LOW SERUM FREE TRI-IODOTHYRONINE HORMONE AS A POSSIBLE PROGNOSTIC FACTOR IN ALCOHOL RELATED LIVER DISEASE.

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ABSTRACT

Introduction: The levels of thyroid hormone & thyroid binding proteins are altered in patients of chronic liver disease. Our aim was to assess the serum freeT3 and serum free T4 levels, in alcohol related liver disease and to find the correlation between thyroid hormone levels and severity of alcohol related liver disease.

Methods: A cross sectional study, with a sample size of 50, was done to assess the serum free T3 andserum free T4 levels of thyroid function andto correlate them with prognostic factors of alcohol related liver disease, i.e.MELD-Na - which is derived by adding serum sodium to the original Model for End-Stage Liver Disease (MELD) score and Maddrey'sDiscriminant Function (DF).Statistical analysis was done with - Chi-Square test, p value <0.001 was considered as statistically significant.

Results: Of the 50 patients, low serum free T3 levels were found in 29 patients, among them15 patients had DF<32; 14 patients had DF>32(p value <0.001), and 14 patients had MELD-Na<24.50; 15 patients had MELD-Na >24.50(p value <0.006). Low serum freeT4 levels were found in 12 patients, among them 4 patients had DF<32;8 patients had DF >32 (p value <0.001), and 8 patients had MELD <24.50; 4 patients had MELD >24.50(p value <0.825).

Conclusion: Significant decrease in the serum free T3 levels was found in patients of alcohol related liver disease with Maddrey'sDiscriminant Function >32 and MELD-Na >24.50 (both prognostic markers of more severe liver disease). Hence, low serum free T3 level can be used as a prognostic indicator of severity of alcohol related liver disease.

Keywords: Thyroid dysfunction, free T3, free T4, TSH, alcohol related liver disease.

Introduction

The levels of thyroid hormone & thyroid binding proteins are altered in patients of chronic liver disease. Liver plays an important role in the metabolism of thyroid hormones. In the production of 3,5,3 triiodothyronine (T3) by the action of selenium dependent 5' deiodinase.[(1)]Low free T3 syndrome is frequently described in patient with cirrhosis of liver and is characterized by, low T3 and decreased T3:T4 ratio. Liver also has a dominant role in the production and secretion of thyroid binding globulin.[(2)]

Thyroid diseases may perturb liver function; liver disease modulates thyroid hormone metabolism; and a variety of systemic diseases affect both the organs.[3] There are clinical and laboratory associations between thyroid and liver diseases. Patients with chronic liver disease may have thyroiditis, hyperthyroidism, or hypothyroidism. Patients with subacute thyroiditis or hyperthyroidism may have abnormalities in liver function tests, which return to normal as the thyroid condition improves. [4]

Thyroid dysfunction has been reported among the medical problems associated with chronic alcohol abuse .[5, 6, 7] In a study by Liappas I et al[8], done on alcohol-dependant individuals , the majority of individuals (70%) presented with slightly altered peripheral thyroid hormone levels at the beginning of detoxification with reduced T3 levels and normal T4 and TSH levels.However, a significant percentage of individuals (30%) showed increased T3 levels, accompanied by normal levels of T4 and TSH.The alterations in peripheral thyroid hormone levels had returned to normal at the end of the detoxification period.

In this study our aim was to assess the freeT3 and free T4 levels, in alcohol related liver disease and to find the correlation between thyroid hormone levels and severity of alcohol related liver disease.

Methodology

A cross sectional study was conducted at Bowring and Lady Curzon hospital, BMCRI.

Inclusion criteria:

Patient between the age group of 18-80 years who were known and established cases of alcohol related liver disease by clinical/radiological (ultrasound abdomen), and/or biochemical study, after completion of a standard alcohol detoxification protocol.

Exclusion Criteria:

Patient withhistory of thyroiddisorder, diabetes mellitus and/or chronic kidney disease.

Patient with history of organ failure, cancer, radio or chemotherapy,

Patient with active infection/sepsis

Patient on drugsthat are known to alter thyroid functions.

Sample Size Calculation:

The following formula was used for calculating the sample size in our cross-sectional study:

$n=Z^2 (1-P)/d^2$

- n = sample size,
- Z= 1.96 (95% confidence interval)
- P (prevalence) = 0.6 (based on the systematic review by Eshraghian A and Taghavi SA, which estimated the prevalence of thyroid abnormalities in cirrhosis of liver as 13% to 61%),
- d (precision) was assumed as 0.15.

The above formula yielded a sample size of 61; however, we managed to enroll 50 patients in our study.

Statistical Analysis

Study population: 50, all of them had alcohol related liver disease/cirrhosis. Statistical Analysis was done using Chi square test – to find the correlation between free T3 & free T4 level with the MELD – Na and Maddrey's Discriminant function (DF).P value <0.001 was considered as significant.

Results

The mean age in our study was 42.4 years, mean free T3 levels was 3.02 pg/dl, mean free T4 levels was 7.38 ng/dl and mean TSH levels was 2.92µg/dl. (Table: 1)

Table 1: Mean value of age and thyroid function test in patient of chronic liver disease.

		Mean ± S.D. – In Present Study
Age (in Years)	---	42.4 ± 9.5 years
Thyroid function test	Normal reference range	Mean ± S.D. – In present study
Free T3	3.10 – 6.80 pg/dl	3.02 ± 1.77 pg/dl
Free T4	12.0 – 22.0 ng/dl	7.38 ± 5.17 ng/dl
TSH	0.27 – 4.20 µg/dl	2.92 ± 1.46 µg/dl

In patients with DF <32, 15 out of 35 (42.8%) had low free T3 levels and in those with DF >32, 14 out of 15 (93.3%) had low free T3 levels, which was statistically significant. (Table: 2)

Table 2: Comparison between Free T3 levels of patients with DF.

