Original Research Paper

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General Medicine

PREVALENCE OF THYROID DYSFUNCTION IN LIVER CIRRHOSIS

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ABSTRACT **Introduction:**Liver plays an imperative role in the metabolism thyroid hormone and its circulation by producing thyroid binding globulin. Present study aimed to find the prevalence of thyroid dysfunction in cirrhosis patient and assess its correlation with severity of cirrhosis.**Materials & Methods:** A hospital based cross-sectional study was conducted at Department of Medicine, Aditya Diagnostics and Hospital, Dibrugarh. Study included 100 patients of cirrhosis diagnosed based on the ground of clinical, biochemical and radiological evidence. Serum T3, T4, fT3, fT4,TSH was determined by Electrochemiluminescence immunoassay. Severity of cirrhosis was calculated by Child Pugh score and correlated with derangement of thyroid functions. **Results:** Overall prevalence of thyroid dysfunction among cirrhotic patients was 35%. Most common thyroid dysfunction seen in chronic liver disease patients was subclinical hypothyroidism (21%) followed by low T3 syndrome (9%). Overt hypothyroidism was seen in 5% cases.Prevalence of thyroid dysfunction was 14.7%, 42.9% and 47.4% in child pugh grades A, B and C respectively ($p<0.05$).Conclusion: Present study observed that derangement in thyroid profile is common in patients with cirrhosis of liver. A statistically significant change was observed in serum T3 and fT3 levels that tend to decline with progressive severity of chronic liver disease and TSH that increases as the severity of chronic liver disease progresses.

KEYWORDS : Chronic Liver Disease, Child Pugh Score, Cirrhosis, Hypothyroidism, Thyroid Dysfunction

INTRODUCTION

Chronic liver diseases (CLD) cause significant morbidity and mortality worldwide. Multiple etiological factors are responsible for development of Cirrhosis, although the rates of progression and clinical course may vary[1,2]. Mortality data is most often used to assess the disease burden and there had been a 46% increase in CLD mortality in the world between period of 1980 to 2013, underscoring the emerging public health importance of CLD.[3]. Chronicity of liver disease is characterised either by duration of liver disease (typically 3-6 months) or by the presence of physical stigmata of chronic liver disease (palmar erythema, spider telengiectasia and hepatosplenomegaly). The severity is variable; and presentation may be different. The affected adults may have only biochemicalor radiological evidence of liver dysfunction, may have stigmata of chronic liver disease, or may present as hepatic failure. As a consequence of greater alcohol consumption, an epidemic of diabetic, obesity and hepatitis B and C infections, the incidence of chronic liver disease is rising worldwide [4].

Etiology of chronic liver disease in adults has a broad spectrum. Overall, the most common causes of chronic liver disease worldwide are alcohol, chronic hepatitis B and C and NAFLD(non-alcoholic fatty liver disease). Primary biliary cirrhosis and autoimmune hepatitis are commonly seen in females, while alcoholism, primary sclerosing cholangitis and hepatitis B are common in males. Genetic diseases such as alpha-1 antitrypsin deficiency, wilson's disease andgenetic cholestatic disease are encountered predominantly in children [4-7].

Liver plays an imperative role in thyroid hormone metabolism and circulation of thyroid hormone by producing thyroid binding globulin [8]. Liver also plays a role in the production of triiodothyronine (T3) by the action of enzyme selenium dependent 5' deiodinase. Besides , the hormonally inactive reverse T3 (rT3) is produced by another selenium independent deiodinase acting on the phenolic ring of thyroxine (T4) [9].

The thyroid hormone levels and thyroid binding proteins are altered in patients of chronic liver disease. Low free T3 syndrome is frequently observed and described in patients with cirrhosis of liver which is characterized by low T3, increased rT3, and decreased T3:T4 ratio [10]. However, Low T3 may be an adaptive thyroid response to reduce the basal metabolic rate of hepatocytes and preserve liver function [11].

Numerous clinicians have reported a sub clinical hypothyroidism in patients with cirrhosis [12-17]. Although studies in different populations and geographical areas vary in their findings of thyroid dysfunction in cirrhosis, low FT3 in the face of a normal TSH and a clinical euthyroidism are consistently found. Free hormone level has been delineated as an indicator of thyroid dysfunction and has been correlated with the degree of severity of liver dysfunction as well.

MATERIALS AND METHODS

A hospital based cross sectional study was conducted at Department of Medicine of Aditya Diagnostics and Hospitals, during the period of one year(1st November 2019 to 31st October 2020). Study included 100 patients with cirrhosis of liver diagnosed by clinical, biochemical and radiological imaging evidence.Patients with known cases of thyroid disorder or on mediations that interfere or interact with thyroid hormone metabolism such as amiodarone, lithium, beta blockers were excluded.

