A Study of Thyroid Profile (FT3, FT4, TSH) in Liver Cirrhosis in Jharkhand - A Hospital based Study

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ABSTRACT

Introduction: Because thyroid hormones and liver hormones are so closely linked, thyroid hormone abnormalities can be found in people with liver disorders.

Aim: To determine the prevalence of thyroid dysfunction in liver cirrhosis patients.

Materials and Methods: This case-control study was carried out in a group of randomly selected liver cirrhosis patients in the Department of Medicine at Rajendra Institute of Medical Sciences (R.I.M.S), Ranchi, Jharkhand (India) between September 2017 to August 2018. The equal number of age (>18 years) and sex-matched cases & controls were included in this study. Radioimmunoassays were used to evaluate early morning fasting blood thyroid-stimulating hormone (TSH), serum total free thyroxine (FT4), and free triiodothyronine (FT3) in 100 index patients with liver cirrhosis who had no history of thyroid disorders.

Results: In the cases that were studied, which consisted of cirrhotic patients, males (80%) outnumbered females (20%). The mean age of cases was 47.9 years, and the maximum numbers of the patient were between 41-55 years of age group (47%). Among the cirrhotic patients, the commonest etiology was alcoholic liver disease which contributed to 78% of the total cases studied. The rest of the cases included cirrhotics from other etiologies, which included NAFLD (22%), HBsAg positive individuals (07%), and other cases of cryptogenic origin. The mean FT3, FT4, and TSH values in cases were 2.29±0.83; 1.20±0.55 & 3.76±2.43 respectively & the mean FT3, FT4, and TSH of the control group were 2.95±0.52; 1.40±0.25 & 2.70±0.94 respectively. From these data, we can say that there is significant derangement of thyroid function in liver cirrhosis in favor of hypothyroidism (p<0.05).

Conclusion: Hypothyroidism, or abnormalities in circulating thyroid hormone concentrations, is seen in people with alcohol-related liver cirrhosis and is linked to more severe liver disease.

Key Words: FT3, FT4, TSH, Hypothyroidism, Liver cirrhosis, NAFLD

INTRODUCTION

The liver is thoroughly involved in proteins, cytokines and interleukins synthesis and destruction. Therefore, abnormal function of endocrine organs is expectable in patients with liver cirrhosis. Similar processes to those seen in sick euthyroid syndrome can occur in several types of liver illness. Still, there are also a variety of modifications specific to the type or stage of liver disease.

The liver monitors and controls the transport, catabolism, and excretion of the thyroid hormones. Thyroxin binding globulin (TBG), the main transport protein of thyroid hormones, is synthesized in the liver and binds over seventy-five percent of the circulating hormones.1 Therefore, dysregulation and dysfunction of thyroid hormones are anticipated in patients with liver cirrhosis.2 According to research utilizing [131I] T4, the liver extracts 5–10% of plasma T4 in a single passage. This result is significantly larger than the quantity of free T4 transported to the liver, implying that there is a significant amount of protein-bound T4 accessible for uptake.3 Although hypothyroidism was more frequently seen in cirrhosis, hyperthyroidism has also been reported in patients with cirrhosis.4 T3 and FT3 concentrations are usually decreased in correlation with the severity of the disease, but this is still controverted.5 This is probably due to reduced deiodinase one activity and subsequent impaired hepatic conversion of
T4 to T3. There are three homologous iodothyronine deiodinases which catalyze these reactions. Type I deiodinase is located in the liver, kidney, and thyroid. In addition to the deiodination to activate and deactivate thyroid hormones, the liver has an essential role in thyroid hormone transport and metabolism.

The endocrine system is a complex, sophisticated system that involves many physiological and pathological processes and functions in the human body. Thyroid hormones regulate BMR in all cells, including hepatocytes, and are necessary for appropriate growth, development, and function of all tissues of the body. Thyroid hormones are metabolized by the liver, which modulates their systemic endocrine effects. Normal thyroid function is required for optimal cell growth, development, and metabolic energy regulation and depends on a normally functioning thyroid and liver axis. Thyroid dysfunction can affect liver function, and liver disease can affect thyroid hormone metabolism, and both organs are affected by a number of systemic diseases.

