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Research Article

A COMPARATIVE STUDY OF THYROID PROFILE IN HEPATITIS B AND C RELATED LIVER CIRRHOSIS

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ABSTRACT

The most vibrant organ of the human body is the liver, which happens to be the second-largest organ in the frame next to the skin. The liver is susceptible to a wide variety of metabolic, toxic, microbial, circulatory, and neoplastic insults. The study aims to compare the thyroid profile with liver cirrhosis viruses of hepatitis B and hepatitis C. The present prospective study carried out from September 2016 to December 2018 at Department of Medical Gastroenterology, Narayana Medical College and Hospital, Nellore. Spearman's rank correlation used to test the relationship between thyroid profile with liver cirrhosis. For evaluating the accuracy of the liver cirrhosis patients for identifying the thyroid profile, the Receiver Operating Characteristic (ROC) curve used. The present study concluded that the level of sensitivity is significantly more in TT4 and fT3 for mild CTPS group. TT3, TT4, and fT3 have shown significant negative correlation except for TSH and fT4 in the MELD group.

Keywords: MELD, CTPS, Liver Cirrhosis, HBV, HCV, Thyroid Profile, ROC curve

1. INTRODUCTION

The liver is one of the most energetic organs of the human body, which happens to be the second-largest organ in the frame next to the skin. The liver maintains the body's metabolic homeostasis, along with the processing of dietary amino acids, carbohydrates, lipids and vitamins, removal of microbes and toxins from splanchnic blood, en route to the systemic circulation, detoxification and excretion into the bile of endogenous waste products. The dominant primary disease of the liver is viral Hepatitis, alcoholic liver disease, and hepatocellular carcinoma [1-3]. Hepatology practice controls infectious liver disorders. Some of the liver cirrhosis causes are viruses, alcohol, NASH, metabolic iron overload, heart failure, and so on. Among them, the leading cause of chronic liver disease in India is Hepatitis B virus and Hepatitis C virus [4-7].

Globally, Liver cirrhosis is the main reason for morbidity and mortality. The liver plays a vital role in thyroid hormone metabolism involved in the conjugation, excretion, peripheral deiodination, and the synthesis of thyroid-binding globulin [8]. Thyroid dysfunction may perturb liver function, liver disease modulates thyroid hormone metabolism, and a variety of systemic diseases affect both organs. The most commonly encountered condition is a Euthyroid Sick Syndrome (ESS), frequent contributors being the underlying disorder, drugs administered, and nutritional status. ESS mainly manifests itself with low free T3 (fT3) levels, although decreases in fT3, free T4 (fT4), and Thyroid-Stimulating Hormone (TSH) may occur in varying combinations [9].

Durand and Valla [10] compared the relationship between CTPS and MELD for assessing the prognosis of liver cirrhosis patients. Earlier studies showed the essential relationship between the liver cirrhosis and thyroid profile, but the results are contradictory [11-17]. They described the low fT3 syndrome of thyroid hormone profile in patients with cirrhosis of the liver [19], and low TT3 may be an adaptive thyroid response to reduce the basal metabolic rate of hepatocytes and preserve liver function [12]. Most of the studies selected the small samples of cirrhosis of patients, and the prevalence of thyroid alterations in cirrhosis concerning the etiology of liver disease has not been settled [13].

In spite of above literature, we aimed to study the thyroid profile and comparison with the liver cirrhosis of patients.

2. MATERIAL AND METHODS

The present prospective study was carried out at the Department of Medical Gastroenterology, Narayana Medical College and Hospital, Nellore from September 2016 to December 2018.

Patients diagnosed with hepatic cirrhosis due to Hepatitis B or C were selected and evaluated for thyroid function. The thyroid hormones correlated with the severity of liver disease by assessing various factors like hepatic encephalopathy, ascites, total bilirubin, albumin, prothrombin time, Child-Turcotte-Pugh (CTP) score, and MELD score.

