

How to Cite:

Razdan, A., Singh, S., Akhtar, S., Yogi, J. P., Fiza, B., & Sinha, M. (2022). Evaluation of thyroid hormones in liver cirrhosis patients on the basis of child pugh score. *International Journal of Health Sciences*, 6(S9), 2462–2470. <https://doi.org/10.53730/ijhs.v6nS9.12953>

Evaluation of thyroid hormones in liver cirrhosis patients on the basis of child pugh score

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Abstract--Introduction: Cirrhosis is an advanced stage of liver fibrosis that is accompanied by distortion of the hepatic vasculature. It is the histological development of regenerative nodules surrounded by fibrous bands in response to chronic liver injury. Objectives: The study was intended to assess serum Triiodothyronine (T₃), Thyroxine (T₄) levels and Thyroid Stimulating Hormone (TSH) on the basis of Child Pugh Score in patients with Liver Cirrhosis. Methodology: 100 clinically diagnosed cases of Liver Cirrhosis patients were enrolled for the study. Estimation of Thyroid Hormones were performed. Statistical evaluation was done for analysis of the results. Result: The study documented a significant decrease in T₃ levels (P= <0.0001), a non-significant increase in T₄ levels (P=0.997) and a slightly significant

increase in TSH levels ($P=0.034$) on the basis of CP Score. Conclusion: The patients with liver cirrhosis have significantly decreased levels of T3 with increased CP Score. The routine liver enzymes like AST, ALT and ALP may be unable to predict the risk of development of liver cirrhosis specially in the early stages. Therefore, screening of serum T3 levels is strongly recommended in patients with early-stage liver diseases like ALD, NAFLD, NASH and CLD.

Keywords--Triiodothyronine, Acute Liver Disease, Chronic Liver Disease.

Introduction

Morphological features of cirrhosis comprise of diffuse fibrosis, regenerative nodules, altered lobular architecture and establishment of intrahepatic vascular shunts between afferent (portal vein and hepatic artery) and efferent (hepatic vein) vessels of the liver.¹ Encapsulation or replacement of injured tissue by a collagenous scar is known as fibrosis. Cirrhosis is an advanced stage of liver fibrosis which is accompanied by distortion of the hepatic vasculature. This condition causes the discharge of the fluid into the abdominal cavity by the liver surface. This fluid accumulates in the peritoneal cavity causing abdominal swelling called ascites. The liver also sends signals to the kidney to retain salt and water, resulting in fluid retention in the legs or abdomen.²

Chronic hepatitis C and heavy alcohol consumption represents the most common cause of cirrhosis. Obesity, associated with non-alcoholic steatohepatitis (NASH), is becoming a common cause of chronic liver disease leading to cirrhosis, either as the sole cause or in combination with alcohol, hepatitis C, or both. Other common causes of cirrhosis may include hepatitis B, hepatitis D, primary biliary cirrhosis and autoimmune hepatitis.³

Deaths from cirrhosis have been estimated to increase and would make it as the 12th leading cause of death in 2020.^{4,5} Based on data from the Global Burden of Disease study, the age standardized incidence rate of cirrhosis was 20.7 per 100,000 in 2015, a 13% increase from 2000.^{6,7} Globally, 1.5 billion persons had CLD in 2017, most commonly resulting from NAFLD (60%), HBV (29%), HCV (9%), and ALD (2%).^{6,8}

Triiodothyronine (T3), thyroxine (T4) and Thyroid Stimulating Hormone (TSH) are the Thyroid Hormones. T4 is entirely a product of thyroid gland, whereas T3 is produced of the thyroid as well as all the tissues in which it is produced by deiodination of T4. Liver is one of the major sites involved in the peripheral conversion of T4 to T3.⁹ The formation of T3 from T4 is catalyzed by iodothyronine-5- deiodinase. This enzyme is predominantly located in the microsomes and plasma membranes of the liver.