In individuals with non-thyroidal diseases, low total and free T3 with normal total T4 and thyrotropin concentrations have been often recorded in the absence of clinical hypothyroidism. In a prospective investigation of 118 individuals with cirrhosis, ultrasonography revealed a 17 percent increase in thyroid glandular volume as compared to controls. Low total and free T3 levels may be regarded as an adaptive hypothyroid state that helps to sustain liver function and total body protein reserves by lowering the basal metabolic rate inside hepatocytes. Indeed, a recent study in cirrhotic patients found that the advent of hypothyroidism during cirrhosis due to intrinsic thyroid illness of various etiologies resulted in a biochemical improvement in liver function (e.g., coagulation profile) when compared to controls. Hypothyroidism has also been linked to a lower degree of cirrhosis breakdown. Controlled hypothyroidism may thus be advantageous in cirrhotic patients, but more research is needed to confirm this concept.

The liver has an important role in thyroid hormone metabolism because it is the manufacturer of proteins that bind thyroid hormones, such as thyroid-binding globulin (TBG), pre-albumin, and albumin. It is also the major site of thyroid hormone peripheral metabolism and is involved in its biliary conjugation excretion, oxidative deamination, and the extrathyroidal deiodination of thyroid (T4) to triiodothyronine (T3) and to reverse T3. On the other hand, the level of thyroid hormone is also important to the normal hepatic function and bilirubin metabolism. Conceivably, the disorders of these two organs would interact or influence each other. As liver abnormalities worsen, the T3 production from T4 is also reduced.

It is believed this reduction of T3, which mainly corresponds to an even lower basic metabolism rate, economically can be useful due to preventing extra energy waste and keeping it for the onset of liver disease or any other related syndrome which consumes further energy. Free T3 concentration corresponds with the state of liver disease, and it seems the serum T3 concentration is directly related to liver abnormalities progress.

Furthermore, it is demonstrated that levels of thyroid hormones and their binding proteins are altered in patients with hepatic disorders, especially cirrhosis; however, almost all are clinically euthyroid. These thyroids' liver associations may cause diagnostic confusions, and neglect of these facts may result in over or under-diagnosis of associated liver or thyroid diseases. Therefore it is suggested to measure free T4 and TSH levels to rule out the coexistent possibility of thyroid dysfunction in any patient with unexplained liver biochemical test abnormalities.

**MATERIAL AND METHODS**

The study was carried out in a group of randomly selected liver cirrhosis patients in the Department of Medicine at RAJENDRA INSTITUTE OF MEDICAL SCIENCES (R.I.M.S) Ranchi, Jharkhand (India), from September 2017 to August 2018, which was preapproved by the Ethical Committee of this institution review board. Equal number of age (>18 years) and sex-matched controls were included in this study.

Patients were selected by adhering strictly to certain inclusion and exclusion criteria mentioned underneath.

**Inclusion criteria:**
- Age more than 18 years.
- Both sexes will be included.
- Patients with evidence of liver cirrhosis by ultrasonography.
- The patient/attendant must give informed consent.

**Exclusion criteria:**
- Patients with a history of recent clinical infection, surgery, or major trauma in the previous month.
- Patients in shock
- Patients with metabolic abnormalities
- Patients with a previous/present history of hypothyroidism/ hyperthyroidism.

**Study design:** Case-control study.

**Period of study:** September 2017 to August 2018.

**Sample size:** 200 participants were enrolled for the present study. 100 Patients with evidence of liver cirrhosis...
by ultrasonography were selected for the study during the study period and 100 participants were without evidence of liver cirrhosis & metabolic abnormalities served as controls.

Method of sampling: Early morning fasting serum thyroid-stimulating hormone (TSH), serum total free thyroxine (FT4), and free triiodothyronine (FT3) were measured by radioimmunoassays in 100 index patients with liver cirrhosis who did not have a history of thyroid diseases.

