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Original research article

Thyroid Dysfunction in Patients with Liver Cirrhosis and its Association with the Severity of Liver Disease: A Cross-sectional Study

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Abstract

Introduction: The majority of cirrhotic liver patients exhibit thyroid problems. The leading global cause of illness and mortality is liver cirrhosis. The metabolism of thyroid hormones is critically impacted by cirrhosis, and via creating thyroid binding globulin, which increases thyroid hormone circulation. Thus, it is evident indicates the severity of liver disease is correlated with thyroid problems. We wanted to investigate how people with thyroid problems' levels of thyroid hormones changed.

Materials and methods In this cross-sectional study, 85 patients who were admitted to tertiary care hospital for symptoms of cirrhosis of liver were evaluated for their thyroid profile along with
other relevant investigations.

Results: There were 15 Female and 70 Male. In individuals with liver cirrhosis, the study found low mean levels of total T4 and free T3, which were substantially linked with Child Pugh grades of liver impairment. There was a correlation between free T3 level and Child Pugh score class. The TSH, total T3, and free T4 mean levels across the Child Pugh classes did not differ in a statistically significant way.

Conclusions: Patients with cirrhosis commonly have thyroid problems. The most frequent problem found was hypothyroidism. Patients with high TSH levels also have a greater rate of problems. Finding thyroid anomalies in cirrhotic patients calls for a healthy dose of caution.

Keywords: Child Pugh score, Cirrhosis, Thyroid hormones

Introduction

When a chronic liver injury results in portal hypertension and end-stage liver disease, regenerating nodules surrounded by fibrous bands emerge histologically as cirrhosis. Clinically, cirrhosis is classified as "compensated" or "decompensated." Having one or more of the following symptoms is referred to as decompensation: jaundice, ascites, hepatic encephalopathy, or bleeding varices. [1,2] Ascites is the initial symptom. None of the aforementioned conditions exist in the compensated cirrhotic patients. Several amino acids and proteins made by the body are metabolised in the liver. Thyroid hormone conjugation and excretion as well as thyroid binding globulin production are two such liver processes. [3,4] Thyroxine (T4) and triiodothyronine are produced by the thyroid gland (T3). In adults, these hormones are in charge of maintaining metabolic and thermogenic balance as well as cell differentiation. Studies show that the amount of T4 generated is significantly larger than the amount of T3. Both of these hormones are linked to plasma proteins such albumin, transthyretin, and thyroxine-binding globulin. 5 Tetraiodothyronine (T4) is converted to triiodothyronine (T3) in the peripheral nervous system by Type-1 deiodinase, which is located in the liver. [5,6] Type-1 deiodinase, which makes up 30 to 40 percent of the liver, is responsible for the liver's additional thyroidal T3 synthesis. Along with all other bodily cells, thyroxine and tri-iodothyronine affect hepatic function through controlling the basal metabolic rate of hepatocytes. By metabolising hormones, the liver also controls the levels of circulating T3 and T4, creating a controlled endocrine system. Type 1 and type 3 deiodinases are the two primary enzymes of the iodothyronine selenodeiodinase enzyme system that function in the liver and are in charge of the extra thyroidal synthesis of T3 and the inactivation of thyroid hormones, respectively. [7] The basal metabolic rate of all cells, including hepatocytes, is regulated by T3 and T4, which modifies hepatic function. Thus, any liver condition affects how thyroid hormone metabolism is regulated. Acute liver failure causes thyroid dysfunction comparable to sick euthyroid syndrome and is accompanied with elevated levels of circulating endotoxins and pro-inflammatory mediators, which is strikingly similar to the clinical presentations of sepsis. Thus, it can be demonstrated that thyroid dysfunction and the severity of liver disease are related. Those who have cirrhosis may experience thyroiditis, hypothyroidism, or hyperthyroidism. When the thyroid issue improves, these patients' abnormal liver function test results typically recover to normal levels. Both the thyroid and the liver are affected by a number of systemic disorders, liver disease can change the metabolism of thyroid hormones, and thyroid dysfunction can affect liver function. [8] Studies to date have shown that cirrhosis causes a decrease in the plasma concentration of total T3 and free T3, while total T4 tends to stay normal or be slightly low.

However, no study has conclusively demonstrated a relationship between the levels of FT4 and thyroid stimulating hormone and the severity of liver disease.

