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"A CLINICAL STUDY OF CIRRHOSIS WITH SPECIAL REFERENCE TO THYROID FUNCTION"

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ABSTRACT

Background-It is known that impaired thyroid function affect the liver function and similarly liver disorders Also affect thyroid function. In this study we looked at the clinical profile of cirrohosis and studied the correlation between cirrhosis and thyroid function.

Methodology- The study was conducted as an observational cross sectional Study on patients with cirrhosis of liver reporting at Department of Medicine, SSMC Rewa (M.P.) during the study period of 15 months i.e. from 1st April 2020 to 30th June 2021. Detailed history regarding risk factors, duration of liver disease, history pertaining to its etiology was obtained. Severity of liver disease was assessed using Child Pugh score. All the patients were then subjected to relevant investigations including Serum T3, T4, TSH.

Results-A total of 100 cases of liver cirrhosis were enrolled in our study with mean age of 53.26±12.54 years. We observed a statistically significant association of Child Pugh Score with T3, T4 as well as TSH ($p<0.05$). We observed a moderate correlation of Child Pugh score with T3 levels and TSH ($r=0.452$ and

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0.311 respectively; $p<0.05$), and weak correlation was observed with T4 ($r=0.240$; $p<0.05$).

Conclusion- In cirrhosis of liver majority of subjects show impaired thyroid functions. Thyroid hormone levels are helpful in assessing the severity as well as course of cirrhosis and among T3,T4,TSH value,TotalT3 faired as better predictor of severity of cirrhosis.

Keywords- Thyroid dysfunction, cirrhosis, Child Pugh, encephalopathy, ascites

INTRODUCTION

The thyroid gland is an endocrine gland which produce two types of hormones i.e. T3, T4 thyroid hormones. These hormones are necessary for meeting the demands of the peripheral tissues and regulate basal metabolic rate. These hormones play an important role in the regulation of growth of nervous tissues, maintaining thermogenic and metabolic homeostasis among adults.[1,2] Normally T4 is the predominant hormone whereas T3 is bioactive hormone which is secreted in very minute quantity.[3]Deiodination is one of the important pathway of metabolism of thyroid hormones due to which inactive T4 is converted into active T3 hormone.[4] The enzyme required in these processes include D1 and D2 deiodinases and Type I deiodinase (D1) is mainly secreted by liver whereas D2 is mainly found in central nervous tissue.[3] Thus, hepatic enzyme D1 is particularly helpful in peripheral conversion of T4 to T3 as well as it is the main site for the clearance of plasma reverse T3.[3,5] Apart from metabolism of thyroid hormones, liver is also involved in conjugation and excretion of thyroid hormones.[6]

Cirrhosis of liver has been described as an end stage of any chronic liver disease and is characterised by alteration of normal lobular structure of liver and fibrosis or nodular formation due to chronic liver injury. Cirrhosis of liver is associated with number of complications including portal hypertension and end stage liver disease.[7]

Literature suggest that thyroid disorders impairs the liver function and similarly liver disorders affect thyroid functions. Hypothyroidism, hyperthyroidism or thyroiditis has been observed in patients of chronic liver disease. Similarly, abnormalities of liver functions have been documented in patients with thyroid dysfunction.[6] Cirrhotic patients with low T3 and T4 levels have comparatively severe liver disease. Low thyroid hormone levels can be used as prognostic markers as well as in predicting the mortality in liver cirrhosis patients.[9] Thyroid function test should be carried out in all patients presenting with cirrhosis of liver

to assess the severity and prognostication of such patients. Data regarding the effect of cirrhosis on thyroid function and correlation of thyroid hormone levels in patients with cirrhosis is scarce and variable especially in low middle income countries. The present study was therefore conducted at tertiary care centre with the aim to study clinical profile of cirrhosis of liver and to assess its correlation with thyroid function.

METHODOLOGY

The study was conducted as an observational cross sectional on patients with cirrhosis of liver reporting to at Department of Medicine, Sanjay Gandhi Memorial Hospital associated with Shyam Shah Medical College, Rewa (M.P.) during the study period of 15 months i.e. from 1st April 2020 to 30th June 2021. All the patients belonging to age range of more than 18 years, diagnosed with chronic Liver Disease and consenting for the study were included whereas patients with **r**enal failure, Nephrotic syndrome , Cardiac failure, Malignancy, pre-existing thyroid disorder, pregnant women, receiving drugs known to interfere with thyroid hormone metabolism and function and not consenting for study were excluded.

After obtaining ethical clearance from Institute's ethical Committee, all participants fulfilling inclusion criteria were included in the study was interviewed and information was recorded on a predesigned, pretested and semi-structured questionnaire. Detailed information regarding addiction especially alcohol, its duration of use was recorded. Data regarding duration of liver disease, history pertaining to its etiology was obtained and documented. All the patients were subjected to detail physical examination. Anthropometry data was obtained and BMI was calculated. Severity of liver disease was assessed using Child Pugh score.