Free T3 levels	DF<32 (n=35)		DF>32 (n=15)		Total (n=50)	
	No. of patients	%	No. of patients	%	No. of patients	%
Low	15	42.85 %	14	93.33%	29	58%
Normal	20	57.15%	01	6.67%	21	42%
$X^2 = 10.982$ (df = 1); p<0.001						

In patients with DF <32, 4 out of 35 (11.4%) had low free T4 levels and in those with DF >32, 8 out of 15 (53.3%) had low free T4 levels, which was statistically significant. (Table: 3)

Table 3: Comparison between Free T4 levels of patients with DF.

Free T3 levels	DF<32 (n=35)		DF>32 (n=15)		Total (n=50)	
	No. of patients	%	No. of patients	%	No. of patients	%
Low	4	11.42 %	8	53.33 %	12	24 %
Normal	31	88.57 %	7	46.67 %	38	76 %
$X^2 = 10.109$ (df = 1); p<0.001						

In patients with MELD-Na <24.5, 14 out of 32 (43.7%) had low free T3 levels and in those with MELD-Na >24.5, 15 out of 18 (83.3%) had low free T3 levels, which was statistically significant. (Table: 4)

Table 4: Comparison between Free T3 levels of patients with MELD – Na Score

Free T3 levels	MELD – Na < 24.5 (n=32)		MELD – Na > 24.5 (n=18)		Total (n=50)	
	No. of patients	%	No. of Patients	%	No. of patients	%
Low	14	43.75 %	15	83.33 %	29	58 %
Normal	18	56.25 %	3	16.67 %	21	42 %
$X^2 = 7.410$ (df = 1); p< 0.006						

In patients with MELD-Na <24.5, 8 out of 32 (25%) had low free T4 levels and in those with MELD-Na > 24.5, 4 out of 18 (22.2%) had low free T4 levels, which was not statistically significant. (Table: 5)

Table 5: Comparison between Free T4 levels of patients with MELD – Na Score

Free T3 levels	MELD – Na < 24.5 (n=32)		MELD – Na > 24.5 (n=18)		Total (n=50)	
	No. of patients	%	No. of Patients	%	No. of patients	%
Low	8	25 %	4	22.22 %	12	24 %
Normal	24	75 %	14	77.77 %	38	76 %
$X^2 = 0.049$ (df = 1); p< 0.825						

Discussion:

Liver diseases are known to have thyroid hormone abnormalities. Thyroid function tests may be abnormal in asymptomatic liver cirrhosis patients. The abnormalities include derangements in T3, T4 in spite of normal TSH values. [9, 10] The serum levels of T3 and the severity of liver dysfunction have an inverse correlation. Derangements in Thyroid profile have been studied as a marker of liver disease prognosis, and were studied in patients awaiting liver transplantation. Cirrhosis of liver constitutes one of the major reasons of presenting to the hospitals both in the departments of Medicine and Gastroenterology in India.[11]Cirrhosis patients constitute a significant proportion of inpatients in our hospital. Many studies were done regarding the thyroid functions in chronic liver disease of various etiologies. Few studies were done in India also, however there is no study of thyroid profile in alcohol related liver disease in this part of the country, where there is major contribution of inpatients by alcoholic cirrhosis. [12, 13]

EARLIER STUDIES

Indian study – done at KGMULucknow, was a cross-sectional study of thyroid function tests in patients of cirrhosis of liver. A sample size of 102 patients includedthose with cirrhosis of liver. Derangement in thyroid profile was common in patient with cirrhosis of liver. Lower free T3 and T4 levels were associated with more severe liver injury and may be used for prognostication in patients with cirrhosis of liver.[14]

International study – done in Sudan, was a case-control study of serum Thyroid Hormone Levels in Sudanese patients with Liver Cirrhosis, with a sample size of 40 patients. The study revealed a significant decrease level of T3 in patients with cirrhosis and an insignificant change in TSH and T4 levels than control groups. [15]

OUR STUDY

In our study, 29 (58%) out 50 patients had low free T3 levels. Among 15 patients with DF>32, free T3 level was low in 93% (14/15).Among 18 patients with MELD – Na> 24.5, free T3 level was low in 83% (15/18).Significantly low level of free T3 was found in patients with DF > 32 and MELD-Na>24.5 (both prognostic markers of more severe liver disease).

Also in our study, 12(24%) out of 50 patients had low free T4 levels.Among 15 patients with DF>32, free T4 level was low in 53% (8/15).Among 18 patients with MELD- Na>24.5, free T4 level was low in 22% (4/18). No significantly low level of free T4 was found in patients with MELD-Na>24.50.

Significant decrease in the free T3 levels were found in patients with alcohol related liver disease.Significant decrease in the free T3 levels were found in patients withalcohol related liver disease, with a Maddrey'sDiscriminant function >32. Significant decrease in the free T3 level were found in patients withalcohol related liver disease, with a MELD-Na>24.50. Hence, low serum free T3 level can be used as a prognostic indicator of severity in patients with alcohol related liver disease.

Conclusions

Low serum free T3 levels can be used as a prognostic indicator of severity in patients with alcohol related liver disease. There is association of significant decrease in serum free T3 level with Maddrey's Discriminant Function more than 32 and MELD-Na score more than 24.50.

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