Original Research Article

Study of association between chronic liver disease and thyroid function tests at a tertiary hospital

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Abstract

Background: Among the various functions of liver, one function is synthesis of carrier proteins and metabolism of hormones and liver diseases, have been shown to be associated with various endocrinal disturbances. Aim of the study was to evaluate the spectrum of chronic liver disease and association between thyroid profile and severity of liver damage at a tertiary hospital. **Material and Methods:** Present study was single-center, hospital based, case-control study, conducted in 88 cases of liver cirrhosis/ chronic liver disease and 88 age/sex matched healthy controls (randomly selected from relatives attending OPD with patients) were studied. Thyroid function tests were done and compared among cases and controls. **Results:** In present study 88 cases of liver cirrhosis/ chronic liver disease and 88 healthy controls were studied. Mean age and gender were comparable in cases and controls and difference was not statistically significant. Most of cases had alcoholic liver cirrhosis (80.7 %), rest had non-alcoholic liver cirrhosis (12.5%) and chronic viral hepatitis (6.8%). As per Child-Pugh Score, most cases were from Child-Pugh B (42%), followed by Child-Pugh C (31.8%) and Child-Pugh A (26.1%). In present study free T3, free T4 and TSH were compared between cases and controls, abnormal values were noted in cases and statistically significant difference was noted. Serum thyroid profile abnormalities were noted as per advancement in Child-Pugh Score Classes and difference was statistically significant for free T3 and free T4. **Conclusion:** Thyroid function test abnormalities in circulating thyroid hormone concentrations were noted in patients liver cirrhosis as compared to healthy subjects and severe abnormalities were associated with advanced Child Pugh score.

Keywords: chronic liver disease; cirrhosis, Liver function tests; Free T3 and T4; TSH;

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INTRODUCTION

Among the various functions of liver, one function is synthesis of carrier proteins and metabolism of hormones and liver diseases, have been shown to be associated with various endocrinal disturbances.[1,2] Cirrhosis and chronic liver failure are leading causes of morbidity and mortality worldwide, majority of cases are preventable and attributed to excessive alcohol consumption, viral hepatitis or nonalcoholic fatty liver disease. Thyroid hormones are essential for normal organ growth, development and function. The major secretory product of the thyroid is a prohormone (T4), which is activated in peripheral tissues by outer ring deiodination to T3. In addition to the deiodination to activate and deactivate thyroid hormones, liver plays an important role in the metabolism of thyroid hormone like conjugation, peripheral deiodination and synthesis of thyroid binding globulin.[3,4] Thyroid diseases may perturb liver function; liver disease modulates thyroid

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hormone metabolism; and a variety of systemic diseases affect both the organs.[4] Aim of the study was to evaluate the spectrum of chronic liver disease and association between thyroid profile and severity of liver damage at a tertiary hospital

MATERIAL AND METHODS

Present study was single-center, hospital based, case-control study, conducted in department of physiology with help from department of internal medicine at Sri Manakula Vinayagar Medical College and Hospital, Puducherry, India. Study duration was of 1 year (April 2013 to March 2014). Institutional ethical committee approval was taken prior to start of study. A written informed consent was taken from all the participants. 88 cases and 88 age/sex matched healthy controls (randomly selected from relatives attending OPD with patients) were studied.

Inclusion criteria for cases: Patients > 18 years, presented with liver cirrhosis/ chronic liver disease

Exclusion criteria for cases: Patients with pregnancy, previously known thyroid disease, diabetes, nephrotic syndrome renal failure or any other acute or chronic illnesses. Patient receiving drugs that may interfere with thyroid hormone metabolism and function like amiodarone, phenytoin, beta blockers, steroids, estrogen and iodine containing drugs/contrast. Patients who refused to give consent.

A detailed history including history suggestive of hypothyroidism, hyperthyroidism and liver cirrhosis was taken followed by a detailed general examination (pallor, icterus, edema, hydration status, asterixis, stigmata of chronic liver disease like alopecia, spider naevi, parotid enlargement, palmar erythema, gynaecomastia and testicular atrophy), thyroid, abdominal and neurological examination. Cases and controls were asked to follow-up in early morning with nil by mouth for 8-10 hours. With all aseptic measures, 5 ml of blood was collected and sent for complete blood count (CBC), random blood sugar, liver function test (LFT) i.e., total bilirubin, direct bilirubin, alanine transaminase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP) total protein and albumin level, renal function test (RFT), hepatitis B surface antigen, hepatitis C virus antibodies and thyroid function tests i.e., free T3 (FT3), free T4 (FT4) and thyroid stimulating hormone (TSH). Also, ultrasonography of abdomen and pelvis was done to note liver size, echotexture, portal vein diameter, presence of collaterals, gall bladder, common bile duct, spleen size, abdominal collection, renal size, echotexture and corticomedullary differentiation. Severity of liver cirrhosis was categorised by Child Pugh score (CPS).