Each patient underwent detailed history taking followed by general and systemic examination,complete history was recorded in a performa and investigated with the following test : Complete hemogram, ESR, Random blood sugar, blood urea, Serum creatinine, Liver function tests, PT/INR, Ultrasound abdomen, fibroscan of liver and thyroid function tests.

Serum T3, T4, fT3, fT4, TSH was determined by Electrochemiluminescence immunoassay (ECLIA). The normal range for thyroid functions in our laboratory was:T3 : 1.3-3.1 nmol / ml; T4 : 66 – 181 nmol / ml; FT3: 3.1—6.8 pmol/L; FT4: 12.0 – 22.0 pmol/L and TSH: 0.25–5.0 µIU/ml.

Any deviation from the normal value range of T3, T4,TSH was considered as thyroid dysfunction [18].

1.Subclinical Hypothyroidism :–T3,T4- within normal limits, TSH- 5-10µIU/ml,
2.Overt Hypothyroidism: - T3,T4- Normal or decreased, TSH- above 10 µIU/ml,
3. Low T3 syndrome- Low T3., TSH- normal,
4. Subclinical Hyperthyroidism- T3 and T4- normal, TSH- decreased or undetectable,
5. Overt Hyperthyroidism- T3, T4- increased., TSH- decreased

Severity of cirrhosis was calculated by Child Pugh score and correlated with derangement of thyroid functions.

Data was entered in Microsoft Excel sheet ver. 2021 and transferred to SPSS ver. 26.0 for statistical analysis. The quantitative data was represented as their mean ± SD. Categorical and nominal data were expressed in percentage. The t-test was used for analysing quantitative data and categorical data was analyzed by using chi-square test. Kandall Tau B correlation co-efficient was used for computing correlation between quantitative variables. The significance threshold of p-value was set at <0.05.

RESULTS

Mean age of the cases with chronic liver disease was 45.34±8.6 years with one third (33%) of the cases were 40 years of age or below. Out of the total 100 cases of chronic liver disease, 71% were males and 29% were females. Severity of chronic liver disease was assessed by child pugh score. Grade A, B and C was observed in 34%, 28% and 38% cases respectively. Low T3 and free T3 levels were seen in 16% and 20% cases while low T4 and free T4 levels were seen in 4% and 3% cases respectively. High TSH was observed in 26% cases (Table 1).

Table 1. Distribution of study cases as per Thyroid Profile

Thyroid Profile	N	%
T3 levels (nmol/ml)		
<1.3	16	16.0%
>/= 1.3	84	84.0%
fT3 levels (pmol/L)		
<3.1	20	20.0%
>/= 3.1	85	85.0%
T4 levels (nmol/ml)		
<66.0	4	4.0%
>/= 66.0	96	96.0%
fT4 levels (pmol/L)		
<12.0	3	3.0%
>/= 12.0	97	97.0%
TSH levels (muIU/ml)		
<0.25	0	0.0%
0.25-5.0	74	74.0%
>5.0	26	26.0%

Low T3 and low free t3 were observed to be significantly associated with increasing CP grade (p<0.05). Similarly, among 26 cases with high TSH levels, 5.9%, 35.7% and 36.8% were in CP grade A, B and C respectively (p<0.05) (Table 2).

Table 2. Association of Thyroid Profile with Chid Pugh Grade

Thyroid Profile	N	CP Grade			p-value
T3 levels (nmol/ml)	A (n-34)	B (n-28)	C (n-38)		
<1.3	16	4	4	8	<0.05
		11.8%	14.3%	21.1%	
fT3 levels (pmol/L)				<0.05	<0.05
<3.1	20	5	5	10	
		14.7%	17.9%	26.3%	
T4 levels (nmol/ml)				0.31	<0.05
<66.0	4	0	2	2	
		0.0%	7.1%	5.3%	
fT4 levels (pmol/L)				0.41	<0.05 <0.05
<12.0	3	0	1	2	
		0.0%	3.6%	5.3%	
TSH levels (muIU/ml)				<0.05	<0.05
<0.25	0	0	0	0	
		0.0%	0.0%	0.0%	
0.25-5.0	74	32	18	24	<0.05
		94.1%	64.3%	63.2%	
>5.0	26	2	10	14	
		5.9%	35.7%	36.8%	

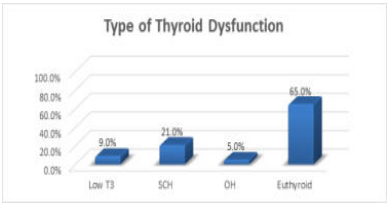
A significant positive correlation was observed between severity of chronic liver disease and TSH levels while an inverse correlation was observed with free and total T3 levels (p<0.01).(Table 3)