All the patients were subjected to routine investigations including CBC, random blood sugar, Liver Function Tests, Renal function Tests, Serum T3, T4, TSH and other relevant investigations .

STATISTICAL ANALYSIS

Data was compiled using Ms-Excel and analysed using IBM SPSS software version 20. Data was grouped and expressed as frequency and percentage whereas numerical data was expressed as mean and SD. Correlation of cirrhosis with thyroid function test was done using spearman correlation coefficient. P value less than 0.05 was considered statistically significant.

RESULTS

A total of 100 cases of liver cirrhosis were enrolled in our study with mean age of

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53.26 ± 12.54 years.

Table 1- Distribution according to baseline variables

Baseline variables		Frequency (n=100)	Percentage
Age (years)	18 – 40	20	20
	41 – 60	49	49
	≥ 60	31	31
Gender	Male	80	80
	Female	20	20
Clinical features	Pallor	73	73
	Icterus	82	82
	Edema	68	68
Grade of ascites	Grade 1	8	8
	Grade 2	35	35
	Grade 3	57	57

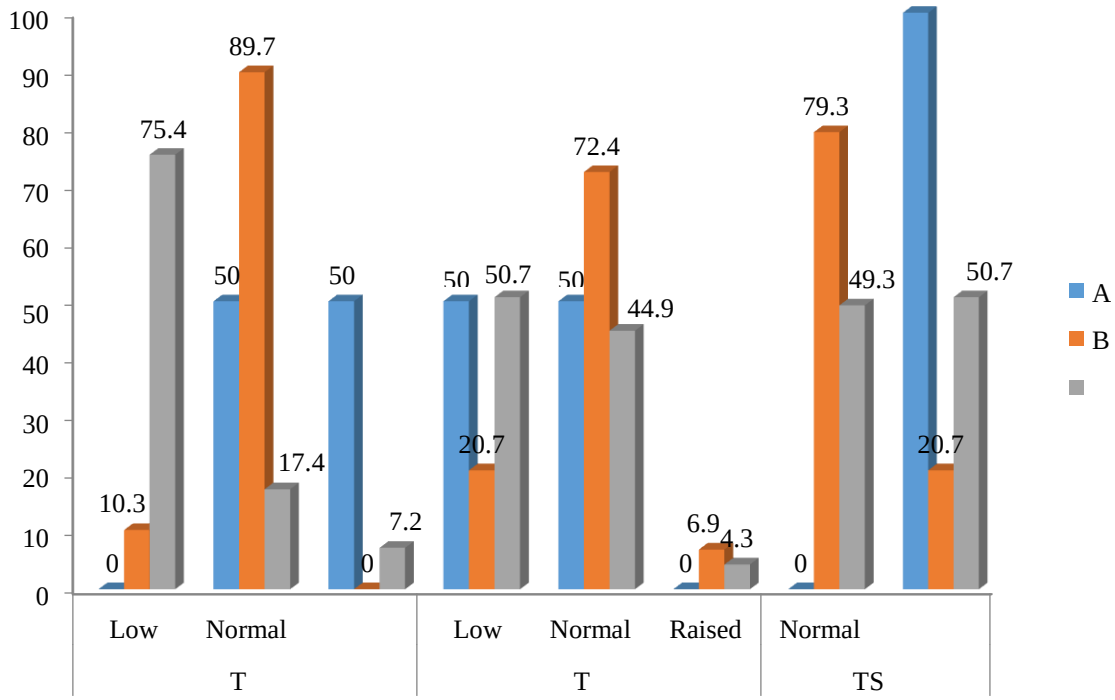
Hepatic encephalopathy	Absent		Grade 0	46	46
	Present	Covert	Grade 1	9	9
		Overt	Grade 2	5	5
			Grade 3	33	33
			Grade 4	7	7
Child Pugh Grade			A	2	2.0
			B	29	29.0
			C	69	69.0
			Mean		10.94 ± 2.64
T3 (ng/mL)			Low	55	55.0
			Normal	39	39.0
			Raised	6	6.0
			Mean		1.02 ± 0.78
T4 (µg / dL)			Low	42	42.0
			Normal	53	53.0

	Raised	5	5.0
	Mean		6.31 ± 3.48
TSH (µUI/mL)	Normal	57	57.0
	Raised	43	43.0
	Mean		4.92 ± 2.44

Majority of cases belonged to 41 to 60 years of age (49%) and male predominance was observed for cirrhosis in a ratio of 4:1.Most common feature in cases with cirrhosis was icterus (82%), followed by pallor (73%) and edema (68%).

