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Study Of Thyroid Function In Patients With Cirrhosis Of Liver

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ABSTRACT

Cirrhosis of liver is a leading cause of morbidity and mortality worldwide. Liver plays a vital role in thyroid hormone metabolism and circulation of thyroid hormones by producing thyroid binding globulin. The liver plays a crucial role in the thyroid hormone synthesis, as it is the most important organ in the extrathyroidal conversion of T4 to T3 by Type 1 deiodinase. With this background, this study is aimed to assess the thyroid function in patients with cirrhosis of liver and correlate the levels of thyroid hormone with the severity of the disease.

Aim: To study the thyroid hormone levels (FT3, FT4, TSH) in patients with cirrhosis of liver and assess the relation of thyroid hormone levels with severity of liver disease.

Material and methods: The study was conducted at Krishna Institute Of Medical Sciences from February 2021 to August 2022 on 97 patients chosen as study subjects. Patients who are admitted in wards and intensive care unit at Krishna hospital were included in the study. All the patients were diagnosed with cirrhosis of liver based on case history, initial clinical evaluation, haematological, biochemical and radiological investigations and were enrolled into the study after applying the exclusion criteria. The severity of liver cirrhosis was determined based on the Child-Turcotte-Pugh grading system. Thyroid function tests (FT3, FT4, TSH) were done.Data was recorded in Microsoft Excel programme and statistical analysis was performed by the SPSS program for Windows, version 25.

Results: A total of 97 patients with diagnosis of cirrhosis of liver were included in this cross sectional study. On comparing the mean serum levels of T3, T4 and TSH in CTP A, B and C groups, it was found the T3 and T4 were lowest in the CTP Class C group (1.501±0.136, 0.843±0.199 respectively),followed by the CTP Class B group (1.866±0.129, 1.111±0.057 respectively) and the CTP Class A group were (2.462±0.435, 2.276±0.191 respectively).The mean TSH was the highest in the CTP Class C group (5.128 ± 0.274), followed by the Class CTP B group (4.688 ± 0.278) and the CTP A group was (3.787 ± 0.096).

Conclusion: In this present study low levels of FT3 levels, normal levels of FT4 and slightly high levels of TSH were observed. It was observed that there was high negative correlation between FT3 and CTP score, high negative correlation between FT4 and CTP score and high positive correlation

between TSH and CTP score . Therefore it can be said that as the severity of the liver cirrhosis increases, the FT3 and FT4 levels decreases and the TSH level increases.

Keywords: *Cirrhosis of liver, Free T3,T4,TSH,CTP score*

INTRODUCTION

Cirrhosis of liver is a leading cause of morbidity and mortality worldwide. Liver plays a vital role in thyroid hormone metabolism and circulation of thyroid hormones by producing thyroid binding globulin.[1] Liver cirrhosis is a progressive disorder that results in inflammation and diffuse process of fibrosis.

The thyroid gland produces two hormones, triiodothyronine (T3) and thyroxine (T4). These hormones, which function through the thyroid hormone receptors are crucial for cell differentiation throughout development and the maintenance of metabolic and thermogenic homeostasis in adults. The thyroid gland secretes T4 about twenty times more than T3. Both hormones are plasma protein bound which include albumin, thyroxine-binding globulin and transthyretin.[2]

The liver plays a crucial role in the thyroid hormone synthesis, as it is the most important organ in the extrathyroidal conversion of T4 to T3 by Type 1 deiodinase.[3,4,5]Type I deiodinase is produced in the liver that performs both the 5'- and 5-deiodination of T4 to T3, which is responsible for 30% to 40% of extrathyroidal synthesis of T3. By the synthesis of thyroid binding globulin, liver also plays a critical role in thyroid hormone metabolism and circulation[6.] The liver is also involved in the conjugation and excretion of thyroid hormone. The liver also plays a role in the metabolism of thyroid stimulating hormone (TSH) and regulates their systemic endocrine effects**.**

Currently, available literatures showed the most common change in thyroid hormone levels in cirrhosis of liver is reduced total and free T3 concentration, which is said to be related to the severity of hepatic dysfunction. However, no study explicitly linked liver cirrhosis severity to FT4 and thyroid-stimulating hormone (TSH) levels. Serum T4 levels are either stable or marginally low. However, serum TSH levels continue to be normal or slightly elevated.[7] With this background, this study is aimed to assess the thyroid function in patients with cirrhosis of liver and correlate the levels of thyroid hormone with the severity of the disease.

