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Thyroid Hormone Levels in Cirrhosis Patients and their Association with Liver Disease Severity

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Abstract

Background: Cirrhosis of the liver, which has a number of etiologies and progresses in a devastating manner, causes significant liver dysfunction. The intricate connection between liver illness and thyroid function has come to light recently in study. The purpose of this study was to determine whether the severity of liver disease in cirrhosis patients was correlated with thyroid hormone levels (free triiodothyronine [FT3], free thyroxine [FT4], and thyroid-stimulating hormone [TSH]).

Methods: Over the course of 18 months (from February 2021 to August 2022) 97 cirrhosis patients were prospectively enrolled. The severity of the liver disease (as measured by the Child-Pugh and MELD scores) and the etiology of cirrhosis were also recorded. Standard assays were used to assess the serum concentrations of FT3, FT4, and TSH. Correlations, multivariate regression, and stratification by Child-Pugh class were all included in the statistical study.

Results: Significant negative relationships between FT3 and FT4 levels and Child-Pugh scores showed that levels decreased as liver disease severity increased (p 0.001). Child-Pugh scores and TSH levels showed a slight positive connection (p = 0.002). The Child-Pugh score's independent predictive significance for the FT3 and FT4 levels was validated by multivariate regression. Further stratification by Child-Pugh class indicated progressively altered thyroid hormones with deteriorating liver disease.

Conclusion: This study clearly links thyroid hormone levels to the severity of liver disease in individuals with cirrhosis. In cirrhosis, particularly in advanced stages, monitoring thyroid function is essential for complete patient care and may help to achieve better clinical results. To clarify underlying causes and treatment implications, more study is required.

Keywords: Thyroid hormones, Cirrhosis, Liver disease, Liver function, Thyroid function

Introduction

The complex and crippling illness of liver cirrhosis is a serious global health issue. Cirrhosis, which is characterized by the progressive replacement of healthy liver tissue with fibrosis and scarring, is caused by a variety of underlying etiologies, such as persistent alcohol misuse, viral hepatitis, non-alcoholic fatty liver disease (NAFLD), and autoimmune illnesses. It is a chronic condition that worsens with time, places a significant strain on healthcare systems, and has far-reaching effects on those who are affected [1-5].

The liver is a vital organ that functions as a metabolic engine and is essential for detoxification, protein synthesis, and the control of several metabolic pathways. Cirrhosis severely impairs the liver's ability to function, which triggers a chain reaction of systemic problems. From hepatic encephalopathy and ascites to coagulopathy and hepatocellular cancer, these problems can present in a variety of ways.

The complex interrelationship between the liver and other organ systems, such as the endocrine system, has recently come to the attention of researchers. Hormones produced by the thyroid gland, a vital organ of the endocrine system, have an impact on growth, metabolism, and overall physiological balance. Triiodothyronine (T3), thyroxine (T4), and thyroid-stimulating hormone (TSH) are the three main hormones that the thyroid gland specifically produces [6-10].

Thyroid hormones are essential for controlling thermoregulation, basal metabolic rate, and energy expenditure. Additionally, they have an impact on the central nervous system, the gastrointestinal tract, and the cardiovascular system. However, there is still research being done and clinical interest in their connection to liver disease, particularly cirrhosis.

The relationship between the thyroid gland and the liver is mediated by a number of processes. The liver is where thyroid hormones are first and mainly made and converted. The liver transforms a sizeable part of T4, the precursor hormone, into T3, which is a more physiologically active version. Therefore, any liver malfunction may possibly interfere with the production and metabolism of thyroid hormones.

Furthermore, liver disease, particularly when it is advanced, might change the binding proteins that carry thyroid hormones in the blood. The levels of free T3 (FT3) and free T4 (FT4), the physiologically active forms of thyroid hormones, may fluctuate as a result. Alterations in thyroid hormone levels can, in turn, have a significant impact on how proteins, lipids, and carbohydrates are metabolized, potentially escalating the metabolic issues seen in cirrhosis. Additionally, the liver is crucial for the elimination and metabolism of neurotransmitters like T3 and T4 as well as other hormones. Hormonal abnormalities may result from the liver's cirrhosis-related metabolic dysfunction, further complicating the clinical picture [11-15].

Although thyroid function and liver disease interact in a fascinating way, our knowledge of this interaction is still lacking. While some research have claimed that cirrhosis can cause hypothyroidism because of reduced thyroid hormone synthesis and clearance, other

investigations have suggested that cirrhotic patients experience a complex pattern of thyroid dysfunction.

In order to better understand the complex relationships between thyroid hormone levels, particularly FT3, FT4, and TSH, and the severity of liver disease in cirrhosis patients, this study work will focus on the complex dynamics between these three thyroid hormones. We conducted a comprehensive study comprising 97 patients with liver cirrhosis over an 18-month period, from February 2021 to August 2022. Our study looked at how variations in thyroid hormone levels may be related to the course of liver disease in order to clarify the precise nature of the association between thyroid function and cirrhosis. We did this in an effort to add to the corpus of knowledge regarding the fascinating nexus between hepatology and endocrinology.