Statistical method: We have analyzed the statistical data by using SPSS statistical software version-20. Descriptive statistics i.e., Mean and Standard deviation (SD) for the continuous variables, and frequency distribution and their percentage for categorical variables were calculated. Independent T-test was calculated for significance. p-value less than 0.05 was considered as the statistical significance level.

RESULTS

Table 1: Sex Incidence of Cases and Controls

<table>
<thead>
<tr>
<th>Sex</th>
<th>Cases</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>%</td>
<td>No.</td>
</tr>
<tr>
<td>Male</td>
<td>80</td>
<td>85</td>
</tr>
<tr>
<td>Female</td>
<td>20</td>
<td>15</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

Table 1 is showing 80% of males and outnumbered females (20%) among the cases, and 85% males and 15% females among the control group.

Table 2: Mean Age of Cases and Controls

<table>
<thead>
<tr>
<th>Mean age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
</tr>
<tr>
<td>Controls</td>
</tr>
</tbody>
</table>

The mean age of cirrhosis occurrence among cases was determined to be 47.90 years in the table -2 above.

Table 3: Distribution of Cases According to Age

<table>
<thead>
<tr>
<th>Age groups (Years)</th>
<th>No. of cases</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>25-40</td>
<td>31</td>
<td>31</td>
</tr>
<tr>
<td>41-55</td>
<td>47</td>
<td>47</td>
</tr>
<tr>
<td>56-70</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>71-85</td>
<td>02</td>
<td>02</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

According to table-3 Maximum numbers of cases were between 41-55 years of age group (47%), and only 2 cases were in 71-85 years of age group.

Table 4: Distribution of Cases According to Past History

<table>
<thead>
<tr>
<th>History</th>
<th>No. of cases</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcoholic</td>
<td>78</td>
<td>78</td>
</tr>
<tr>
<td>Non-Alcoholic</td>
<td>22</td>
<td>22</td>
</tr>
<tr>
<td>HBsAg +ve</td>
<td>07</td>
<td>07</td>
</tr>
<tr>
<td>HBsAg -ve</td>
<td>93</td>
<td>93</td>
</tr>
<tr>
<td>Anti HCV +ve</td>
<td>Nil</td>
<td>-</td>
</tr>
</tbody>
</table>

Above table-4 is showing alcoholic cirrhosis is the most common cause (78%), other causes include NAFLD (22%), HBsAg +ve (07%) & no one was Anti HCV +ve.
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**TABLE 5: Mean FT3, FT4 and TSH Levels in Cases and Controls**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Cases</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>FT3</td>
<td>Mean-SD: 2.29±0.83</td>
<td>2.95±0.52</td>
</tr>
<tr>
<td></td>
<td>‘t’ Value: -6.752</td>
<td></td>
</tr>
<tr>
<td></td>
<td>‘p’ Value: 0.000</td>
<td></td>
</tr>
<tr>
<td>FT4</td>
<td>Mean-SD: 1.20±0.55</td>
<td>1.40±0.25</td>
</tr>
<tr>
<td></td>
<td>‘t’ Value: -3.195</td>
<td></td>
</tr>
<tr>
<td></td>
<td>‘p’ Value: 0.002</td>
<td></td>
</tr>
<tr>
<td>TSH</td>
<td>Mean-SD: 3.76±2.43</td>
<td>2.70±0.94</td>
</tr>
<tr>
<td></td>
<td>‘t’ Value: 4.07</td>
<td></td>
</tr>
<tr>
<td></td>
<td>‘p’ Value: 0.000</td>
<td></td>
</tr>
</tbody>
</table>

The above table-5 is showing mean FT3, FT4 & TSH among cases are (2.29±0.83), (1.20±0.55) & (3.76±2.43) and in controls (2.95±0.52), (1.40±0.25), (2.70±0.94) respectively and is statistically significant (p<0.05).

