Research Article

Correlation of Thyroid Function Tests in Patients with Liver Cirrhosis Due to Hepatitis C

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Abstract

Objective: To determine correlation of thyroid function test in patients with liver cirrhosis due to hepatitis C.

Methods: A cross-sectional study with non-probability purposive sampling technique was carried out at gastroenterology OPD Unit 1 LGH, Lahore from October 2019 to September 2020 after approval from ethical review board of PGMI/ LGH. Total 110 patients diagnosed with liver cirrhosis (Child Pugh Scores A, B, C) due to hepatitis C on abdominal ultrasound and 110 healthy individuals were included. After informed consent and physical examination, data was recorded and blood sample was taken for analysis of all liver enzymes (total bilirubin, aspartate aminotransferase, alanine aminotransferase and alkaline phosphatase, serum albumin) and thyroid function tests (free T3, free T4 and TSH). Pearson correlation and ANOVA test were applied to analyze data.

Results: Out of 110 cirrhotic patients, 61.81% were males and 38.18% were females and mean age was 50.12+7.06. There were 58(52.72%) patients in Class C, 58(52.72%) patients in Class B according to Child Pugh Score. The level of free T3 was 2.43±1.78, free T4 was 12.19±3.20 and TSH was4.18±3.98 in cirrhotic patients. Significant correlation was found between aspartate aminotransferase, alanine aminotransferase and alkaline phosphatase with both FT3 and FT4. Correlation was also significant statistically between Free T3 ($p < 0.005$) and Free T4 (p 0.045) with CPS.

Conclusion: Patients with liver cirrhosis due to hepatitis C have significantly low free T3 and free T4 as compared to controls and significantly correlated with the liver disease severity. Hence, thyroid levels in cirrhotic patients may be used as a prognostic marker. Low FT3 and high TSH might be used as a predictor of mortality in liver cirrhosis.

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Key Words: Hepatitis C, Cirrhosis, thyroid function tests.

Introduction

Liver cirrhosis is the late stage of different types of liver disorders characterized by scarring and histological alteration of the hepatic tissue with the development of regenerative nodules[1]. Cirrhosis is currently the 11th most common cause of death globally. Almost 3% of the population of world has hepatitis C virus infection and more than 350, 000 die due to HCV related conditions like cirrhosis and hepatic carcinoma[2]. In Pakistan, the prevalence of cirrhosis due to HCV is 13.5 % [3]. The liver has key role in activation and deactivation of thyroid hormones. In liver, thyroxine (T4) is converted into triiodothyronine (T3) in presence of deiodinase. Thyroid gland secretes T4 which is mostly bound to plasma

proteins[4]. The conjugation, excretion of thyroid hormone and the synthesis of thyroid binding globulin also occurs in liver. Furthermore, level of the T3, T4, free triiodothyronine (FT3) and free tetraiodothyronine (FT4) depend on the stage of the liver cirrhosis As, the disease progresses there is systematic reduction in the thyroid hormone levels[5].Serum triodothyronine level can be used as a marker to estimate the damage caused to the liver due to cirrhosis[6]. Cirrhotic patients may have hypothyroidism, hyperthyroidism or thyroiditis. Previous studies claimed that levels of thyroid hormones & binding proteins are deranged among hepatic cirrhotic patients. The reduction in total T3 and FT3 levels is the utmost common change in blood levels of thyroid hormones, which is related to hepatic derangement[7]. Till date no study clearly mentioned the correlation of thyroid hormones levels with liver cirrhosis due to hepatitis C. This study was conducted on patients with hepatitis C related cirrhosis to observe spectrum of thyroid profile and prognosticate the liver damage in such patients. The aim of this study was to assess the correlation of thyroid function test in patients with cirrhosis due to hepatitis