2.1. Inclusion Criteria

1. Patients are having the age group of 20 to 60 years.
2. Patients with symptoms, signs with clinical, biochemical, and radiological evidence of cirrhosis of the liver.
3. Those patients are willing to participate in the study.

2.2. Exclusion Criteria

1. The patient's age is less than 20 years.
2. Patients who have diabetes.
3. Pregnant women.
4. Patients are having a prior history of thyroid disease.
5. Patients have any other chronic illness (except liver disease).

2.3. Statistical Analysis

The data entered into MS-Excel, and statistical analysis was done by using IBM SPSS Version 25.0. The numbers and percentages expressed to the categorical variables. The mean and standard deviation expressed to the continuous variables. The student's t-test and ANOVA test used to test the mean difference between the two and three groups. To examine the relationship between the thyroid profile and CTPS and MELD scores, Spearman's rank correlation used. For evaluating the diagnosis of liver cirrhosis in the thyroid profile, the Receiver Operating Characteristic (ROC) curve was used. A P-value of less than 0.05 was considered statistically significant.

3. RESULTS

Out of 31 patients, 23 (74.19%) patients were males, and 8 (25.81%) were females. The Mean±SD age was 56.06±13.41 years, with ranges from 20 to 77 years. Sex ratio was Male:Female::2.88:1. The Mean±SD age of females (54.75±13.89 years) were higher than the Mean±SD age of males (52.48±13.51 years), and there was no statistically significant difference between males and females for the age [P = 0.687]. The physical examination revealed that 15 (48.4%) patients were having the habit of alcohol, 28 (90.3%) patients were ascites, 2 (6.5%) patients having SBP, and each one (3.2%) patient had bleeding and HE. The mean±SD of TT3, TT4, TSH, fT3 and fT4 were 1.37±0.45, 7.65±1.56, 2.94±1.77, 2.41±0.62, and 1.02±0.30 respectively. The mean±SD of MELD and CTP scores were 8.52±2.17 and 19.19±6.78, respectively.

In the CTPS group, 7 (22.58%) were mild patients, 14 (45.16%) were moderate patients, and 10 (32.26%) were severe patients. The mean±SD age for the severe group was higher (54.70±11.64) than the moderate group (52.50±11.91) and the mild group (51.86±19.54). However, there was no statistically significant difference for the mean age of the CTPS group [P = 0.898, Not Significant]. Among 23 (74.2%) patients of males, five (21.7%) patients were in the mild group, 10 (43.50%) patients were in the moderate group, and eight (34.80%) patients were in the severe group. In eight (25.80%) patients of females, two (25.0%) patients were in the mild group, four (50.0%) patients were in a moderate group, and two (25.0%) patients were in the severe group. The mean±SD value of the total T3 in the severe group was significantly lower (1.05±0.54) than the moderate group (1.48±0.29) and the mild group (1.61±0.32) [P = 0.012, Significant]. The mean±SD value of the total T4 of the severe group is significantly lower (6.74±1.21) than the moderate group (7.75±1.68) and the mild group (8.72±1.09) [P = 0.029, Significant]. The mean±SD value of the TSH of the moderate group was higher (3.52±1.61) than the severe group (2.89±2.22) and the mild group (1.82±0.60). However, it does not show any statistically significant difference for TSH in the CTPS group [P = 0.121, Not Significant]. The mean±SD value of the free T3 of the severe group was significantly lower (1.98±0.47) than moderate group (2.50±0.54) and the mild group (2.86±0.62) [P = 0.007, Significant]. The mean±SD value of the fT4 of severe group was higher (1.09±0.21) than moderate group (1.04±0.40) and the mild group (0.86±0.13) [P = 0.308, Not Significant] and these are shown in Table 1. Table 3 showed the correlation between thyroid profile with CTPS group and it revealed that there was a significant negative correlation for TT3 [r-value = -0.462; P = 0.009, Significant], TT4 [r-value = -0.437; P = 0.014, Significant], fT3 [r-value = -0.479; P = 0.006, Significant] and fT4 [r-value = 0.358; P = 0.048,