Aim

To study the thyroid hormone levels (FT3, FT4, TSH) in patients with cirrhosis of liver and assess the relation of thyroid hormone levels with severity of liver disease.

MATERIAL AND METHODS

The study was conducted at Krishna Institute Of Medical Sciences from February 2021 to August 2022 on 97 patients chosen as study subjects. Patients who are admitted in wards and intensive care unit at Krishna hospital were included in the study. All the patients were diagnosed with cirrhosis of liver based on case history, initial clinical evaluation, haematological, biochemical and radiological investigations and were enrolled into the study after applying the exclusion criteria. The severity of liver cirrhosis was determined based on the Child-Turcotte-Pugh grading system. Thyroid function tests (FT3, FT4, TSH) were done. The normal range of thyroid profile are FT3 2.1 to 4.4 pg/ml, FT4 – 0.8 to 2.7 ng/dl, TSH – 0.4 to 4.0 mIU/ml.

Inclusion criteria

• All patients aged more than 18 years, admitted with cirrhosis of liver were considered for enrolment into the study.

Exclusion criteria

- Patients with known thyroid disorders such as hypothyroidism, thyroiditis, hyperthyroidism, autoimmune thyroiditis without liver cirrhosis
- Patients who use medications such as propylthiouracil, levothyroxine, carbimazole, amiodarone, and beta blockers which affect the thyroid hormone metabolism.
- Patients with active infections such as cardiac, pancreatic, renal or bone and muscle disorders

- Patients who have refused consent to the study.

Ethical clearance has been taken from ethical committee. Ec No- KIMSDU/IEC/01/2021. Data was recorded in Microsoft Excel programme and statistical analysis was performed by the SPSS program for Windows, version 25. Continuous variables were presented as mean ± SD, and categorical variables were presented as absolute numbers and percentage. Data was checked for normality before statistical analysis. Descriptive analysis was performed to obtain general characteristic of the study population. Appropriate statistical tests like ANOVA test, Pearson correlation test were applied. $p<0.05$ was considered statistically significant.

RESULTS

A total of 97 patients with diagnosis of cirrhosis of liver were included in this cross sectional study. Majority were in the age group of 51 to 60 years (31.9%) followed by 41 to 50 years (22.7%), 31 to 40 years (22.7%), 61 to 70 years (16.5%) and > 70 years (5.2%). Of total 97 patients with cirrhosis of liver included in the present study,73 (75.3%) were male and 24 (24.7%) were female.

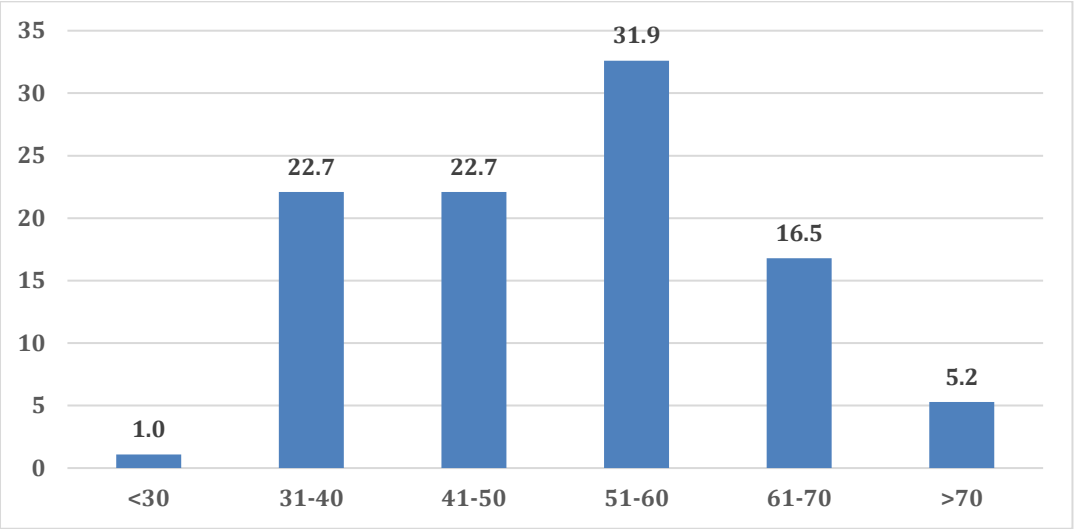

FIGURE 1: Frequency distribution of age group for the study population

Of total 97 patients with cirrhosis of liver included in the present study, 31 (32%) of the population belonged to CTP class A, 50 (51.5%) belonged to CTP class B and 16 (16.5%) belonged to CTP class C.

