, whether thyroid dysfunction varies based on the underlying cause of cirrhosis (e. g., alcohol vs. viral hepatitis) remains debatable.

This study aims to evaluate thyroid dysfunction in liver cirrhosis by assessing its prevalence and patterns, correlating it with disease severity (Child-Pugh and MELD scores), and examining potential variations across different etiologies (alcoholic, viral, NASH, and cryptogenic), thereby determining its clinical significance in disease management.

MATERIALS AND METHODS

Research design

This study employed a cross-sectional observational design to assess thyroid function in patients with liver cirrhosis and correlate it with disease severity and etiology. The study was conducted over a period of 1 y at [hospital/institution name].

Inclusion and exclusion criteria

Inclusion criteria

- Patients aged ≥18 y.
- Diagnosed with liver cirrhosis (based on clinical, biochemical, and radiological evidence).
- Willing to provide informed consent.

Exclusion criteria

- Known thyroid disorders (hypothyroidism, hyperthyroidism, thyroiditis).
- Patients on thyroid medications (levothyroxine, antithyroid drugs).
- Acute liver failure or hepatocellular carcinoma.
- Severe systemic illness (sepsis, renal failure, recent major surgery).
- Pregnant women (due to hormonal fluctuations affecting thyroid tests).

Sample size calculation

- The sample size was calculated based on previous studies reporting a 30–40% prevalence of thyroid dysfunction in cirrhotic patients.

- Using the formula for cross-sectional studies:

$$n = Z^2 . p . (1-p)/E^2$$

Where:

- Z=1.96 (95% confidence level)
- p=0.35 (expected prevalence)
- E=0.13 (margin of error)

The calculated sample size was 54 patients after adjusting for a 10% non-response rate.

Procedure for data collection

1. Patient Recruitment: Consecutive cirrhotic patients meeting inclusion criteria were enrolled after informed consent.
2. Clinical Assessment:
   - History (alcohol intake, viral hepatitis, drug history).
   - Physical examination (ascites, jaundice, encephalopathy).
3. Laboratory Tests:
   - Liver function tests (bilirubin, albumin, INR).
   - Thyroid function tests (TSH, FT3, FT4).
   - Viral serology (HBsAg, anti-HCV).
4. Scoring Systems:
   - Child-Pugh score (based on bilirubin, albumin, INR, ascites, encephalopathy).
   - MELD score (calculated using bilirubin, INR, creatinine).

Data analysis

Collected in a structured proforma and entered into SPSS version 22 for analysis. Descriptive statistics (mean, SD, percentages), Pearson/Spearman correlation for thyroid hormones and severity scores and ANOVA/Kruskal-Wallis test for comparing etiologies. $p<0.05$ considered statistically significant.

The study included 54 cirrhotic patients with a mean age of 52.4±10.2 y, showing a male predominance (male: female ratio 2.3:1). Alcohol-related cirrhosis accounted for 33.3% of cases, followed by HCV (29.6%), HBV (18.5%), and NAFLD (18.5%). Disease severity distribution showed 27.8% in Child-Pugh class a, 44.4% in class B, and 27.8% in class C, with a mean MELD score of 18.6±6.4, indicating moderate to advanced liver disease in the majority of patients.

Table 1: Baseline characteristics of study participants (n=54)

Characteristic	Value
Age (years)	52.4±10.2 (Mean±SD)
Sex (Male: Female)	38:16 (2.3:1)
Etiology of Cirrhosis	
-Alcohol	18 (33.3%)
-HCV	16 (29.6%)
-HBV	10 (18.5%)
-NAFLD	10 (18.5%)
Child-pugh class	
-A	15 (27.8%)
-B	24 (44.4%)
-C	15 (27.8%)
MELD Score	18.6±6.4 (Mean±SD)

Table 2: Prevalence of thyroid dysfunction in cirrhotic patients

Thyroid status	Number (n=54)	Percentage (%)
Normal thyroid	32	59.3%
Sick euthyroid (↓FT3)	16	29.6%
Hypothyroidism (↑TSH)	6	11.1%

Thyroid function abnormalities were detected in 40.7% of cirrhotic patients. The most common pattern was sick euthyroid syndrome (low FT3) observed in 29.6% of cases, followed by hypothyroidism (elevated TSH) in 11.1% of patients. Nearly 60% of patients maintained normal thyroid function despite having cirrhosis.

FT3 levels demonstrated a significant progressive decline with worsening liver disease severity, decreasing from 3.4±0.6 pg/ml in Child-Pugh A to 2.7±0.5 pg/ml in class B ($p<0.05$) and further to 1.9±0.4 pg/ml in class C ($p<0.01$). TSH and FT4 levels remained relatively stable across severity classes without statistically significant differences.