Significant] except for TSH [r-value = 0.112; P = 0.548, Not Significant] in CTPS group. Table 4 showed the ROC curve analysis of thyroid profile with CTPS group and it revealed that there The ROC curve analysis showed that the TT4 [AUC value = 0.24, P = 0.022, Significant], fT3 [AUC value = 0.20; P = 0.007, Significant] and TT3 [AUC value = 0.18; P = 0.005, Significant] was significant except for fT4 [AUC = 0.68; P = 0.118, Not Significant] and TSH [AUC value = 0.45; P = 0.627, Not Significant] for assessing the risk of mortality in severe CTPS group. Whereas in mild case of CTPS group, the TT4 [AUC value = 0.78; P = 0.028, Significant] significantly more accurate than the fT3 [AUC value = 0.76; P = 0.042, Significant]. However, TT3 [AUC value = 0.72; P = 0.085, Not Significant] is also having higher AUC value and for TSH [AUC value = 0.26; P = 0.059, Not Significant] and FT4 [AUC value = 0.30; P = 0.103, Not Significant] but it does not show any statistically significant result for assessing the risk of mortality and graphical presentation of ROC curve analysis was shown in Fig.1.

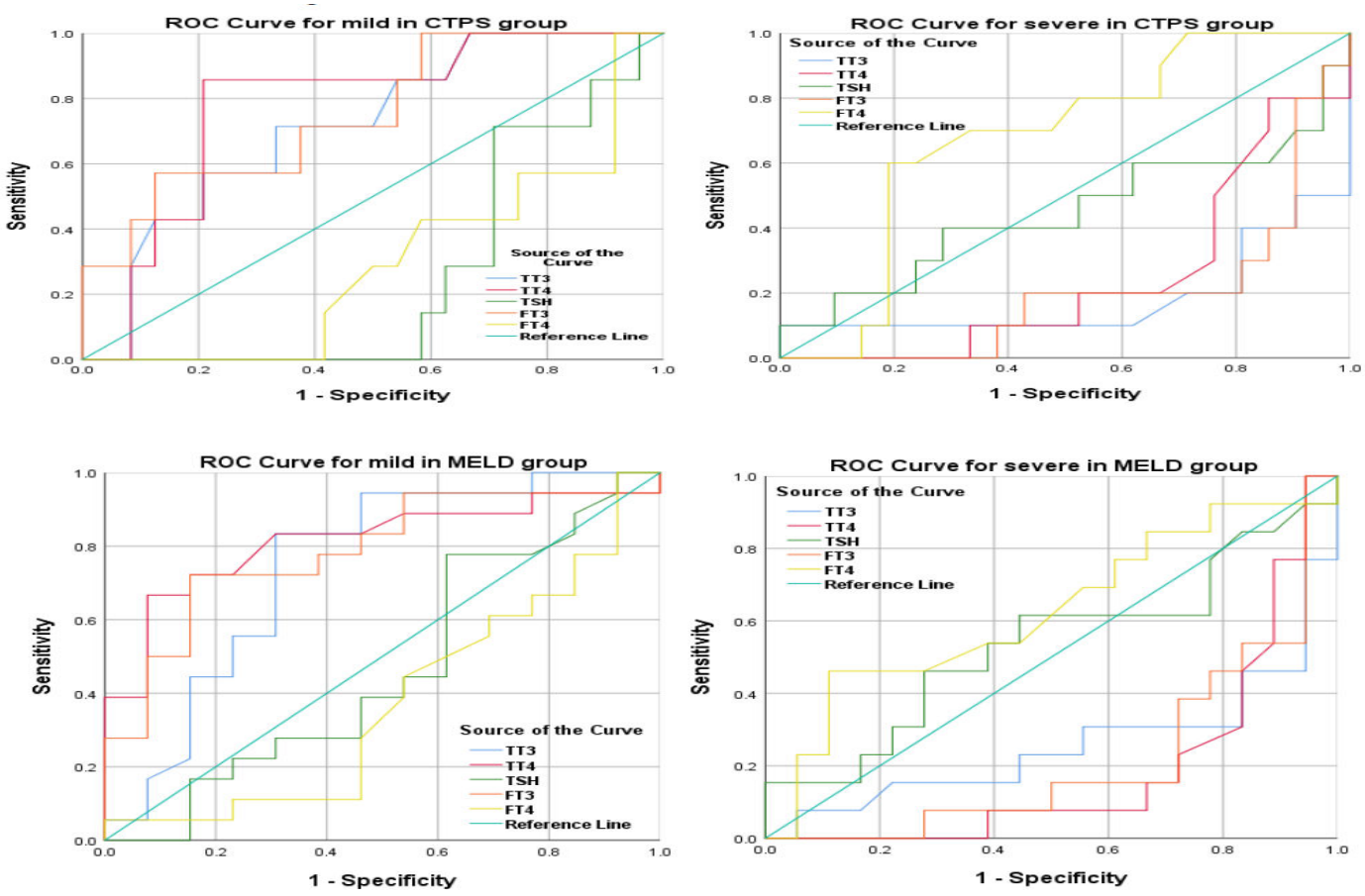

Fig. 1: Receiver Operating Characteristic (ROC) curve of thyroid profile in the CTPS and MELD group.

Table 1: Patient's demographic and clinical profile for the CTPS group

Variable (s)	Mild (n = 7)	Moderate (n = 14)	Severe (n = 10)	Total (n = 31)	F value	P-value