It has been noted that there aren't many Indian studies on the functional effects of thyroid hormone in cases of chronic liver disorders. The research of thyroid hormone function tests will shed light on the functional aspects of liver disorders and help treat chronic liver diseases by improving understanding of chronic liver disease and how it interacts with thyroid function. In light of the aforementioned ideas, we want to investigate the relationship between thyroid anomalies in liver cirrhosis patients and learn how they relate to the severity of the liver illness.

Objectives

To assess the association between the thyroid hormone levels and severity of liver disease, expressed in terms of child pugh score in tertiary care hospital.

Materials and Methods

This cross-sectional study was done in 85 patients in the outpatient department, in-patient department and intensive care unit of General Medicine Department of tertiary care hospital coming with symptoms of cirrhosis of liver and were evaluated for their thyroid profile during the study period mentioned. A detailed history and clinical examination was done for all such patients in order to confirm the diagnosis of liver cirrhosis and later sent for thyroid profiling.
Inclusion Criteria: Patients of liver cirrhosis with age more than 18 years, both male and female showing signs of hepatocellular dysfunction, portal hypertension evident clinically and radiologically were included for the study.

Exclusion Criteria: Patients with sepsis, cardiac failure, diabetes, renal failure, nephrotic syndrome, pregnancy and family history of thyroid diseases and patients on drugs known to affect thyroid functions were excluded from the study. Also, the other patients who are non-alcoholic but suffer from cirrhosis were excluded.

The diagnosis of cirrhosis was established by radiological means using ultrasound findings showing shrunken coarse echotexture of liver supported by clinical and biochemical parameters. The thyroid hormone levels were estimated using electro-chemiluminescence assay after collecting an early morning fasting blood sample within 24 hours of admission once the patient satisfied the inclusion criteria.

Child turgott Pugh scoring system

The Child Turgott Pugh scoring system is used to predict prognosis and mortality in patients with liver cirrhosis. Child Pugh score is calculated using serum bilirubin, serum albumin, prothrombin time, grade of hepatic encephalopathy and ascites [9-11]. Scores representing the increasing severity of liver dysfunction:

- Score 5-6: Class A
- Score 7-9: Class B
- Score 10-15: Class C

Ethical Aspects The study protocol for the purpose of research was approved by the Ethical and Research Committee. Before going about with the evaluation of thyroid profiles, an informed and written consent was taken from the patients explaining about the procedure and purpose of the study.
Procedure

An extensive history was taken, together with a clinical examination and ultrasound results, to diagnose cirrhosis. These patients were referred for thyroid profiling after being diagnosed with cirrhosis. Electrochemiluminescence immunoassay was used to assess thyroid function. The following is the thyroid profile's normal range: T3: 0.79–1.58 ng/ml; T4: 4.0–11.0 g/dl; TSH: 0.39–3.55 l/ml We assessed the relationship between the severity of the liver illness and the thyroid abnormalities based on these values. In order to determine the concomitant effects thyroid abnormalities had on the liver, the liver function test was also performed on these patients. The relationship between the thyroid and liver was improved by this investigation.
Data Analysis: The data was entered and analysed with trial version of Statistical Package for Social Sciences (SPSS) software version 14.0. The continuous variables were expressed in mean±SD while categorical variables were expressed in frequency and percentage. The analysis of variance was used to test the significance of continuous variables within classes. In all tests a p-value <0.05 was considered statistically significant.

Result

The level of T4 and free T3 among the various child pugh score classes varied significantly. F statistics were respectively 3.05 and 3.40. Compared to other classes of Child Pugh scores, class B's mean difference was found to be greater. (Table 1)

Table 1: Distribution of Thyroid function test mean differences and standard deviations for various Child Pugh scores

Thyroid Function tests (TFts)		Mean difference (Mean±Sd)	Standard Error	95% CI for mean		F Statistic	p-value
				lower bound	upper bound		
Total T3 (ng/mL)	Class A	0.54±0.23	0.06	0.41	0.67	0.36	0.55
	Class B	0.84±0.39	0.07	0.68	1.00		
	Class C	0.73±0.34	0.04	0.63	0.81		
	Total T3	0.72±0.33	0.03	0.65	0.79		
Total T4 (µgm/dL)	Class A	4.61±1.24	0.32	3.93	5.30	3.05	0.02
	Class B	6.00±1.93	0.38	5.22	6.78		
	Class C	4.81±1.83	0.24	4.33	5.28		
	Total T3	5.11±1.81	0.18	4.75	5.47		
TSH (µIU/mL)	Class A	1.65±0.85	0.22	1.17	2.11	2.17	0.068
	Class B	1.92±1.01	0.19	1.51	2.33		
	Class C	1.46±1.14	0.15	1.17	1.76		
	Total T3	1.62±1.09	0.11	1.41	1.84		
Free T3 (pg/mL)	Class A	1.25±0.33	0.09	1.07	1.43	3.40	0.017
	Class B	2.04±0.70	0.14	1.75	2.32		
	Class C	1.49±0.65	0.09	1.32	1.66		
	Total T3	1.59±0.63	0.06	1.47	1.72		
Free T4 (µgm/dL)	Class A	0.71±0.11	0.03	0.65	0.77	0.51	0.459
	Class B	0.91±0.18	0.04	0.84	0.98		
	Class C	0.86±0.20	0.03	0.81	0.92		
	Total T3	0.85±0.18	0.02	0.82	0.89		