**DISCUSSION**

Males (80 percent) outweighed females in the cases investigated, which included cirrhotic individuals (20 percent). The average age of the cases was 47.9 years, with the majority of patients falling into the 41-55 year age bracket (47 percent). The most common aetiology among cirrhotic patients was alcoholic liver disease, which accounted for 78 percent of the total cases investigated. Cirrhosis from various etiologies, such as NAFLD (22 percent), HBsAg positive persons (07 percent), and other cryptogenic cases, made up the balance of the cases. Mean serum bilirubin was 2.45 mg/dl, Mean SGOT was 370.29 IU/L, Mean SGPT was 159.14 IU/L, Mean ALP was 146.80 U/L, Mean serum Albumin was 2.47 g/dl, and Mean prothrombin time was 10.59 sec. The controls that were selected were having an almost similar pattern of distribution of the cases with males (85%) and females (15%). Their mean age distribution was 52.26 years.

When the thyroid profiles of patients and controls were compared, some extremely interesting discoveries emerged. The mean FT3, FT4, and TSH values in cases were 2.29±0.83; 1.20±0.55 & 3.76±2.43 respectively & the mean FT3, FT4, and TSH of the control group were 2.95±0.52; 1.40±0.25 & 2.70±0.94 respectively. Based on these findings, we may conclude that thyroid function is significantly altered in liver cirrhosis, favouring hypothyroidism (p<0.05). Despite this biochemical imbalance, it’s worth noting that none of our patients displayed any clinical signs or symptoms of hypothyroidism. G. Deepika et al.21 have carried out a retrospective, cohort study in which the medical records of cirrhosis patients who had been enrolled and found that there was a sig-
nificant increase 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, these findings are consistent with our study.

Thyroid hormone levels in patients with stable liver cirrhosis were compared to healthy controls without liver disease in Vincken S et al.22 Cirrhotic individuals had considerably lower FT3 and FT4 levels than healthy subjects (p = 0.001 and 0.002, respectively).

Joeimon J L et al.23 have estimated the prevalence of thyroid dysfunction in patients with liver cirrhosis. Hypothyroidism was seen in 24 out of 111 patients (21.6%). Only serum TSH increase was seen in 12 patients (10.8%) and Serum TSH increased along with FT3 and FT4 decrease in 12 patients out of 111 patients (10.8%) as observed in our study.

In a case-control research involving 100 decompensated liver cirrhosis patients, Punekar P et al.24 found that cirrhosis patients had a statistically significant lower level of FT3 (p 0.0001) and FT4 (p 0.0001), but a statistically significant higher level of TSH (p 0.0001). They eventually determined that in liver cirrhosis patients, mean FT3 and FT4 levels were much lower, while mean TSH levels were significantly higher, as compared to healthy controls; these findings are congruent with ours.

Cirrhosis was linked to a considerable deviation of thyroid dysfunction in favour of hypothyroidism in our study. And this hypothyroidism may have an impact on the patients’ long-term survival. These factors may be overlooked, resulting in the identification of related liver or thyroid disorders and, as a result, inaccuracies in patient prognosis. To rule out or rule in coexisting thyroid dysfunctions, it is recommended to check free thyroxine (FT4) and thyroid-stimulating hormone (TSH), which are usually normal in euthyroid patients with liver disease, and to look for thyroid dysfunction in any patients with liver problems.

CONCLUSION

The fact that thyroid hormone dysfunction is associated with liver disease has been substantiated by our data, which revealed that there is a clear trend towards abnormalities in circulating thyroid hormone concentrations, i.e. hypothyroidism, which is seen more frequently in those with ethanol-related liver cirrhosis and is linked to more advanced liver disease.

In our study population, the most common cause of chronic liver disease and cirrhosis was alcoholism, and men outnumbered females in all categories, indicating that alcoholic cirrhosis is more prevalent in Jharkhand, necessitating further research and implementation of health awareness among the general public.

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Authors’ Contribution:

Vishwanath Malkappa Jalawadi – Concept, Study design, data analysis, manuscript preparation and statistical analysis.

Upendra Prasad Yadav – Data collection, manuscript drafting

Ajit Dungdung – Manuscript preparation

Dr(Prof) Bindey Kumar – Guidance.

Rashmi Sinha – Co-guidance and statistical analysis.

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