AGE	51.86±19.54	52.50±11.91	54.70±11.64	53.06±13.41	0.108	0.898
TT3	1.61±0.32	1.48±0.29	1.05±0.54	1.37±0.45	5.195	0.012*
TT4	8.72±1.09	7.75±1.68	6.74±1.21	7.65±1.56	4.043	0.029*
TSH	1.82±0.60	3.52±1.61	2.89±2.22	2.94±1.77	2.360	0.113
fT3	2.86±0.62	2.50±0.54	1.98±0.47	2.41±0.62	5.874	0.007*
fT4	0.86±0.13	1.04±0.40	1.09±0.21	1.02±0.30	1.230	0.308

*Values are expressed as mean± standard deviation; * P< 0.05 – Significant.*

Table 2: Patient's demographic and clinical profile for the MELD group

Variable (s)	Mild (n = 18)	Severe (n = 13)	Total (n = 31)	t-value	P-value
AGE	52.56± 14.11	53.77± 12.91	53.06±13.41	-0.245	0.808
TT3	1.52± 0.34	1.17±0.51	1.37±0.45	2.297	0.029*
TT4	8.32± 1.56	6.72±1.02	7.65±1.56	3.228	0.003*
TSH	2.84±1.61	3.07±2.02	2.94±1.77	-0.365	0.718
fT3	2.65±0.61	2.07±0.47	2.41±0.62	2.864	0.008*
fT4	0.98± 0.32	1.07±0.29	1.01± 0.30	-0.773	0.446

*Values are expressed as mean± standard deviation; * P< 0.05 – Significant*

Table 3: Correlation analysis for thyroid profile with the CTPS and the MELD score

		TT3	TT4	TSH	FT3	FT4
CTPS	Correlation Coefficient	-0.462*	-0.437*	0.112	-0.479*	0.358*
	P value	0.009	0.014	0.548	0.006	0.048
MELD	Correlation Coefficient	-0.509*	-0.446*	0.032	-0.533*	0.171
	P value	0.003	0.012	0.864	0.002	0.358

** P< 0.05 – Significant*

Table 4: Receiver Operating Characteristic (ROC) curve analysis of thyroid profile for CTPS score