Post-hoc analysis reveals that the only significant difference between group B and class c's mean free T levels. On post hoc analysis, the difference in mean total T levels between each class of child pugh classes was not statistically significant (Table 2).

Table 2: Comparing the mean difference and standard deviation of thyroid function test results across different Child Pugh scores using a post hoc analysis

TFts vs Child Pugh class			Mean difference	Standard Error	p-value	95% CI	
						lower Bound	upper Bound
Total T4 (µgm/ dL)	Class A	B	0.28	0.45	0.54	-0.79	1.35
		C	0.91	0.4	0.04	-0.04	1.86
	Class B	A	-0.38	0.62	0.75	-1.86	1.1
		C	0.88	0.45	0.12	-0.19	1.95
	Class C	A	-1.18	0.52	0.05	-2.41	0.05
		B	-0.82	0.42	0.11	-1.82	0.18
Free T3 (pg/mL)	Class A	B	-0.02	0.15	0.23	-0.59	0.15
		C	0.1	0.14	0.49	-0.23	0.43
	Class B	A	0.3	0.21	0.31	-0.21	0.82
		C	0.44	0.16	0.02	0.07	0.82

Discussion

The patients suffering from liver disease commonly face endocrine dysfunction. The purpose of the current study was to evaluate the relationship between thyroid hormone levels and the severity of liver disease as measured by the kid pugh score. Males made up the majority of the study participants. According to the kid pugh classification, the majority of the study participants belonged to the child pugh class C and as a result, had severe liver dysfunction. Patients with higher child pugh scores were found to have lower mean total T and free T levels. When mean thyroid hormone levels were compared between the three child pugh classes of liver disease severity, it was found that there was a substantial difference in mean T and free T. This result points to a correlation between mean T and free T among child pugh class classes. The levels of T, free T, and TSH, on the other hand, did not show a similar statistical correlation among the child pugh classes. These results are comparable to those of a study conducted in in Rajasthan, India, by Patira NK et al which indicated that patients had decreased free levels. Similar findings were reported by. Verma SK et al., Lucknow, India, Tas ¸ A et al., in Turkey and Kayacetin E et al., in Turkey [10-12].

The low amounts of free T found in severe liver illness have been the subject of numerous hypotheses. Reduced Type I deiodinase levels, and consequently reduced peripheral conversion of T to T, are the most frequently proposed explanations for the low free T levels in liver illness. Additionally, it has been proposed that the production of inflammatory cytokines, which operate by lowering deiodinase activity, is a factor causing low thyroid hormone levels in liver illness [13].

Across the child pugh classes of liver impairment, there was no significant correlation between free T and TSH levels in the current investigation. This discovery matched that made by according to investigations conducted by Borzio M et al. in the United States, Penteado et al. in Brazil. There was no correlation between TSH levels and the severity of liver dysfunction, in study done by Mansoer P et al. in Iran and Malik R et al. in London [14-16].

Only the mean free T levels between group B and class C appear to be significantly different, according to the post hoc analysis. On post hoc analysis, the difference in mean total T levels between each class of child pugh classes was not statistically significant. To confirm these findings, a larger investigation with a larger sample size is required due to the confounding degree of significance on post hoc analysis. [3,4]

Conclusion

Patients with cirrhosis commonly have thyroid problems. The most frequent problem found was hypothyroidism. Statistically significant values for TSH and liver enzymes show a positive association between TSH and the severity of the condition. Patients with raised TSH levels also experience a higher rate of problems. Finding thyroid anomalies in cirrhotic patients calls for a healthy dose of caution. It follows that people with cirrhosis should be advised to get thyroid function testing while the disease is still in its early stages because they may also have hypothyroidism.

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