TABLE 1

Child Pugh Score	Frequency	Percent
A	31	32%
B	50	51.5%
C	16	16.5%
Total	97	100

In the total 97 patients with cirrhosis of liver included in the present study, the mean value of FT3 (pg/ml) level was found to be (1.99±0.44), the mean value of FT4 (ng/dl) level was (1.44±0.60) and the mean value of TSH level (IU/ml) was (4.47 ± 0.55).

TABLE 2: Mean and Standard Deviation of Thyroid function test profile.

Thyroid function profile	Mean	SD(±)
FT3 (pg/ml)	1.99	0.44
FT4 (ng/dl)	1.44	0.60
TSH (IU/ml)	4.47	0.55

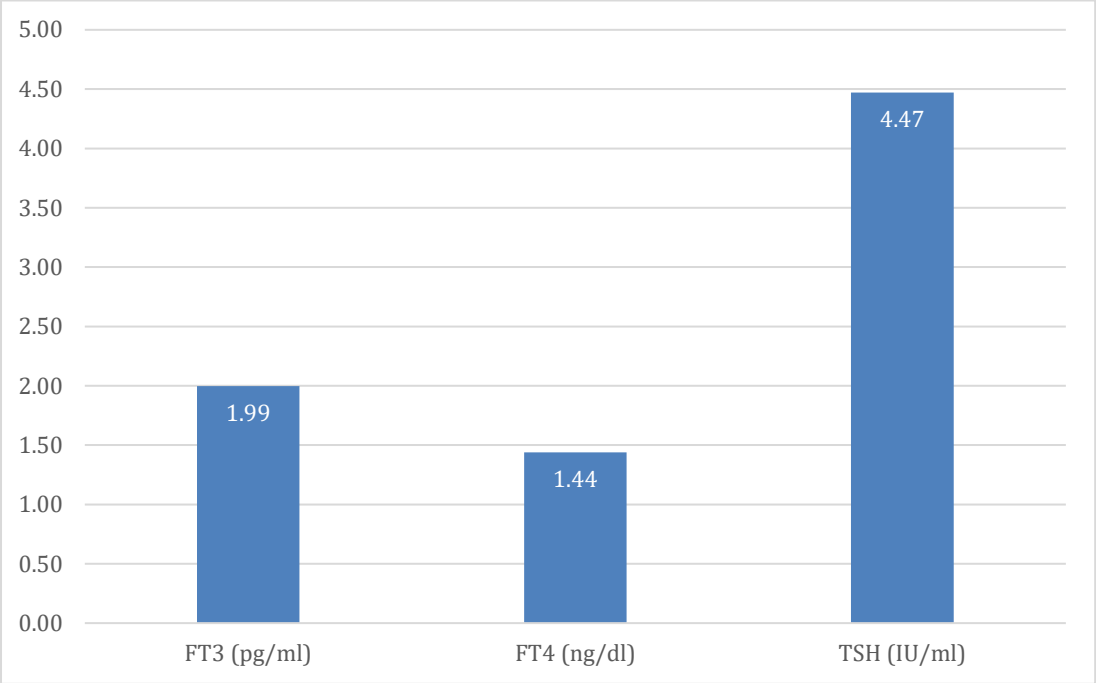

FIGURE 2 : Mean and Standard Deviation of Thyroid function test profile.

A total of 97 patients with cirrhosis of liver were included in the present study. On comparing the mean serum levels of T3, T4 and TSH in CTP A, B and C groups, it was found the T3 and T4 were lowest in the CTP Class C group (1.501±0.136, 0.843±0.199 respectively), followed by the CTP Class B group (1.866±0.129, 1.111±0.057 respectively) and the CTP Class A group were (2.462±0.435, 2.276±0.191 respectively).The mean TSH was the highest in the CTP Class C group (5.128 ± 0.274), followed by the Class CTP B group (4.688 ± 0.278) and the CTP A group was (3.787 ± 0.096)