Data was collected and compiled using Microsoft Excel, analysed using SPSS 23.0 version. Frequency, percentage, means and standard deviations (SD) was calculated for the continuous variables, while ratios and proportions were calculated for the categorical variables. Difference of proportions between qualitative variables were tested using chi- square test or Fisher exact test as applicable. P value less than 0.5 was considered as statistically significant.

RESULTS

In present study 88 cases of liver cirrhosis/ chronic liver disease and 88 healthy controls were studied. Mean age and gender were comparable in cases and controls and difference was not statistically significant. Most of cases had alcoholic liver cirrhosis (80.7 %), rest had non-alcoholic liver cirrhosis (12.5 %) and chronic viral hepatitis (6.8 %). As per Child-Pugh Score, most cases were from Child-Pugh B (42 %), followed by Child-Pugh C (31.8 %) and Child-Pugh A (26.1 %).

Table 1: General information

General information	Cases (n=88) No. of cases (%)	Controls (n=88) No. of cases (%)	P-Value
Mean Age	51.5 ± 13.7	52.1 ± 15.7	0.72
Gender			0.82
Male (n %)	73 (83.0 %)	70 (79.5 %)	
Female (n %)	15 (17.0 %)	18 (20.5 %)	
Diagnosis			
Alcoholic liver cirrhosis	71 (80.7 %)		
Non-alcoholic liver cirrhosis	11 (12.5 %)		
Chronic Viral Hepatitis (HBV/HCV)	6 (6.8 %)		
Classification according to Child-Pugh Score			
Child-Pugh A	23 (26.1 %)		
Child-Pugh B	37 (42 %)		
Child-Pugh C	28 (31.8 %)		

In present study free T3 , free T4 and TSH were compared between cases and controls, abnormal values were noted in cases and statistically significant difference was noted.

Table 2: Comparison of Serum thyroid profile

	Reference range	Cases (n=310)	Controls (n=250)	P-Value
Free T3 (pg/ml)	2.3 - 4.1	1.86 ± 0.62	2.87 ± 0.56	< 0.001
Free T4 (ng/dl)	0.9 - 1.7	0.62 ± 0.49	1.29 ± 0.81	< 0.001
TSH (mIU/ml)	0.3-4.5	0.93 ± 1.26	3.23 ± 2.35	< 0.001

Serum thyroid profile abnormalities were noted as per advancement in Child-Pugh Score Classes and difference was statistically significant for free T3 and free T4cx.

Table 3: Comparison of Serum thyroid profile among Child-Pugh Score Classes

Thyroid function	CPS categories (Mean ± Standard Deviation)			Total (n=110)	P-value
	CPS A (n=13)	CPS B (n=35)	CPS C (n=62)		
Free T3	1.92 ± 0.92	1.36 ± 0.81	1.01 ± 0.55	1.56 ± 0.62	0.002
Free T4	0.84 ± 0.29	0.67 ± 0.44	0.46 ± 0.54	0.62 ± 0.49	0.005
TSH	1.90 ± 1.06	1.23 ± 0.96	0.99 ± 0.69	0.93 ± 1.26	0.308

