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Original Research Article

A Study of Thyroid Dysfunction in Cirrhosis of Liver and Correlation with Severity of Liver Disease

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Abstract

Background: Liver plays an important role in the metabolism of thyroid hormones, as it is the most important organ in the peripheral conversion of tetraiodothyronine (T4) to triiodothyronine (T3) by Type 1 deiodinase.

Methods: This cross-sectional study was carried out at a tertiary care hospital, in central Rajasthan among 360 cases of cirrhosis of liver from all causes getting admitted in Medicine & Gastroenterology wards of JLN Medical college & Associated Hospitals, Ajmer after prior written and informed consent. Ethical approval was obtained from the Ethical Committee of this institution.

Results: The mean FT3 levels were found to decrease (p=0.03) while the TSH levels increased (p=0.002) with increase in MELD score in the present study. This is due to impaired peripheral conversion of T4 to T3 by Type I deiodinase in cirrhotic liver. The sensitivity of FT3 in detecting the cirrhosis of liver at cut off of 1.05 MELD score was 91.8% and specificity 88.5%. The sensitivity of FT4 in detecting the cirrhosis of liver at cut off of 0.32 MELD score was 95.9% and specificity 84.7%. The sensitivity of TSH in detecting the cirrhosis of liver at cut off of 0.88 was 100% and specificity was 70.9%.

Conclusion: The mean FT3 levels were found to be decreasing, while the TSH levels were found to be increasing with increase in MELD score due to impaired peripheral conversion of T4 to T3. The mean portal vein diameter was observed to increase with increase in MELD score because of development of portosystemic collaterals in cirrhotic liver which results in portal hypertension and dilatation of portal vein.

Keywords: MELD, T4, T3, Liver disease.

Introduction

In clinical terms, cirrhosis is described as are either "compensated" or "decompensated." Decompensation means cirrhosis complicated by one or more of the following features: jaundice, ascites,

hepatic encephalopathy (HE), or bleeding varices. Ascites is the usual first sign. Hepatorenal syndrome, hyponatremia, and spontaneous bacterial peritonitis are also features of decompensation, but in these patients, ascites invariably occurs first. Compensated cirrhotic patients have none of these features. [1]

The thyroid gland produces two-related hormones, thyroxine (T4) and triiodothyronine (T3). Acting through thyroid hormone receptors α and β, these hormones play a critical role in cell differentiation during development and help maintain thermogenic and metabolic homeostasis in the adult. T4 is secreted from the thyroid gland in about twenty-fold excess over T3. Both hormones are bound to plasma proteins, including thyroxine-binding globulin, transthyretin (formerly known as thyroxine binding prealbumin), and albumin. [2]

The liver plays an important role in the metabolism of thyroid hormones, as it is the most important organ in the peripheral conversion of tetraiodothyronine (T4) to T3 by Type 1 deiodinase. [3,4] Type I deiodinase is the major enzyme in the liver and accounts for approximately 30%–40% of extrathyroidal production of T3, it can carry out both 5'-and 5-deiodination of T4 to T3. Moreover, the liver is involved in thyroid hormone conjugation and excretion, as well as the synthesis of thyroid binding globulin. T4 and T3 regulate the basal metabolic rate of all cells, including hepatocytes, and thereby modulate hepatic function. The liver metabolizes the THS and regulates their systemic endocrine effects. Thyroid diseases may perturb liver function; liver disease modulates thyroid hormone metabolism; and a variety of systemic diseases affect both the organs. [5-6] 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. [6]

Material and Methods

Source of the Study

This cross-sectional study was carried out at a tertiary care hospital, in central Rajasthan among 360 cases of cirrhosis of liver from all causes getting admitted in Medicine & Gastroenterology wards of JLN Medical college & Associated Hospitals, Ajmer after prior written and informed consent. Ethical approval was obtained from the Ethical Committee of this institution.

Study Design: Cross-sectional study

Sample Size: From previous studies prevalence of dyslipidemia with cirrhosis was 36.6% and prevalence of hypothyroidism was 62% with cirrhosis of liver.

The sample size was estimated based on prevalence of disease and using formula, $n = z^2pq / d^2$, where; n=sample size, z=1.96(considering 0.05 alpha, 95% confidence limits and 80% beta), p = assumed probability of occurrence or concordance of results, q = 1 – p and d = marginal error (precession).

STUDY PERIOD: September 2021 to September 2022.

Inclusion Criteria

- Patients age more than 18 years with cirrhosis of liver

Exclusion Criteria

- History of thyroid disease prior to development of liver disease
- Patients on thyroid medications already eg. levo-thyroxine, propylthiouracil
- Patients on lipid lowering drugs eg. Statins, fibrates
- Drugs altering the thyroid profile levels. eg. Amiodarone, Lithium, Phenytoin
- Drugs altering the lipid profile levels eg. Amiodarone, Loop and thiazide diuretics,

- Diabetes mellitus
- Hypertension
- Cerebrovascular disease
- Cardiovascular disease
- Pancreatitis
- Pregnant women
- Patients on long term Beta- blockers therapy.