TABLE 3: Comparison of thyroid profile with Child Pugh Score

Thyroid profile	Child Turcotte Pugh Score		
	A	**B**	**C**
FT3 (mean± SD)	2.462±0.435	1.866±0.129	1.501±0.136
FT4 (mean± SD)	2.276±0.191	1.111±0.057	0.843±0.199
TSH (mean± SD)	3.787±0.096	4.688±0.278	5.128±0.274

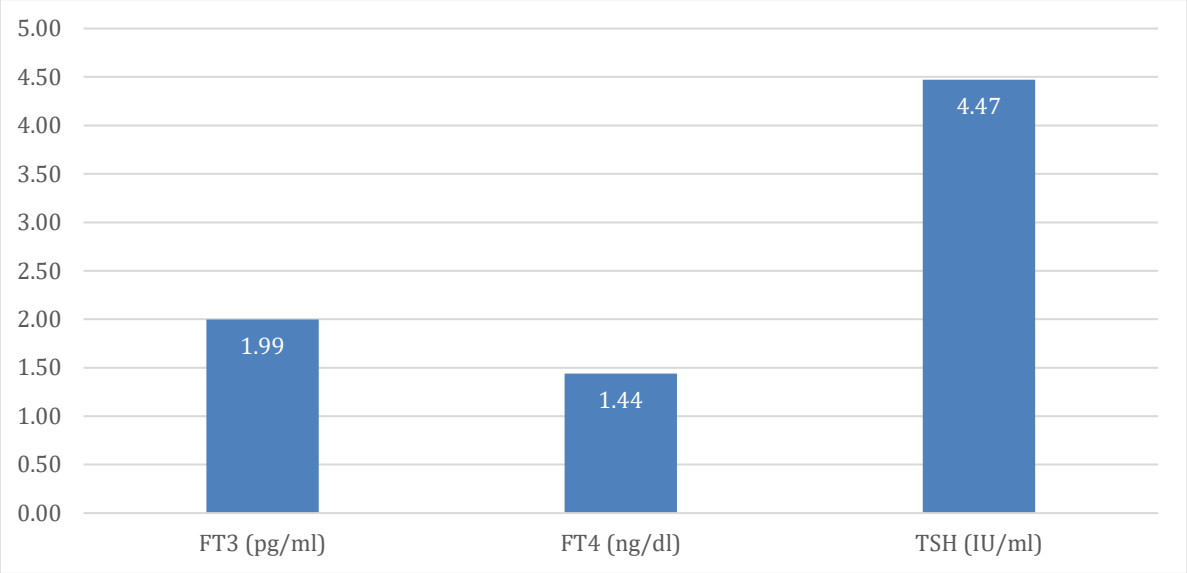

FIGURE 3: Mean and Standard Deviation of Thyroid function test profile.

On correlating between Child Turcotte Pugh score and FT3 levels, it has been observed that FT3 and CTP score had high negative correlation (r = -0.786).

TABLE 4: Correlation between Child-Turcotte-Pugh score and FT3 level

		CHILD PUGH SCORE	FT3 (pg/ml)
CHILD PUGH SCORE	**Pearson Correlation**	1	-0.786
	Sig. (2-tailed)		0.000
	N	97	97
FT3 (pg/ml)	**Pearson Correlation**	-0.786	1
	Sig. (2-tailed)	0.000	
	N	97	97

On correlating between Child Turcotte Pugh score and FT4 levels, it has been observed that FT4 and CTP score had high negative correlation (r = -0.768).

TABLE 5: Correlation between Child-Turcotte-Pugh score and FT4 level

		CHILD PUGH SCORE	FT4 (ng/dl)
CHILD PUGH SCORE	**Pearson Correlation**	1	-0.768
	Sig. (2-tailed)		0.000
	N	97	97
FT4 (ng/dl)	**Pearson Correlation**	-0.768	1
	Sig. (2-tailed)	0.000	
	N	97	97

On correlating between Child Turcotte Pugh score and TSH levels, it has been observed that TSH and CTP score had high positive correlation (r = 0.752).