Table 3. Correlation of CP Grade with Thyroid Profile

Kendall's Tau B Correlation		
CP GRADE	r-value	p-value
T3	-0.23	<0.01
T4	-0.03	0.6
fT3	-0.52	<0.01
fT4	-0.05	0.4
TSH	0.82	<0.01

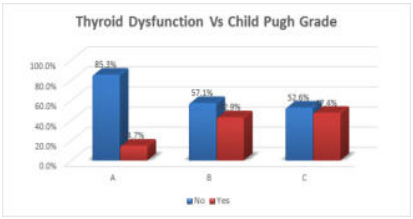
Overall prevalence of thyroid dysfunction among chronic liver disease patients was 35% (Figure 1).Most common abnormality in thyroid function seen was subclinical hypothyroidism (21%) followed by low T3 syndrome (9%),Overt hypothyroidism (5%) \

Figure 1. Type of thyroid dysfunction



No significant association was observed between thyroid dysfunction with gender, age or any specific etiology of cirrhosis (p>0.05).A significant association was observed between presence of thyroid dysfunction and severity of chronic liver disease. Prevalence of thyroid dysfunction was 14.7%, 42.9% and 47.4% in child pugh grades A, B and C respectively (p<0.05) (Figure 2).

Figure 2. Severity of CLD &presence of thyroid dysfunction



DISCUSSION

In this study, it was observed that the prevalence of thyroid dysfunction in cirrhosis patients was 35%. Most common thyroid dysfunction was subclinical hypothyroidism (21%) followed by low T3 syndrome (9%), overt hypothyroidism(5%) . Low T3 and free T3 levels were seen in 16% and 20% cases while low T4 and free T4 levels were seen in 4% and 3% cases respectively. High TSH was observed in 26% cases.

In the study conducted by Kharb et al. [19], thyroid dysfunction was present in 16% of patients. 7% of patient had sick euthyroid syndrome , followed by subclinical hypothyroidism(3.5%), subclinical hyperthyroidism(2.3%), thyrotoxicosis(2.3%) and overt hypothyroidism(1%) . Joeimon JL et al. [20] in their study found hypothyroidism in 21.6%(24 out of 111 patients) . 10.8% had subclinical hypothyroidism and10.8% had overt hypothyroidism(12 out of 111 patients). Verma SK et al. [21] observed low free T3 and T4 in 72.5% and 26.47% of patients respectively and TSH towards the upper limit of normal range in 52.3% of patients. Punekar P et al. [22] observed that cirrhotic patients had statistically significant lower level of FT3 and FT4 amd higher level of TSH compared with the controls. Overall, the most common abnormality observed was low T3 (low FT3) syndrome (41%) followed by hypothyroidism (20%). Patira NK et al. [23] observed prevalence of subclinical hypothyroidism in cirrhosis as 62%.

In this study, Low T3 and low free T3 were observed to be significantly associated with increasing Child Pugh grade (p<0.05). Similarly, among 26 cases with high TSH levels, 5.9%, 35.7% and 36.8% were in Child Pugh grade A, B and C respectively (p<0.05). A significant positive correlation was seen between severity of chronic liver disease and TSH levels while an inverse correlation was seen with T3 and fT3 levels (p<0.01). Prevalence of thyroid dysfunction was 14.7%, 42.9% and 47.4% in Child Pugh grades A, B and C respectively (p<0.05). A significant association was observed between presence of thyroid dysfunction and severity of liver disease and presence of hepatic encephalopathy. Similar findings were concluded by Joeimon JL et al. [20], Verma SK et al.[21], Punekar P et al. [22], Patira NK et al. [23] , Ray AC et al. [24].

The study showed low T4 and free T4 only in 4% and 3% respectively. No significant association was seen between low T4 and/or free T4 with increasing Child Pugh grade. This was in contrast to studies conducted by Verma SK et al.[21], Punekar P et al. [22], Patira NK et al. [23] , Ray AC et al. [24], which shows serum fT4 reduces as the severity of cirrhosis increases.

LIMITATION

The present study was a cross-sectional study therefore a causal relationship between thyroid abnormalities and cirrhosis of liver could not be show. In addition, it is a single-centred study with limited sample size. So,we need to conduct more multi centric study that involves patients of different geographical areas and larger sample size to support our findings. Another limitation was liver biopsy that was not peformed to confirm cirrhosis. Being an invasive procedure, it was avoided. Detailed work up for thyroid profile like reverse T3 and thyroid antibodies [like thyroperoxidase (TPO) antibody, thyroglobulin] were also not done.

CONCLUSION

Present study concluded that derangement in thyroid profile is common in patients with cirrhosis of liver. A statistically significant change was observed in serum T3 and fT3 levels that tend to decline with progressive severity of chronic liver disease irrespective of etiology. Present study thus recommend that all cirrhotic patients should undergo evaluation of thyroid function evaluation as these patients develop thyroid dysfunction, especially hypothyroid status.

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