Methods

A cross-sectional study with non-probability purposive sampling technique was carried out at gastroenterology OPD Unit 1 LGH, Lahore from October 2019 to September 2020 after approval from ethical review board of PGMI/ LGH. Sample size was calculated using Rao soft calculator. After informed consent, total 110 patients with age range 18-65 years, both male & female diagnosed with liver cirrhosis (Child Pugh scores A, B, C) due to hepatitis C on abdominal ultrasound and 110 healthy individuals were also enrolled in the study. Patients with known thyroid disease, pregnancy or any other metabolic disorder were excluded. After detailed history and physical examination, blood sample was taken for analysis of all liver enzymes (total bilirubin, alanine aminotransferase and aspartate aminotransferase, alkaline phosphatase, serum albumin) and thyroid function tests (free T3, free T4 and TSH). LFT was measured by using fully automated biochemistry analyzer (HITACHI). Serum free triidothyronine, free tetraidothyronine & TSH were analyzed by ELISA method. Abdominal ultrasound was performed in every patient. Prognosis of liver cirrhosis was categorized by Child Pugh score.

SPSS version 21 was used to evaluate data. The qualitative data was measured as frequency and percentage. The quantitative data was calculated as mean and standard deviation. Pearson correlation was used to find relationship between thyroid function tests and liver enzymes. Association between the thyroid function tests and Child Pugh score classes was found by ANOVA test. p value ≤ 0.05 was taken as statistically significant.

Results:

A total 110 patients with cirrhosis due to hepatitis C participated including 68(61.81%) males and 42 (38.18%) females. Average age of cirrhotic patients was 50.12±7.06 years. 72 (65.45%) patients with cirrhosis were in group of age ranges between 41 to 65 years. The mean level of free T3 was 2.43±1.78, free T4 was 11.29±3.20 and TSH was 4.18±3.98 in cirrhotic patients whereas normal values for free T3, free T4 and TSH are 2.3 - 4.1 pg /ml, 12- 30 pg/ml and 0.5 to 4.0 µIU/ml respectively. Descriptive variable, clinical and lab data of patients having cirrhosis and healthy patients is reported in **Table I**

Table I: *Descriptive, clinical and lab data of patients having cirrhosis and healthy patients*

Parameter		Cirrhotic patients n = 110	Healthy controls n = 110
Age (years)		50.12±7.06	39.42±9.06
Age groups	18-40 yrs	38(34.54%)	60(54.54%)
	41-65yrs	72(65.45%)	50(45.45%)
Gender	Male	68(61.81%)	70(63.63%)
	Female	42(38.18%)	40(36.36%)
SBP (mmHg)		114.57±13.58	110.23±15.43
BMI (kg/m^2)		23.43±3.42	21.98±2.61
Total Bilirubin (mg/dl)		3.10±2.07	1.20±0.27
ALT (U/L)		75.63±58.13	18.25±14.28
AST (U/L)		80.77±29.32	19.45±8.75
ALP (U/L)		210.35 ±95	185.02±21.29
Albumin (mg/dl)		3.21±1.39	4.21±0.49
Free T3 (pg/ml)		2.43±1.78	3.5±1.5
Free T4 (pg/ml)		11.29±3.20	15.8±2.2
Thyroid stimulating hormone (µIU/ml)		4.18±0.98	3.3±0.5

The results showed that correlation between ALT, AST and ALP was statistically significant with both FT3 and FT4 as shown in **Table II.**

Table II: *Relationship between Thyroid function test & liver function tests*

Lab parameters		Total bilirubin (mg/dl)	ALT (U/L)	AST (U/L)	ALP (U/L)	Albumin (mg/dl)
free T3 (pg /ml)	Pearson correlation	0.121	0.231*	0.217*	0.221*	0.232
	p-value	0.781	0.012	0.031	0.015	0.861
free T4 (pg /ml)	Pearson correlation	0.461	0.278*	0.251*	0.183*	-0.041
	p-value	0.654	0.002	0.122	0.041	0.713
thyroid stimulating hormone (µIU/ml)	Pearson correlation	-0.007	-0.054	-0.018	0.004	-0.035
	p-value	0.943	0.521	0.784	0.872	0.691