Materials and Methods

Research Design: From February 2021 to August 2022, an 18-month prospective observational research was conducted. The goal of the study was to determine whether there was a connection between the levels of thyroid hormones (FT3, FT4, and TSH) and the severity of liver disease in cirrhotic patients.

Study Subjects: This study comprised 97 patients with liver cirrhosis who had received a diagnosis. Patients were gathered from a tertiary care hospital's hepatology division. Prior to their involvement in the study, all individuals gave their informed consent. The Institutional Review Board (IRB) of the hospital granted ethical approval.

1. Adults who are at least 18 years old are required to be included.
2. A cirrhosis diagnosis that has been verified using histological, radiological, biochemical, and clinical criteria.
3. Accessibility to entire medical data, including thyroid hormone profiles and liver function testing.

Patients with a history of thyroid illness or thyroid hormone replacement medication are excluded from consideration.

1. Patients who have already undergone radiation treatment or thyroid surgery.
2. People with concurrent endocrine conditions that impact thyroid function.
3. Patients with serious comorbid conditions such as chronic or acute infections, cancer, or other serious illnesses.

Data collection: Clinical and demographic information, such as age, gender, the cause of cirrhosis, and comorbidities, were taken from electronic medical records. The Child-Pugh score and the Model for End-Stage Liver Disease (MELD) score were used to determine the severity of liver disease. Three groups of Child-Pugh scores were determined: A, B, and C on the Child-Pugh scale denote mild, moderate, and severe liver disease, respectively.

Thyroid Hormone Evaluation: Following an overnight fast, blood samples were taken from each participant. Standard laboratory assays were used to assess the levels of FT3, FT4, and TSH in the serum. Certified clinical laboratory staff used automated analyzers to perform

thyroid function testing. The standard values from the laboratory were used to construct reference ranges for thyroid hormones.

Statistical Analysis: Version 25 of the Statistical Package for the Social Sciences (SPSS) software was used for the statistical analysis. Demographic and clinical data were summarized using descriptive statistics. The relevant means, standard deviations (SD), or medians with interquartile ranges (IQR) were used to express continuous variables. Frequencies and percentages were used to present categorical variables.

Suitable statistical tests, such as the Pearson's correlation coefficient for normally distributed data and Spearman's rank correlation for non-normally distributed data, were used to evaluate the correlations between thyroid hormone levels and the severity of liver disease. In order to find independent predictors of thyroid hormone levels in cirrhosis patients, multivariate regression analysis was used, with potential confounders such age, gender, cirrhosis etiology, and comorbidities being taken into account.

To highlight major findings and data trends, tables and figures were created. Statistical significance was defined as a p-value 0.05.

Quality Control: To guarantee the accuracy and dependability of data collection and laboratory analysis, quality control procedures were put in place throughout the project. All laboratory tests were carried out in accordance with established procedures by trained staff. Laboratory apparatus was routinely calibrated and maintained in accordance with manufacturer instructions.

Results

The demographic details of the study population are shown in Table 1. The participants' average age was 57.4 years, and 72% of them were men. Alcohol consumption was the most frequent cause of cirrhosis (46.4%), then viral hepatitis (28.9%), non-alcoholic fatty liver disease (NAFLD, 16.5%), and other causes (8.2%). The distribution of thyroid hormone levels (FT3, FT4, and TSH) in patients with cirrhosis is shown in Table 2 by Child-Pugh class. Notably, the Child-Pugh score shows a tendency for declining FT3 and FT4 values with increasing severity of liver disease. On the other side, a slight rise in TSH levels is associated with deteriorating liver function.

The Child-Pugh score, a metric for the severity of liver disease, and thyroid hormone levels (FT3, FT4, and TSH) are shown to be correlated in Table 3. As liver disease progresses, thyroid hormone levels tend to decline, as seen by the substantial negative association between FT3 and FT4 levels and the Child-Pugh score. The Child-Pugh score, on the other hand, shows a positive connection with TSH levels.

The findings of multivariate regression analysis, which examined thyroid hormone level predictors in cirrhosis patients while controlling for potential confounders, are shown in Table 4. In patients with cirrhosis, the Child-Pugh score continues to be a reliable predictor of FT3 and FT4 levels, indicating its link to changes in thyroid hormone levels.

Our research yields numerous important conclusions:

1. Alcohol use disorders accounted for the majority of the cirrhosis patients in our study, indicating a common etiological component in liver disease.
2. The Child-Pugh score, which assesses the severity of liver disease, revealed an inverse relationship between thyroid hormone levels (FT3 and FT4) and liver disease. This shows that thyroid hormone levels tend to decline as liver disease worsens.
3. TSH levels showed a little positive connection with the Child-Pugh score, suggesting that TSH levels tend to rise as liver disease develops.
4. Multivariate regression analysis supported the Child-Pugh score's continued independence as a predictor of FT3 and FT4 levels, highlighting the importance of the score in cirrhosis patients' thyroid hormone changes.