	Mild			Severe		
Thyroid profile	AUC (95% CI)	Std. Error	P-value	AUC (95% CI)	Std. Error	P-value
TT3	0.72 (0.52-0.92)	0.102	0.085	0.18 (0.00-0.37)	0.10	0.005*
TT4	0.78 (0.59 - 0.96)	0.093	0.028*	0.24 (0.07 - 0.42)	0.09	0.022*
TSH	0.26 (0.09 - 0.44)	0.088	0.059	0.45 (0.20 - 0.69)	0.12	0.627
fT3	0.76 (0.55 - 0.96)	0.103	0.042*	0.20 (0.03 - 0.36)	0.09	0.007*
fT4	0.30 (0.09-0.50)	0.102	0.103	0.68 (0.48-0.87)	0.10	0.118*

*AUC: Area under the curve; *p<0.05 - Significant*

In the MELD group, 18 (58.06%) were mild patients, and 13 (41.94%) were severe patients. The mean±SD age (years) was lower in the severe group (53.77±12.91) than the mild group (52.56±14.11) [P = 0.808, Not Significant]. Among 23 (74.2%) patients of males, six (26.1%) were mild patients, and seventeen (73.90%) were severe patients. In eight (25.80%) patients of females, three (37.50%) were mild patients, and five (62.5%) were severe patients. The mean±SD value of the total T3 of the severe group was significantly lower (1.17±0.51) than the mild group (1.52±0.34) [P = 0.029, Significant]. The mean±SD value of the total T4 of the severe group was significantly lower (6.72±1.02) than the mild group (8.32±1.56) [P = 0.003, Significant]. The mean±SD value of the TSH of the severe group is higher (3.07±2.02) than the mild group (2.84±1.61). However, the mean difference was not shown statistically significant for TSH in the MELD group [P = 0.718, Not Significant]. The mean±SD value of the fT3 of the severe group was significantly lower (2.07±0.47) than the mild group (2.65±0.61) [P = 0.008, Significant]. The mean±SD value of the fT4 of the severe group was higher (1.07±0.29) than the mild group (0.98±0.32). However, the mean difference was not shown statistically significant for fT4 in the MELD group [P = 0.446, Not Significant] and these are shown in Table 2. Table 3 showed the correlation between thyroid profile with MELD group and it revealed that there was a significant negative correlation for TT3 [r-value = -0.509; P = 0.003, Significant], TT4 [r-value = -0.446; P = 0.012, Significant] and fT3 [r-value = -0.533; P = 0.002, Significant] except for TSH [r-value = 0.032; P = 0.864, Not Significant] and fT4 [r-value = 0.171; P = 0.358, Not Significant] in MELD group.

Table 5 showed the ROC curve analysis of thyroid profile with MELD group and The ROC curve analysis for MELD score of severe group showed that the TT3 [AUC value = 0.25; P = 0.021, Significant] was significantly more accurate than the fT3 [AUC value = 0.21; P = 0.007, Significant], TT4 [AUC value = 0.19; P = 0.003, Significant] except for fT4 [AUC value =

0.62; P = 0.246, Not Significant] and TSH [AUC value = 0.53; P = 0.749, Not Significant]. Whereas in mild case of MELD, the TT4 [AUC value = 0.81; P = 0.021, Significant] was significantly more accurate than the fT3 [AUC value = 0.79; P = 0.007, Significant], TT3 [AUC value =0.75; P = 0.021, Significant] except for TSH (AUC value = 0.47; P = 0.749, Not Significant] and FT4 [AUC value = 0.38; P = 0.246, Not Significant] and graphical presentation of ROC curve analysis was shown in Fig.1.