The Child-Pugh scoring system also called the Child-Pugh-Turcotte score was conceptualized and designed by Child and Turcotte in 1964 to predict the severity

and mortality in cirrhosis patients. The scoring system uses five laboratory and clinical criteria to categorize patients: serum bilirubin, serum albumin, prothrombin time (PT), distension or ascites and hepatic encephalopathy.¹⁰ This ultimately categorizes patients into three categories: A - good hepatic function, B - moderately impaired hepatic function, and C - advanced hepatic dysfunction.

Materials and Methods

The study was conducted in the Department of Biochemistry in collaboration with the Department of Gastroenterology, Mahatma Gandhi Medical College & Hospital, Jaipur. 100 diagnosed patients of Liver Cirrhosis were enrolled for the study. Blood samples were collected and analyzed for the parameters by these methods:

- ❖ Triiodothyronine: CLIA (Chemiluminescent immunoassay).
- ❖ Thyroxine: CLIA (Chemiluminescent immunoassay).
- ❖ Thyroid Stimulating Hormone: CLIA (Chemiluminescent immunoassay).

Inclusion Criteria:

- Clinically Diagnosed Cases of Liver Cirrhosis.
- Age between 30-65 years, either gender.
- Patients willing to participate in the study.

Exclusion criteria:

- Age <30 and >65 years.
- Patients with prior history of thyroid disease.
- Patients undergoing thyroid medications.
- Patients with history of any other chronic disease.
- Pregnant and Lactating females.

Statistical Evaluation

The results obtained during the study were recorded and presented as mean \pm SD (standard deviation). Enrolled patients were grouped according to severity based on CP scoring. Results obtained were analyzed by applying one-way ANOVA test, P-value of ≤ 0.05 was considered as statistically significant.

Results

Out of total 100 patients the highest percentage of cases was in CP C with 69%, followed by 24% in CP B and only 7% in CP A category. On the basis of CP Score a significant decrease in T3 levels ($P < 0.0001$), a slight significant increase in TSH levels ($P = 0.034$) and a decrease in T4 levels were observed but the decrease was non-significant ($P = 0.997$).

Table I: Scoring systems in cirrhosis

MEASURE	1 POINT	2 POINTS	3 POINTS
Total Bilirubin($\mu\text{mol/l}$)/(mg/dl)	<34/<2	34-50/2-3	>50/>3
Serum Albumin(g/dl)/(g/l)	>3.5/35	2.8-3.5/28-35	<2.8/28
Prothrombin Time/INR	<4.0/<1.7	4.0-6.0/1.7-2.3	>6.0/>2.3

Ascites	None	Mild	Moderate to Severe
Hepatic Encephalopathy	None	Grade 1-2	Grade 3-4

Table 2: Distribution of Liver Cirrhosis patients on the basis of CP Score

CP Score		
CP Score	No. of cases	Percentage (%)
A	7	7
B	24	24
C	69	69
Total	100	100

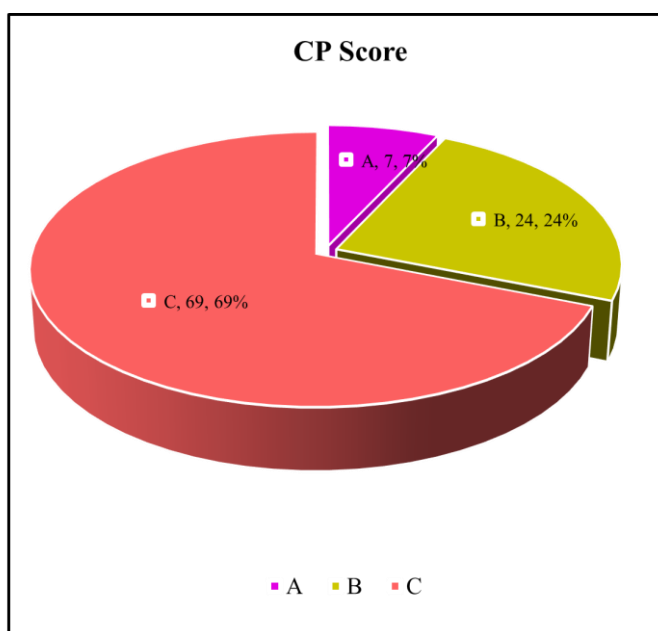


Figure 1: Distribution of Liver Cirrhosis patients on the basis of CP Score

Table 3: Comparison of Serum T₃ on the basis of CP Score

T ₃ Levels				
CP Score	No. of cases	T ₃	f-value	P-value
A	7	0.71±0.21	18.49	<0.0001
B	24	0.64±0.21		
C	69	0.49±0.07		