Table 1: Demographic Characteristics of Study Population

Characteristic Total (n=97)	Mean ± SD (or Median, IQR)
Age (years)	57.4 ± 8.9
Gender (Male/Female)	72/25
Etiology of Cirrhosis	
- Alcohol-related	45
- Viral Hepatitis	28
- NAFLD	16
- Other	8

Table 2: Distribution of Thyroid Hormone Levels by Child-Pugh Class

Child-Pugh Class	FT3 (pg/mL)	FT4 (ng/dL)	TSH (μIU/mL)
Class A (n=35)	3.21 ± 0.87	1.14 ± 0.23	2.85 ± 1.17
Class B (n=42)	2.98 ± 0.94	1.09 ± 0.22	3.12 ± 1.10
Class C (n=20)	2.65 ± 0.83	1.05 ± 0.19	3.45 ± 1.21

Table 3: Correlations between Thyroid Hormone Levels and Child-Pugh Score

Thyroid Hormone	Correlation with Child-Pugh Score	p-value
FT3	-0.471	<0.001
FT4	-0.395	<0.001
TSH	0.326	0.002

Table 4: Multivariate Regression Analysis for Predictors of Thyroid Hormone Levels

Predictor	FT3	FT4	TSH
Age (years)	-0.028	-0.014	0.043
Gender (Male)	-0.131	-0.047	-0.056
Etiology (Alcohol)	-0.079	-0.045	0.067
Child-Pugh Score	-0.232	-0.195	0.121

Discussion

In this study, we looked at the relationship between the levels of thyroid hormones (FT3, FT4, and TSH) and the severity of liver disease in patients with cirrhosis. The results of our study add to the corpus of information about the intricate interactions between the thyroid and liver in cirrhosis patients.

The Child-Pugh score's tendency toward worsening FT3 and FT4 levels along with the severity of the liver disease raises significant concerns about the underlying causes. Although the precise pathophysiological processes are still not fully understood, a number of potential explanations can be taken into consideration [15,16].

The liver's critical function in thyroid hormone metabolism is one probable explanation. Through the action of deiodinase enzymes, the liver is in charge of converting the prohormone thyroxine (T4) into its physiologically active form, triiodothyronine (T3). This metabolic conversion may become compromised when cirrhosis worsens and liver function declines, which would diminish the synthesis of T3. As a result, as our study showed, FT3 levels may be reduced in cirrhosis patients [17-19].

Impaired thyroid hormone synthesis and clearance in the liver may possibly be to blame for the observed drop in FT4 levels. Due to liver failure brought on by cirrhosis, the liver may not be able to manufacture enough transport proteins like thyroxine-binding globulin (TBG), which can change the levels of free thyroxine (FT4).

The fact that TSH levels and the Child-Pugh score correlated favorably was another interesting discovery. This finding raises the possibility that, as liver disease worsens, the anterior pituitary gland's production of TSH may rise in response to a fall in thyroid hormone levels. The purpose of this balancing mechanism is to encourage the thyroid to generate more hormones. However, in cirrhosis patients, reduced hepatic clearance of TSH, leading to higher blood TSH levels, may restrict the efficacy of this compensatory response.

The importance of the Child-Pugh score as an independent predictor of FT3 and FT4 levels was further supported by our multivariate regression analysis. This supports the idea that the degree of liver disease is a key factor in affecting thyroid hormone changes in cirrhosis patients. Regression analysis also took into account age, gender, and the cause of the cirrhosis, emphasizing the significance of these variables in interpreting thyroid hormone profiles in cirrhotic people [19,20].

These discoveries have therapeutic ramifications for how cirrhosis patients are treated. Patients with cirrhosis, especially those with severe liver disease, should have routine clinical examinations that include monitoring thyroid function, including FT3, FT4, and TSH values. Alterations in thyroid hormones may have an effect on the metabolic profile and contribute to the emergence of problems such muscular atrophy, osteoporosis, and changes in cardiovascular function. The quality of life for cirrhosis patients may be improved if thyroid dysfunction is detected early and treated appropriately.

Our findings encourage additional investigation into the underlying mechanisms tying liver illness and thyroid dysfunction together, in addition to clinical issues. Future research may examine the function of particular liver enzymes and transport proteins in the cirrhosis-related thyroid hormone metabolism. Researching the effects of various cirrhosis etiologies on thyroid function may shed light on the various patterns of thyroid hormone abnormalities observed in various patient populations.

Conclusion

Finally, our work illuminates the complex link between thyroid hormone levels and liver disease severity in cirrhosis patients. As liver disease progresses, FT3 and FT4 levels were inversely linked with the Child-Pugh score, indicating a thyroid hormone reduction. A slight positive connection between TSH levels and liver disease severity suggests a compensatory response to thyroid hormone changes. Multivariate regression study showed that the Child-Pugh score predicts FT3 and FT4 levels independently.

These findings emphasize the clinical importance of thyroid function monitoring in cirrhosis patients, especially those with advanced liver disease. Early thyroid dysfunction detection and treatment may enhance cirrhosis prognosis and quality of life. Thyroid hormone changes in liver illness require further study to understand their causes and clinical effects.

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