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Original Research Article

Thyroid in Acute and Chronic Liver disease

A Study of Thyroid Hormone Patterns in Patients with Acute and Chronic Liver Disease

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Abstract: Thyroxine and tri-iodothyronine are essential for normal organ function, growth, and development. Thyroxine and tri-iodothyronine regulate the basal metabolic rate, which includes hepatocytes, thereby modulating liver function. The liver plays a vital role in the metabolism of thyroid hormones and the peripheral conversion of thyroxine to triiodothyronine by type I deiodinase. To date, some previous studies have shown that the most common change in the plasma level of thyroid hormones is a reduction in the total T3 and free T3 concentration associated with the severity of hepatic dysfunction. The current study aims to evaluate thyroid function in patients with acute and chronic liver diseases. Objectives of the study include assessing the severity of liver dysfunction in patients with hypothyroidism and hyperthyroidism. This prospective, hospital-based cross-sectional study was conducted in the inpatient department of General medicine from October 2019 to October 2021. A comprehensive physical examination was conducted, followed by a thorough review of their hospital records. Patients with acute hepatitis (acute onset of jaundice and three-fold rise in serum transaminases) and chronic liver disease (evidence of liver disease of more than 6 months' duration and portal hypertension on ultrasonography or upper gastrointestinal endoscopy) were included in the study. Results showed a significant positive correlation between TSH and prothrombin time, child-pugh score, and total bilirubin. Total T3, free T3, and free T4 showed a significant positive correlation with albumin and a significant negative correlation with prothrombin time, child-pugh score, and total and direct bilirubin. So, thyroid hormone patterns may help assess the prognosis of patients with liver disorders as they show a significant correlation with established markers of prognosis of liver diseases.

Keywords: Acute liver disease, chronic liver disease, Thyroid hormone pattern, Prognostic indices, Hypothyroidism, Hyperthyroidism.

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1. INTRODUCTION

Thyroxine(T4) and tri-iodothyronine(T3) are essential for normal organ function, growth, and development. These regulate the basal metabolic rate, including hepatocytes, thereby modulating liver functions (ref). The liver plays a vital role in the metabolism of thyroid hormones and the peripheral conversion of thyroxine to triiodothyronine by type I deiodinase[1,2]. Hence, the liver is involved in conjugation, peripheral deiodination, excretion, and the synthesis of thyroid-binding globulin[3]. Thyroid dysfunction may perturb liver function, where liver disease modulates thyroid hormone metabolism, and various systemic diseases affect both organs.[4] Among the liver's various functions, one function of the liver is the synthesis of carrier proteins and hormone metabolism. Hence liver diseases are associated with various endocrinal disturbances.[5-6] Thyroid gland secretes two iodine-containing amine hormones derived from the amino acid tyrosine, Levothyroxine (T4), and Tri-Iodothyronine (T3). FreeT4 and FreeT3 enter every cell through its plasma membrane and bind to a nuclear T3 receptor. This thyroid receptor is a part of the nuclear group of receptors, namely Retinoic acid, vitamin D, Retinoid X, and peroxisome proliferator receptor.[7] In normal individuals, the thyroid gland secretes triiodothyronine(T3) of 10 nmol and thyroxine(T4) of 110nmol every day.[8] T3 has ten times greater efficacy and affinity than T4 for the nuclear receptor. Though T4 is quantitatively secreted at much higher levels, it must be considered a pro-hormone that requires deiodination and conversion to T3 to become biologically active.[9] There are three groups of enzymes that regulate the metabolism of thyroid hormone, forming part of the iodothyronine seleno-deiodinase enzyme system, namely type 1 = D1, type 2 = D2, and type 3 = D3 which are responsible for the activation of T4 to T3, inactivation of T4 to rT3 and the conversion of rT3 and triiodothyronine to T2(ref). In extrathyroidal tissue, the conversion of Thyroxine to T3 occurs through the D1 enzyme system, a rapidly occurring equilibrating pool, and through the D2 system, a slowly occurring equilibrating pool. Type 1 deiodinase is majorly found in the liver and the kidney, for about 30–40% of extrathyroidal production of T3 (12 nmol).[10] Type 2 deiodinase is present in the central nervous system, pituitary gland, and skeletal muscle, contributing to 60–70% of the extrathyroidal production of T3(about 30 nmol).[11] Though the D2 enzyme system performs similar actions to that of D1, enzyme kinetics, regulation, and susceptibility to propylthiouracil[12] are different. Though both D1 and D2 enzyme systems can also inactivate T4 and T3, the major inactivator is the D3 system, which primarily causes inner-ring deiodination. It is found in the Central nervous system, skin, and liver, converting Thyroxine to rT3 and triiodothyronine to T2; both are inactive metabolites. Again, D3 also converts reverseT3 to rT2.[13] This enzyme system is expressed in the placenta, which helps protect the developing fetus from maternal thyroid hormones.[14] In addition to the central role in deiodination to activate and deactivate thyroid hormones, the liver specifically performs thyroid hormone transport and metabolism functions. The liver extracts 5–10% of plasma thyroxine during a single passage, as shown in studies using w131IxT4. Its value is much higher, which can be accounted for by the amount of free Thyroxine delivered to the liver, indicating that a considerable amount of T4, bound to protein, is available for uptake.[15] A stereospecific active transport mechanism is identified for transporting Thyroxine and T3 across the hepatocytes. The free hormone levels are high intracellularly than the plasma levels.[16] The liver provides a large, rapidly exchangeable pool of circulating thyroid hormones by synthesizing plasma proteins that bind to lipophilic thyroid hormones for about 99% of thyroid hormones bound to thyroxine-binding globulin, thyroxine-binding prealbumin, and albumin in plasma. The free component of hormone within the plasma is in equilibrium with the hormone, which is protein bound; this free fraction of hormone, which accounts for the hormone's activities. Hence tissue thyroid status depends not only on the secretion of thyroxine but also on the metabolism of normal thyroid hormones, delivery of triiodothyronine to nuclear receptors, and distribution of receptors and their function.[17] Cirrhosis is the histological development of regenerative nodules surrounded by fibrous bands due to chronic liver injury, which results in portal hypertension and end-stage liver disease.[18] To date, some previous studies showed that the most common change in the plasma level of thyroid hormones is a reduction in the total T3 and free T3 concentration associated with the severity of hepatic dysfunction. But no report shows an association between FT4 and thyroid-stimulating hormone (TSH) levels and the severity of liver cirrhosis. Changes in thyroid hormone levels are well established that some researchers used them as a sensitive index of liver function.[19-20] The current study aims to evaluate the thyroid function of patients with acute and chronic liver diseases. Objectives of the study include assessing the severity of liver dysfunction in patients with hypothyroidism and hyperthyroidism.