Methodology

This was cross sectional study to assess correlation of lipid profile and thyroid profile in severity of cirrhosis of liver among 360 patients admitted to the Medicine & Gastroenterology wards of JLN Medical College and Associated hospitals, Ajmer with cirrhosis of liver due to various causes diagnosed clinically, biochemically and radiologically. Fasting serum lipid profile & Thyroid profile was measured in all patients diagnosed with cirrhosis.

Triglycerides and HDL was measured by direct method and serum LDL shall be calculated by using Friedewald formula. LDL cholesterol = Total cholesterol – {HDL cholesterol-TG/5}.

Serum free T3 (FT3) & free T4 (FT4) was measured by direct Radio immuno assay. S. TSH was measured by chemiluminenescence immuno assay (CIA).

All the patients was assessed by detailed history and physical examination and was also be asked about past history of jaundice, blood transfusion, marital and sexual history and duration of alcoholism (if present), history of thyroid disease before the development of liver disease.

Physical examination in search of stigmata of chronic liver disease was routinely done in all patients. Ophthalmologic examination (Slit- lamp examination) was done to look for KF ring. Detailed cardiovascular and neurological examination shall be done.

Every patient was investigated in the following order after the completion of physical examination

Statistical Analysis

Statistical analysis was performed using SPSS 20 software and the analyzed data was expressed in percentages. P-value equal to or less than 0.05 was considered to be significant.

Results

Table 1. Socio-demographic profile

Mean age	45.05±11.36 yrs
Male : Female	40:360

Table: 2. Mean thyroid profile value with severity of cirrhosis (meld score) of liver

	MELD SCORE								P value
	≤10		11 to 18		19 to 24		>24		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
FT3 (pg/ml)	2.05	0.86	1.93	0.58	1.801	0.49	1.68	0.54	0.03
FT4 (ng/dl)	0.86	0.35	1.006	0.62	0.99	0.41	0.93	0.59	0.64
TSH (µIU/ml)	4.38	2.38	5.94	2.69	6.69	1.98	6.43	1.77	0.002

Table 3: ROC analysis for thyroid profile to predict meld score

	Area Under the Curve	Cutt off	P value	Sensitivity	Specificity
FT3 (pg/ml)	0.516	1.05	0.01 (S)	91.8%	88.5%
FT4 (ng/dl)	0.581	0.32	0.64	95.9%	84.7%
TSH (µIU/ml)	0.561	0.88	0.01 (S)	100%	70.9%

Discussion

In patients with MELD score ≤10, mean FT3, FT4, and TSH levels were 2.05±0.86 pg/ml, 0.86±0.35 ng/ml and 4.38±2.38 µIU/ml respectively.

In patients with MELD score 11-18, mean FT3, FT4, and TSH levels were 1.93±0.58 pg/ml1.006±0.62 ng/ml and 5.94±2.69 µIU/ml respectively.

In patients with MELD score 19-24, mean FT3, FT4, and TSH levels were 1.801±0.49 pg/ml1.0.99±0.41 ng/ml and 6.69±1.98 µIU/ml respectively.

In patients with MELD score >24, mean FT3, FT4, and TSH levels were 1.68±0.54 pg/ml1.0.93±0.59 ng/ml and 6.43±1.77 µIU/ml respectively.

The mean FT3 levels were found to decrease while the TSH levels increased with increase in MELD score in the present study as peripheral conversion of T4 to T3 impaired in cirrhotic liver. The alterations in FT4 were non-significant.

In study by Punekar P et al., [7] the mean FT3 levels and mean FT4 levels were decreasing with increase in disease severity assessed by MELD score. The mean FT4 levels had a correlation with MELD scores but they were statistically non-significant. But a significant correlation between the mean TSH and MELD score was observed. The mean TSH levels tend to increase with increase in MELD score which is comparable to our study.

In study done by Buden RP et al., [8] the mean FT3 and FT4 level were found to be significantly decreased and mean TSH level were significantly increased with increase in MELD score which is comparable to our study in terms of FT3 and TSH.

Mobin et al [9] observed that among all(n=76) patients with decompensated cirrhosis, 76.3% had low T3 levels,14.47% had low T4 levels, while 2.63% had increased levels of TSH. [10] Similar findings were observed in study by Punekar P et al., [7]

Conclusion

The mean FT3 levels were found to be decreasing, while the TSH levels were found to be increasing with increase in MELD score due to impaired peripheral conversion of T4 to T3. The mean portal vein diameter was observed to increase with increase in MELD score because of development of portosystemic collaterals in cirrhotic liver which results in portal hypertension and dilatation of portal vein.

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