*p value = <0.05 statistically significant

When the thyroid function tests were compared with Child Pugh Score, the research results showed that there was a significant relationship between levels of Free T3 p =< 0.005 and Free T4 p =0.045 with Child Pugh Score whereas TSH levels were in significant as shown in **Table III.**

Table III: *Association between thyroid function test with Child Pugh score*

Thyroid function test	Child Pugh score	n (%)	Level (Mean ± SD)	p value
Free T3 (pg/ml)	A	15(13.63%)	2.85 ± 0.8	< 0.005*
	B	37(33.63%)	2.82 ± 0.9	
	C	58(52.72%)	2.62 ± 0.5	
Free T4 (pg/ml)	A	15(13.63%)	14.89 ± 1.6	0.045*
	B	37(33.63%)	13.74 ± 2.1	
	C	58(52.72%)	12.02 ± 1.3	
Thyroid stimulating hormone (µIU/ml)	A	15(13.63%)	2.69 ± 4.6	0.312
	B	37(33.63%)	3.41 ± 2.4	
	C	58(52.72%)	4.3 ± 3.2	

*p value = ≤0.05 statistically significant

Discussion:

Thyroid hormones help in maintaining body temperature and metabolic homeostasis. T3, T4 and TSH play important role in cell differentiation[8]. The association of the normal hepatic function and normal level of thyroid hormone profile is important as they both directly relate to each other[9]. In this study the average age of cirrhotic patients was 50.12±7.06 years with 61.81% males. Study done by Patira NK. et al, showed similar results. There were 72% patients in age group 41-60 years & more male (78%) as compared to females were present in the study[10]. Chaudary S. et al, in his study showed same results where males (71%) were involved[11]. In this study, most patients were presented in the advanced phases of liver cirrhosis. In current study, 58(52.72%) patients were in class C of Child Pugh score followed by 37(33.63%) in class B and 15(13.63%) were in class A. Similar result was observed in a study where 56.86% patients were classified as class C and 39.22% as class B[12].

The level of free T3 and free T4 was found low and serum TSH level was high in patients with cirrhosis as compared to normal healthy controls. A study by

Punekar P. et al, reported that in all cirrhotic patients T3 levels and serum T4 levels were low and TSH levels were raised[13]. These findings are similar with our study outcomes i.e. low serum T3 levels (2.43±1.78), low serum T4 levels (11.29±3.20) and increased serum TSH levels (4.18±0.98) as compared to healthy controls. The reason of these altered results includes change in level of thyroid binding proteins, reduced hepatic clearance of reverse T3 and impaired conversion of T4 to T3. In patients with cirrhosis, Type 1 deiodinase is inhibited due to fibrosis hence there is decreased conversion of T4 to T3[14]. Low FT3 levels were the most consistent finding in many studies. In the studies by Deepika et al and D'costa, the levels of FT3 were significantly low in liver cirrhosis patients[15,16].

In this study free T3 and free T4 were correlated positively whereas TSH levels were negatively correlated with total bilirubin, aspartate transaminase (AST) and alanine transaminase. A study by Yadav *et al* showed similar results but Mansour-Ghanaei et al reported negative correlation of T3 levels[17,18]. The lowest levels of free T3 was found in the Child C 2.2±0.5 group followed by the Child B group while the Child A group was 2.85±0.8 in this study which are similar with study done by Vincken S et al [19]. A local study in 2012 also stated that free T3 levels were significantly low in Child C score [20]. Correlation between different CPS categories was statistically significant with FT3 (p=<0.005) and FT4 (p=0.045). A study done by Shergill GS. et al showed similar results with significant relationship between Child Pugh scores and free T3 and free T4[21].

Conclusion:

Patients with liver cirrhosis due to hepatitis C have significantly low free T3 and free T4 as compared to controls and significantly correlated with the liver disease severity. Hence, thyroid levels in cirrhotic patients may be used as a prognostic marker. Low FT3 and high TSH might be used as a predictor of morbidity & mortality in liver cirrhosis.

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