Table 5: Receiver Operating Characteristic (ROC) curve analysis of thyroid profile for MELD score

	Mild			Severe		
Thyroid profile	**AUC (95% CI)**	**Std. Error**	**P-value**	**AUC (95% CI)**	**Std. Error**	**P-value**
TT3	0.75 (0.55 -0.94)	0.098	0.021*	0.25 (0.06 -0.45)	0.098	0.021*
TT4	0.81 (0.66 - 0.97)	0.079	0.003*	0.19 (0.03 - 0.34)	0.079	0.003*
TSH	0.47 (0.25 - 0.68)	0.111	0.749	0.53 (0.32 - 0.75)	0.111	0.749
fT3	0.79 (0.62 - 0.95)	0.084	0.007*	0.21 (0.05 - 0.38)	0.084	0.007*
fT4	0.38 (0.17 -0.58)	0.106	0.246	0.62 (0.42 -0.83)	0.106	0.246

*AUC: Area under the curve; *p<0.05 - Significant*

4. DISCUSSION

This study describes the comparison of the thyroid profile with liver cirrhosis viruses of hepatitis B and hepatitis C patients. In the present study, 74% of males and 26% of females were studied. Whereas in other studies, it to be 67% of males and 33% of females [16] and 71% of males and 29%of females, respectively [17]. From these, we inferred that the male preponderance of disease compared with females, probably because of high-risk behavior in males. The physical examination revealed that 48.4% of patients were having the habit of alcohol, 90.3%of patients were ascites, 6.5% of patients having SBP, and each one 3.2% of patients had bleeding and HE. Whereas in other studies, 46% of patients had etiology with alcohol, 74% of patients had ascites, 38% of patients had HE [17].

In a study of Patira *et al.* [18], 26% were mild, 52% were moderate, and 22% were severe patients; whereas in the present study, 23% were mild, 45% were moderate, and 32% were severe patients in CTPS group. The level of fT3 and fT4 significantly decreased, and the mean of TSH increased in chronic hepatitis C virus with cirrhosis compared with chronic hepatitis C virus without cirrhosis patients for the CTPS group. These results coincided with El-Feki *et al.* [16], and Punekar *et al.* [17], Patira *et al*. [18]. The present study is contradictory to the results of El-Feki *et al*. [16], Punekar *et al.* [17], and Patira *et al.* [18], and comparison of mean values of fT4 for CTPS group. In other studies, TT3, fT3, and fT4 had shown a significantly negative correlation for the CTPS group [9, 18]. In this study, there was a significant low negative correlation between TT3 Vs. CTPS group and also the TT4 Vs. CTPS group.

In the present study, 58% were mild patients, and 42% were severe patients in the MELD group, and the mean values for TT3, TT4, fT3, fT4in the severe group were shown significantly lower compared with the mild group except for the TSH. In a study by Punekar *et al.* [17], the mean value significantly decreased in fT3, fT4 been reduced, and TSH was significantly increased compared with controls in the MELD group. In other studies, TT3, fT3, and fT4 had shown a significantly negative correlation for the MELD group [9, 17, 18]. In this study, there was a significant low negative correlation between TT3 Vs. MELD group, TT4 Vs. CTPS group, and fT3 Vs. MELD group. In a study by Tas *et al.* [9], the AUC value of the fT3 shown significantly higher value in the MELD group, which coincides with the present study.

The limitations of the present study are, it is a hospital-based study and not a population-based study, and the sample size is very less; a thyroid profile of healthy people not included as a control group in this study. Hence, we recommend a multicenter randomized study of thyroid profile with the liver cirrhosis viruses with long term follow up and an adequate number of patients.

5. CONCLUSION

We concluded that the mean values for TT3, TT4, and free T3 in the CTPS group and the mean values for the TT3, TT4, and free T3 in the MELD group were shown significantly decreased by increasing the level of severity. There is a significant negative correlation of TT3, TT4 and free T3 for both CTPS and MELD groups. The level of sensitivity is significantly more in the free T4, TT4, free T3 and TT3 for severity of CTPS

group and TT4 and free T3 for mild CTPS group, whereas the level of sensitivity is also significantly more in the TT3, free T3, and TT4 for severity of MELD group and the TT4, free T3 and TT3 for mild MELD group. Thus, the thyroid profile in liver cirrhosis of patients can be used as prognostic indicator.

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