Correlation Of Serum Ft3 Level With Serverity Of Liver Dysfunction In Patients With Chronic Liver Disease

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INTRODUCTION

Chronic liver disease in the clinical context is a disease process of the liver that exceeds more than 6 months. It involves a process of progressive destruction and regeneration of the liver parenchyma that leading to fibrosis and cirrhosis[1]. The liver has pivotal role in thyroid hormone metabolism because it is the manufacturing house of various proteins that bind thyroid hormone such as thyroxine binding globulin (TBG), pre-albumin and albumin.[2] It is also the major site of thyroid hormone peripheral metabolism in the form of conjugation, biliary excretion, oxidative deamination and the extra thyroid deiodinnation of thyroxine (T4) to tri iodothyronine (T3) and to reverse T3.[3] hence it is as expected that thyroid dysfunction have been reported in various spectra of liver disease and associated with severity of liver disease.[4,5]

Type I deiodinase is the major enzyme in the liver disease, this study was done to measure FT3, FT4 and TSH serum levels in patients with CLD and to look for any correlation between TFT abnormalities and severity of CLD.

AIMS AND OBJECTIVES

1. To estimate thyroid hormone levels (FT3, FT4 and TSH) in patients with CLD.
2. To see the correlation between FT3, FT4 and TSH levels with severity of the disease.

2) MATERIALS AND METHODS :

a) Study design: Hospital based observational study, FAAMCH, Barpeta, Assam.

b) Study period: 1 Year, from1st March 2020 to 31st February 2021.

c) SAMPLING METHOD : The sample size was calculated based on the systematic review by Eshraghian A and Taghavi SA.(6) According to this review, the prevalence of thyroid abnormalities in cirrhosis of liver ranges from 13% to 61%. The total sample size was calculated according to the formula; $N = z^2pq/L^2$ (where z=1.96, p stands for prevalence (61%), q=100- p, L= relative error= 15% of p), the corrected sample size was 113. However, we managed to enroll 100 patients in our study during the period of 1 year. Out of which 73 were male and 27 females.

d) Study participants with inclusion and exclusion criteria: The study enrolled 100 Chronic liver disease patients irrespective of etiological agents out of which were 73 male and 27 females .Written informed consent was obtained from all patients..

i. Inclusion Criteria:

(1) Patients with symptoms, signs, biochemical and radiological features of chronic liver disease irrespective of causes.
(2) Patients >18 years of age.

ii. Exclusion Criteria:

1) Patients below 18 years
2) Patients with known thyroid disorder and known Diabetic.
3) Patients on any regular medication that might interfere with thyroid metabolism.
4) Patients with other causes of sick euthyroid syndrome.
5] Ascites due to other causes.

e) SOURCE OF DATA: Department of General Medicine, OPD and IPD, Fakhruddin Ali Ahmed Medical College and Hospital, Barpeta.

f) ETHICAL COMMITTEE APPROVAL: The present study was approved by the ethical committee.

g) Diagnostic tool: Diagnosis of cirrhosis was based on case history, clinical examination, biochemical,ascitic fluid analysis, endoscopic and abdominal ultrasound findings.

Functional **s**everity of chronic liver disease was assessed by Child Turcotte Pugh (CTP) scoring systm: **Child class A:** score of **5-6**; **Child class B:** score of **7-9**; **Child class C:**score of **10-15**.

The severity of encephalopathy is classified using the WEST-HAVEN CRITERIA**.**

Thyroid Hormonal assessment:
Serum free T3 (FT3), free T4 (FT4) and TSH were measured by Chemiluminescence Immunoassay (CLIA).
The normal ranges for thyroid functions in our laboratory are as follows:
FT3 : 2.1- 3.8 nmol/lit
FT4 : 0.82 - 1.63 nmol/lit
TSH = 0.465- 4.680 µIU/ml

h) Type of biological materials :5 ml of freshly drawn early morning fasting venous blood sample.

STATISTICAL ANALYSIS:

The data was analyzed using SPSS version 25 software.

Results: A total of 100 patients with Chronic liver disease were enrolled in this study. The results of this research are explained by the following tables:

Table 1: Distribution of patients according to Child-Pugh score:

	Class-A	Class-B	Class-C	Total
Female	3	8	16	27(27%)
Male	5	21	47	73(73%)
	8(8%)	29(29%)	63(63%)	100(100%)

8% cases belong to CPS-A, 29% in B, 63% in C. Thus most of our patients presented to us in advanced stage of decompensated cirrhosis of liver.