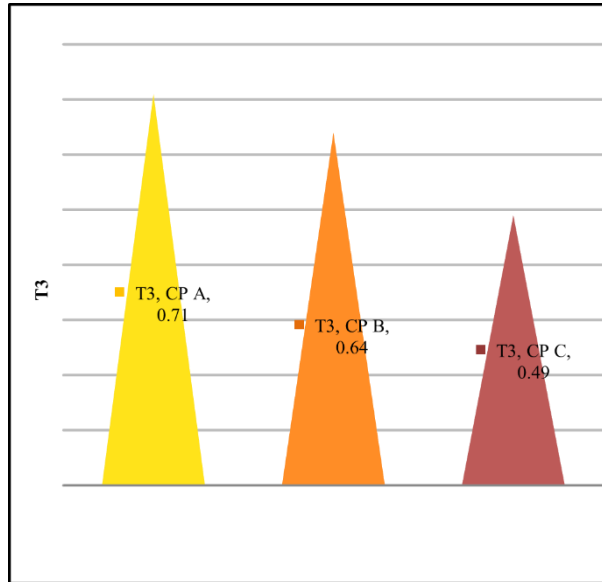


Figure 2: Comparison of Serum T₃ on the basis of CP Score

Table 4: Comparison of Serum T₄ on the basis of CP Score

T ₄ Levels				
CP Score	No. of cases	T ₄	f-value	P-value
A	7	6.34±1.85	0.001	0.997
B	24	6.26±2.53		
C	69	6.27±2.52		

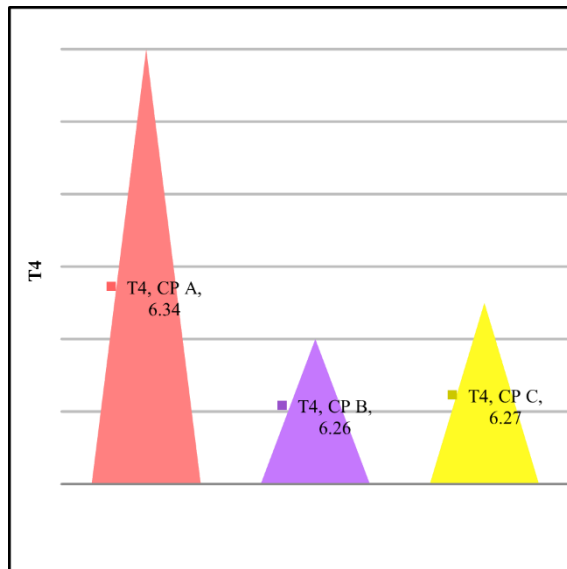


Figure 3: Comparison of Serum T₄ on the basis of CP Score

Table 5: Comparison of Serum TSH on the basis of CP Score

		TSH Levels		
CP Score	No. of cases	TSH	f-value	P-value
A	7	2.14±0.62	3.5	0.034
B	24	3.68±1.71		
C	69	3.88±2.07		