TABLE 6: Correlation between Child-Turcotte-Pugh score and TSH level

		CHILD PUGH SCORE	TSH (IU/ml)
CHILD PUGH SCORE	**Pearson Correlation**	1	0.752
	Sig. (2-tailed)		0.000
	N	97	97
TSH (IU/ml)	**Pearson Correlation**	0.752	1
	Sig. (2-tailed)	0.000	
	N	97	97

DISCUSSION

In the present study, the incidence of cirrhosis of liver was maximum in age group of 51-60 years (31.9%) followed by 31-40 years (22.7%) and 41-50 years (22.7%). Epidemiological studies in the United States reported a higher prevalence among patients > 50 years of age compared to those 20 to 49 and 6 to 19 years of age, irrespective of ethnicity.[8]

In the present study, more than half (51.5%) patients were categorized according to Child Pugh Score B followed by Score A (32%) and C (16.5%). On comparing the mean serum levels of FT3, FT4 and TSH in CTP Class A, B, and C, it was found the FT3 and FT4 were the least in the CTP Class C group . It was also found that the CTP Class C group had the highest mean TSH level.

When we observed for each individual thyroid function parameter, we found the mean FT3 was (1.99±0.44), that of FT4 was (1.44±0.60) and it was (4.47 ± 0.55) for TSH. Our findings were similar to that of Punekar *et.al*[9] study, where the mean FT3 was (1.95 ± 0.57), the mean FT4 was (1.27±0.54) and the mean TSH was (4.09 ± 1.70).

In our study, on comparing the mean levels of FT3, FT4 and TSH in CTP Classes A, B, and C groups, it was observed that the CTP Class C group had the lowest levels of FT3 and FT4(1.501±0.136,0.843±0.199 respectively), followed by the CTP class B group (1.866±0.129, 1.111±0.057respectively), and the mean levels of FT3 and FT4 in CTP class A group were the highest (2.462±0.435, 2.276±0.191 respectively). In our study, the mean level TSH was the highest in the CTP class C group (5.128 ± 0.274), followed by CTP class B group (4.688 ± 0.278) and CTP class A group (3.787 ± 0.096). We found that free T3 and free T4 levels were inversely correlated with the Child-Pugh class and previous studies also suggested similar results. On comparing patients with HE with non-HE, Punekar et al. study found significantly lower FT3 levels ($P < 0.0001$) in patients with liver cirrhosis with hepatic encephalopathy than patients without hepatic encephalopathy, although FT4 ($P < 0.09$) and TSH levels ($P < 0.60$) were not statistically significant.

Our study showed that patients with liver cirrhosis had low FT3 levels, normal FT4 levels and slightly elevated TSH levels which were statistically significant. In Chang Liu *et al* [10] study, the FT3 and FT4 levels in cirrhosis group are lower than that of control group and TSH levels were higher than that of control group .It also showed that FT3 levels correlate negatively with the Child-Pugh score. Our findings are consistent with these studies. In studies like Deepika *et al*.,[11] D'costa and Dhume,[12] Kayacetin *et al*.,[6] El-Sawy and Tawfi,[13] etc., the FT3 levels were significantly low in patients with cirrhosis of liver.

Kayacetin *et al*.[6] reported that serum levels of FT3 and total T4 were significantly lower in all cirrhotic patients with hepatic encephalopathy compared to cirrhosis without hepatic encephalopathy. Our FT3 results are similar to this study.

In several studies, the most common abnormalities of serum thyroid hormone levels in patients with liver cirrhosis were low FT3 levels, normal to slightly low FT4 and normal to slightly raised TSH levels. There may be numerous factors responsible for the abnormalities of thyroid hormones such as inhibition of Type 1 (D1) deiodinase enzymes that lead to decreased conversion of T4 to T3 in patients with liver cirrhosis due to severe hepatic inflammation and fibrosis, decrease in the plasma level of thyroid binding proteins, changes in the binding of T4 and T3 to their carrier protein and reduced hepatic clearance of reverse T3.

CONCLUSION

In the present study, a total of 97 patients were included, of which majority belonged to the age group 51 to 60 years predominated by male gender. Majority of the patients belonged to CTP Class B group. In this present study low levels of FT3 levels, normal levels of FT4 and slightly high levels of TSH were observed. It was observed that there was high negative correlation between FT3 and CTP score(r=-0.786), high negative correlation between FT4 and CTP score(r=-0.768) and high positive correlation between TSH and CTP score (r=0.752). Therefore it can be said that as the severity of the liver cirrhosis increases, the FT3 and FT4 levels decreases and the TSH level increases. As a result, thyroid function tests should be performed on all cirrhotic patients for prognosis and treated accordingly.

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