Table 2-Mean value of TSH with respect to different Child Pugh class:

TSH	CPS-A	CPS-B	CPS-B	P value
Mean± SD	2.7 ± 1.7	3.6 ± 3	3.3 ± 2.9	0.7162

Mean values of TSH in CPS-A, B and C were 2.7 ± 1.7, 3.6 ± 3 and 3.3 ± 2.9 respectively and the difference in means was statistically insignificant with a P value of 0.7162.

Table 3-Mean value of FT3 with respect to different Child Pugh class :

FT3	CPS-A	CPS-B	CPS-C	P value
Mean± SD	2.8 ± 0.6	2.1 ± 0.9	1.6 ± 0.8	0.0472

Mean values of FT3 in CPS-A, B and C were 2.8 ± 0.6 , 2.1 ± 0.9 and 1.6 ± 0.8 respectively and the difference in means was statistically significant with a P value of 0.0472.

Table 4- Mean value of FT4 with respect to different Child Pugh class:

FT4	CPS-A	CPS-B	CPS-C	P value
Mean± SD	1.4 ± 0.2	1.3 ± 0.3	1.4 ± 0.3	0.4396

Mean values of FT4 in CPS A, B and C were 1.4 ± 0.2,1.3 ± 0.3 and 1.4 ± 0.3 and the difference in means was statistically insignificant with a P value of 0.4396 .

Table 5: Correlation between TSH,FT3,FT4 and Child-pugh score :

Correlations				
		TSH	FT-3	FT-4
CPS	Pearson Correlation	0.005	-0.377	0.137
	P-Value	0.962	0.001	0.180

TSH and FT4 are found to be positively correlated with Child-pugh score with correlation co-efficient of 0.005 and 0.137 respectively, with statistically insignificant P values of 0.962 and 0.180.

FT3 is found to be negatively correlated with Child-pugh score with correlation co-efficient of -0.377 with statistically significant P value of 0.001.

DISCUSSION:

This study shows that most of the patients presented in advanced stage of chronic liver disease (decompensated).
We found a significant decrease in FT3 level in accordance with the severity of liver dysfunction according to Child-Pugh classification, where patients with Child-Pugh C showed significantly decreased FT3 level compared to Child's A and Child's B patients.

These results are in agreement with **Abd Allah Ahmed El-Sawy** et al.[7] **, Agha F et al[8]** , **Fariborz Mansour-Ghanaei et al**[9] .

However in our study, no statistically significant correlation observed between FT4 and TSH with Child Pugh score.

Low FT3 levels may be due to alterations of two main enzymes acting in the liver as part of the iodo-thyronine seleno-deiodinase enzyme system. The type1 and type 3 deiodinases are responsible for extra-thyroidal production of T3 and inactivation of thyroid hormones, respectively. The decrease in total T3 is probably reflecting a reduced deiodinase type1 activity, resulting in reduced conversion of T4 to T3 and an increase in conversion of T4 to reverse T3 by the deiodinase type 3 system in the liver of cirrhotic patient. Although, despite alteration in serumT3, serum TSH and T4 are reported to be steady, indicating adaptive mechanisms by which the body reduces basal metabolic rate and preserve the liver function[9,10] .

The significant correlation in our Study between serum FT3 and the severity of liver dysfunction as well as a progressive decrease in FT3, suggests that FT3 concentrations in patients with advanced liver cirrhosis may be considered as a helpful indicator of severity. It also appears that the degree of depression of serum FT3 correlate well with the severity of liver disease, and maybe helpful in assessing the course and diagnosis of liver cirrhosis.

CONCLUSION:

This study revealed that Free T3 level decreases as the Childpugh class (A-C) increases. FT3 levels were inversely correlated with the Child Pugh class and previous studies also suggested similar results.

Thus low FT3 level is associated with more severe liver injury, hence FT3 can be used as a marker of severity in cirrhosis of liver.

LIMITATIONS OF THE STUDY:

- The present study was a single centred hospital based study with small sample size so results obtained in this study cannot be generalised.
- Liver biopsy was not done to confirm liver cirrhosis due to logistic constrains and as it is an invasive procedure.
- Detailed work up for thyroid profile like reverse T3 and thyroid antibodies like thyroperoxidase antibody, thyroglobulin were also not carried out.

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