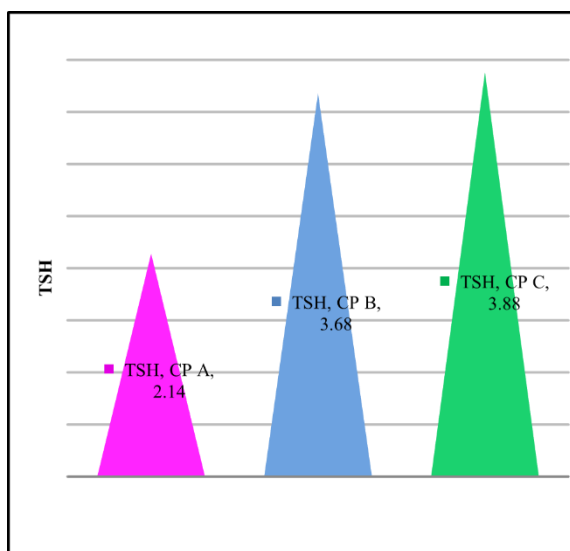


Figure 4: Comparison of Serum TSH on the basis of CP Score

Discussion

Liver Cirrhosis is one of the most common diseases and is characterized pathologically by inflammation of hepatocytes, fibrosis and nodule formation with loss of liver architecture.¹¹ Clinically cirrhosis may be compensated or decompensated, depending upon the absence or presence of the complication of cirrhosis.¹² The present study was planned to determine the role of Thyroid Hormone in 100 Liver Cirrhosis patients on the basis of CP Score. Patients were selected on the basis of predefined inclusion and exclusion criteria and after obtaining informed consent.

When the cases were distributed on the basis of CP Score, serum T3 levels were observed to decrease significantly ($P < 0.001$). Thyroid hormone abnormalities in Liver Cirrhosis patients were also demonstrated by Harischandra P et.al., 2020¹³, Joeimon J L et.al., 2017¹⁴ and Mobin A et.al., 2016.¹⁵ They concluded in their studies that the level of T3 decreased in Liver Cirrhosis patients. Another study by Moustafa A et.al., 2009¹⁶, concluded that, serum total T3 levels as biomarkers for liver disease might be a beneficial tool, helping in monitoring the state of liver disease patients. Ghanaei F M et.al., 2012¹⁷ reported the similar pattern in T3 levels in Liver Cirrhosis patients. They concluded in their study that serum T3

concentration is a good index of hepatic function, decreasing by the severity of liver damage.

A decrease in T4 levels was observed with an increase in the severity of Liver Cirrhosis ($P=0.997$) but the observed decrease was not significant as shown in Table 8, Figure 8. T4 levels decrease, due to decreased production of thyroid binding globulin and due to the action of peripheral binding inhibitors. Total T4 levels were found to be insignificantly reduced or unchanged in studies conducted by Vijaykumar S et.al, 2020¹⁸, Joeimon J L et.al., 2017¹⁴ and Harischandra P et.al., 2020.¹³ They reported abnormalities in circulating thyroid hormone concentrations and thyroid dysfunction in patients with Liver Cirrhosis. Hence, thyroid function tests should be carried out in all cirrhotic patients to assess the severity of such patients.

A slight significant increase in the levels of TSH were observed ($P=0.034$). Similar pattern in TSH levels were reported by Antonelli A et.al., 2004¹⁹ and Moustafa A et.al., 2009.¹⁶ A study by Verma S K et.al., 2017²⁰, also demonstrated the increase in TSH levels among Liver Cirrhosis patients and concluded that derangement in thyroid profile is common and may be used for prognosis in patients with Cirrhosis of Liver. Another study by Joeimon J L et.al., 2017¹⁴, concluded that abnormalities in circulating thyroid hormone concentrations i.e. hypothyroidism is noted especially in those with ethanol related liver cirrhosis and it is associated with more advanced liver disease and Vijaykumar S et.al., 2020¹⁸, in their study concluded that Thyroid dysfunction is common in cirrhosis of liver hence thyroid function tests should be carried out in all cirrhotic patients to assess the severity and prognosis of such patients.

Conclusion

The present study therefore suggests that decreased T3 level is strongly associated with increased severity in patients with Liver Cirrhosis on the basis of CP Score. Various liver diseases like ALD, NAFLD, NASH and CLD lead to Liver Cirrhosis and further to HCC. Therefore, screening of patients for thyroid levels specially T3 level in the early stages of liver disease can be helpful and used as a marker for identifying patients who are at a risk of Liver Cirrhosis.

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