Majority of cases with cirrhosis had grade 3 ascites (57%), and overt encephalopathy was seen in (45%) cases. Mean Child Pugh score in patients with liver cirrhosis was 10.94 ± 2.64 and majority of cases had severe cirrhosis i.e. grade C (69%), followed by 29% cases with grade B and only 2% cases belonged to grade A. Low T3, T4 and raised TSH corresponding to hypothyroidism was noted in 55%, 42% and 43% cases respectively. However, T3 and TSH were raised in only few cases (Table 1).

Figure 1 - Association of Child Pugh score with thyroid function tests



In present study, majority i.e. 75.4% cases with Child Pugh Grade C had low T3 levels whereas 50.7% cases had low T4 and high TSH levels each. The present study observed a statistically significant association of Child Pugh Score with T3, T4 as well as TSH ($p<0.05$).

Table 2- Correlation of Child Pugh Score with Thyroid function test

CPS	R	R Square	Adjusted R Square	Std. Error of the Estimate	F	Sig.
T3	0.4	0.204	0.196	0.	25.12	0.

	52			7.02	9	0.001
T4	0.240	0.058	0.048	3.398	5.984	0.016
TSH	0.311	0.097	0.088	2.331	10.520	0.002

We observed a moderate correlation of Child Pugh score with T3 levels and TSH (r=0.452 and 0.311 respectively; $p<0.05$), and weak correlation was observed with T4 (r=0.240; $p<0.05$).

DISCUSSIONS

Cirrhosis of liver is an end stage of any chronic liver disease and is characterised by alteration of normal lobular structure of liver and fibrosis or nodular formation due to chronic injury. Liver is involved in major metabolic processes and in cirrhosis the hormones which are metabolized in the liver are affected. The enzyme involved in thyroid metabolism i.e. Type I deiodinase (D1) is mainly secreted by liver which is helpful in peripheral conversion of T4 to T3 as well as it is the main site for the clearance of plasma reverse T3.[3,5] Thyroid hormones are also known to affect the function and regulation of hepatocytes, playing an important role in modulating liver function.[6]

In present study, a total of 100 cases of liver cirrhosis were enrolled with varying severity of cirrhosis using Child Pugh Score. Mean Child Pugh Score was

10.94± 2.64 and majority of cases belonged to Child Pugh C (69%). our study findings are concordant with the findings of Chaudhary et al where majority of cases were in Child Pugh Class C (56.36%) followed by Class B (31.82 %).[10] However, in a study of Samarthanaet al, majority of cirrhotic belonged to Class B

(45%) followed by class C (31%).[11] Majority of patients with cirrhosis in a study of Punekar et al belonged to Child C class and MELD in the range of 10 to 19 these findings concordant to findings of our study .[12]

The aim of our study was to assess the TFT by biochemical assay of T3, T4, TSH in subjects who were diagnosed with cirrhosis and to correlate these levels with severity of cirrhosis. T3 levels were lower in 55% cases whereas T4 levels were low in 42% cases. Raised TSH were observed in 43% cases. We observed a negative association as well as correlation of severity of liver cirrhosis using Child Pugh with T3 and T4 levels whereas with increase in severity of cirrhosis, increase in TSH was observed ($p<0.05$). Amongst various thyroid hormones, T3 showed moderate correlation with Child Pugh score whereas both T4 and TSH were weakly correlated. Our study findings were concordant to the finding of previous studies and the results were equivalent to those studies comparing free hormonal levels rather than total. Thus, not only free, total thyroid hormone (free +bound) are affected in liver disorders. Samarthana et al[11] documented hypothyroidism in 64% cases with liver cirrhosis. High TSH and low total T3levels were correlated significantly with the severity of disease. The authors also assessed free T3 levels along with total T3 and concluded FT3 to be more sensitive marker in assessing the severity of cirrhosis.[11] Harischandra et al in their case control study documented significantly lower T3 and T4 levels in cases as compared to controls but the TSH levels were similar in both the groups.[13]

Neeralagi et al, also showed that thyroid dysfunction was noted in approximately one fourth patients of liver cirrhosis, and thyroid dysfunction especially hypothyroidism was significantly associated with higher Child Pugh score.[14] Chaudhary et al observed low FT3 and FT4 levels in 24.6% and 10% cases with cirrhosis whereas 22.7% cases had high TSH levels. The authors documented a significant correlation of CPC with FT3 ($p=0.0048$) and FT4

(p=0.045).[10] Verma et al also observed a significant inverse correlation of free T3 and free T4 with severity of liver disease.[15]

CONCLUSION

Thyroid functions are significantly altered in patients with cirrhosis of liver. Thyroid hormonal levels are helpful in assessing the severity as well as course of cirrhosis. Amongst T3, T4, TSH value, total T3 is better predictor of severity of cirrhosis. Depending upon the availability, thyroid function tests (whether free or total) must be assessed in all the cases with cirrhosis to not only assess the severity but also to assess the prognosis of such patients.

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