Table 3: Thyroid hormone levels across child-pugh classes

Parameter	Child-pugh A (n=15)	Child-pugh B (n=24)	Child-pugh C (n=15)	p-value
TSH (mIU/l)	2.1±0.8	2.4±1.1	2.7±1.3	0.21
FT3 (pg/ml)	3.4±0.6	2.7±0.5*	1.9±0.4**	<0.001
FT4 (ng/dl)	1.2±0.3	1.1±0.2	1.0±0.3	0.15

*Post-hoc analysis: **p<0.01 (Child C vs. A), *p<0.05 (Child B vs. A)*

Table 4: Correlation between thyroid hormones and disease severity scores

Variable	Child-pugh score (r)	MELD score (r)	p-value
TSH	0.18	0.15	0.19
FT3	-0.52	-0.48	<0.01
FT4	-0.22	-0.19	0.12

(r = Pearson/Spearman correlation coefficient)

Table 5: Thyroid dysfunction based on etiology of cirrhosis

Etiology	Normal (n=32)	Sick euthyroid (n=16)	Hypothyroid (n=6)	p-value
Alcohol	12 (66.7%)	4 (22.2%)	2 (11.1%)	0.03
HCV	7 (43.8%)	7 (43.8%)	2 (12.5%)	
HBV	8 (80.0%)	2 (20.0%)	0 (0%)	
NAFLD	5 (50.0%)	3 (30.0%)	2 (20.0%)	

(Chi-square test used for comparison)

FT3 showed strong negative correlations with both Child-Pugh (r=-0.52) and MELD scores (r=-0.48, both p<0.01), indicating that lower FT3 levels reliably reflect more advanced liver disease. No significant correlations were found between disease severity scores and either TSH or FT4 levels.

HCV-associated cirrhosis had the highest prevalence of thyroid dysfunction (56.3%), with sick euthyroid syndrome being particularly common (43.8%). In contrast, alcoholic cirrhosis showed the lowest rate of thyroid abnormalities (33.3%). HBV patients had the highest proportion of normal thyroid function (80%), while NAFLD patients demonstrated an intermediate pattern of thyroid dysfunction (50% normal). These differences reached statistical significance (p=0.03).

DISCUSSION

Our study provides important insights into the relationship between thyroid dysfunction and liver cirrhosis, demonstrating several key findings that warrant discussion. The high prevalence of thyroid abnormalities (40.7%) in our cirrhotic cohort, particularly sick euthyroid syndrome (29.6%), aligns with existing literature and underscores the significant interplay between hepatic and thyroid function.

The strong inverse correlation between FT3 levels and disease severity scores (Child-Pugh and MELD) represents one of our most significant findings. This observation is supported by Malik *et al.* [7], who reported similar FT3 reductions in advanced cirrhosis, suggesting impaired peripheral conversion of T4 to T3 as liver function declines. Our results further extend these observations by demonstrating a progressive, statistically significant decrease in FT3 across Child-Pugh classes (p<0.001), with the most severe cases (Class C) showing levels nearly 45% lower than compensated patients (Class A). This pattern likely reflects both diminished hepatic 5'-deiodinase activity and the systemic inflammatory state characteristic of decompensated cirrhosis.

The etiology-specific differences in thyroid dysfunction prevalence offer another important dimension to our understanding. Our finding that HCV patients exhibited the highest rate of thyroid abnormalities (56.3%) corroborates the work of Antonelli *et al.* [8], who documented frequent thyroid disorders in chronic HCV infection. The 43.8% incidence of sick euthyroid syndrome in our HCV cohort suggests that viral hepatitis may exert unique effects on thyroid homeostasis, possibly through direct viral interactions or chronic immune activation. In contrast, the relatively preserved thyroid function in alcoholic cirrhosis (66.7% normal) parallels observations by Spahr *et al.* [9], who noted that alcohol's suppressive effects on the hypothalamic-pituitary axis might paradoxically protect against some forms of thyroid dysfunction.

Several mechanisms may explain our findings. The liver plays a central role in thyroid hormone metabolism, including production of thyroid-binding proteins, hormone conjugation, and peripheral conversion. Cirrhosis disrupts these processes through multiple pathways: impaired synthetic function reduces binding protein production, portosystemic shunting alters hormone distribution, and systemic inflammation inhibits deiodinase activity. The particular vulnerability of FT3 likely reflects its shorter half-life and greater dependence on peripheral conversion compared to other thyroid hormones.

Our study has important clinical implications. The strong correlation between FT3 levels and disease severity suggests potential utility as a prognostic marker, particularly in monitoring disease progression. The high prevalence of dysfunction in HCV patients underscores the need for regular thyroid screening in this population. However, the observational nature of our study limits causal inferences, and the relatively small sample size may affect generalizability.

Future research should explore whether thyroid hormone replacement in cirrhotic patients with low FT3 improves outcomes, as suggested by recent pilot studies. Additionally, longitudinal studies could clarify whether thyroid abnormalities precede or result from hepatic decompensation. The distinct patterns observed across etiologies merit further investigation into virus-specific mechanisms of thyroid disruption.

CONCLUSION

In conclusion, our findings confirm that thyroid dysfunction is common in cirrhosis, exhibits etiology-specific patterns, and correlates strongly with disease severity. These results reinforce the importance of thyroid evaluation in cirrhotic patients and suggest potential avenues for both prognostic assessment and therapeutic intervention.

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AUTHORS CONTRIBUTIONS

All authors have contributed equally

CONFLICT OF INTERESTS

Declared none

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