DISCUSSION

The liver plays a central role in thyroid hormone metabolism, transport, and clearance by producing thyroid binding globulin, albumin and transthyretin.[5] In India, alcohol is the commonest cause of cirrhosis (34.3%) and almost 20% of all liver disease patients and a significant proportion of liver-related mortality of unknown etiology may well be attributable to alcohol.[6] Non-alcoholic fatty liver disease (NAFLD) defined by hepatic fat accumulation in the absence of hereditary and autoimmune conditions, drug-induced liver injury, alcohol consumption, or viral etiology. The prevalence of NAFLD has increased substantially during the past decades, genetics, obesity, unhealthy lifestyle, and other metabolic risk factors could be responsible for the burgeoning evolution.[7,8] The low total and FT3 levels may be regarded as an adaptive hypothyroid state that serves to reduce the basal BMR within hepatocytes and preserve liver function and total body protein stores.[4] Patira NK *et al.*[9] noted that majority of patients (72%) belonged to age group 41-60 years with male predominance (78%). While Punekar *et al.*[10] noted that males (71%) were involved more than female. Similar findings were noted in present study. Ashish Kumar *et al.*[11] studied 50 patients, (35 males and 15 females, male to female ratio of 2.33) with liver cirrhosis. 21 patients had alcoholic liver disease, 20 had Hepatitis C, 5 had hepatitis B and 4 patients had cryptogenic cirrhosis. On assessment of severity of cirrhosis 26 patients belonged to CTP A, 19 to CTP B and 5 to CTP C. Subclinical hypothyroidism was seen in 5 out of 50 patients (10 %) and hyperthyroidism was observed in 2 cases (4%). Among the patients with hypothyroidism, 3 had ethanol related liver cirrhosis, 1 had Hepatitis C whereas 1 had cryptogenic cirrhosis. Two Patients with hyperthyroidism belonged to CTP A; one had cryptogenic cirrhosis and one has hepatitis C. High incidence of abnormalities in circulating thyroid hormone concentrations i.e. hypothyroidism is noted especially in those with ethanol related liver cirrhosis and it is associated with more advanced liver disease. Chaudhary S *et al.*[12] studied 110 patients with liver cirrhosis and 110 healthy controls, mean age of patients was 51.1±12.13 years and Male : Female ratio of 4:1. According to Child Pugh score (CPS) 62 (56.36%) patients were in Class C, 35 (31.82 %) patients were in Class B. Low level of FT3 was seen in 27 (24.6%) patients, low level of FT4 was in 11 (10 %) patients and high TSH level was seen in 25 (22.7 %) patients. Overall abnormal TFT levels were seen in 43 (39.1 %) patients. overt hyperthyroidisms in 3 (2.7%) patients, subclinical hypothyroidism in 14 (12.7%) patients, overt hypothyroidism in 11 (10%) patients. Isolated low FT3 level was seen in 15 (13.06 %) patients. Correlation between AST, ALT and ALP were found to be statistically significant with both FT3 and FT4. Correlation between different CPS categories was found to be statistically significant with mean score of FT3 (p=0.0048), and mean score of FT4 (p=0.045). G. Deepika *et al.*,[13] studied 310 cirrhotic patients and 250 control subjects. They noted that there was a significantly increased between cirrhotic patients and non-cirrhotic subjects for TSH and slightly decreased T3 and T4 where the p value is 0.039, 0.014 and 0.245 respectively. The mean of TSH levels of cirrhotic patients is higher than the mean of non-cirrhotic subjects and show significant difference. And also there is significant difference for T4 between two groups, but T3 seems no significant difference between two groups. Punekar P *et al.*, [10] noted that, the mean FT3 and FT4 levels were significantly c and mean TSH levels were significantly increase in liver cirrhosis patients and also correlated with the severity of liver disease. Jaswanth Kumar P *et al.*,[14] studied 70 alcoholic liver disease patients to assess and compare the levels of thyroid hormones- free T3, free T4, Thyroid Stimulating Hormone (TSH) and Gamma Glutamyl Transferase (GGT) before and after treatment. Serum GGT levels decreased free T4, T3 levels increased and TSH

levels are not altered significantly with treatment. Additionally, free T3 showed a significant correlation with GGT before and after treatment and free T4 and TSH showed a significant correlation with GGT after treatment. Thyroid hormones levels, particularly free T3 and free T4, need to be evaluated in chronic alcoholic liver disease patients and during the withdrawal and abstinent periods as decreased hormone levels may increase withdrawal effects and craving for alcohol. He W *et al.*,[15] conducted a meta-analysis and noted a strong epidemiological evidence for the relationship between hypothyroidism and non-alcoholic fatty liver disease (NAFLD). Both individuals with subclinical and overt hypothyroidism are at higher risk for NAFLD than euthyroid subjects. Knowledge of the association between hypothyroidism and deranged biochemical markers of liver function is important for the clinician to consider an evaluation of thyroid function in the workup of the patient with altered liver function tests. Limitations of present study were single center, small sample size and diagnosis of cirrhosis in each case was not confirmed histopathologically.

CONCLUSION

Thyroid function test abnormalities in circulating thyroid hormone concentrations were noted in patients liver cirrhosis as compared to healthy subjects and severe abnormalities were associated with advanced Child Pugh score.

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