2. MATERIALS AND METHODS:

The study was a prospective hospital-based cross-sectional study conducted in the In-patient department, Department of General Medicine,

2.1 Study Period

October 2019 - October 2021.

2.2 Source of patients

Patients older than 18 were admitted and diagnosed with acute and chronic liver disease in DR PSIMS & RF.

2.3 Sample size calculation

As per the study done by Panekar et al., the prevalence of thyroid abnormalities was 41% among patients with liver disorders.[21] Using Epi Info Software, the sample size was calculated as per the population survey model: $N=Z^2PQ/E^2$, where N=sample size, Population proportion:41%, Q=1-P, E-Error: 10%, Confidence level:85%. After calculation, the minimum sample size came to 51. As the data is incomplete for 6 subjects, 45 patients were included. The study sample consisted of 45 subjects, of which 30 patients belonged to chronic liver disease and 15 to the acute liver disease group.

2.4 Sampling method

Simple Random sampling method.

2.5 Inclusion criteria

• Patients aged above 18 years
• Males and females diagnosed with acute and chronic liver disease based on clinical features, laboratory parameter ultrasonography features.

2.6 Exclusion criteria

1. Patients with known thyroid dysfunction or on the treatment of the same.
2. Patients using drugs known to alter thyroid.
3. Patients with renal failure, cardiac and pulmonary failure
4. Pregnant and lactating women

2.7 Ethical considerations

Institutional Ethical Committee permission was taken before the commencement of the study (Ref no: ECR/804/Inst/AP/2019-RR-19). Informed consent was taken from every patient who participated in the study.

2.8 Sample collection and measurements:

Blood samples were collected and analysed at the biochemistry laboratory of the hospital. T3, T4, free T4, and free T3 were measured based on the competition principle of Electrochemiluminescence. TSH was measured based on the sandwich model of Electrochemiluminescence. The normal range considered as T3 -0.5 to 2.0 ng/ml, T4 -4.4 to 12 mcg/dl, TSH-0.3 to 6.02miu/ml, Free T4-0.8-2.7ng/dl, Free T3-2.1-4.4 pg/ml. The phlebotomist collected the sample at the sample collection point, and analysis was done at the Biochemistry laboratory of our tertiary care hospital. The liver function test (LFT) was done using a fully-automated analyser.

The normal range considered as:

Total bilirubin: Up to 1.2 mg/dl
Direct bilirubin: Up to 0.2 mg/dl

Indirect bilirubin was calculated by subtracting total bilirubin and direct bilirubin.

2.9 Study Tools and Data collection procedure

All patients were interviewed and clinically examined. Patients with acute hepatitis (acute onset of jaundice and three-fold rise in serum transaminases) and chronic liver disease (evidence of liver disease of more than 6 months' duration and portal hypertension on ultrasonography or upper gastrointestinal endoscopy) were included in the study. In practical clinical terms, diagnosis of chronic liver disease is made in the presence of duration >6 months. Coarse echoes and features were considered markers of chronic liver disease. An ophthalmological examination was done for patients with the Kayser Fleischer ring. Ascites were graded into three categories; 0- no ascites, 1- easily controlled ascites, and 2- difficult to control ascites.[22] Hepatic encephalopathy was graded into 3 categories; 0-none, 1-minimal and 2-advanced.[23]All patients underwent an abdominal ultra-sonogram to confirm the diagnosis. Child Pugh's score is assessed as follows:[24]

- Encephalopathy: None = 1 point, Grade 1 and 2 = 2 points, Grade 3 and 4 = 3 points
- Ascites: None = 1 point, slight = 2 points, moderate = 3 points
- Bilirubin: under 2 mg/ml = 1 point, 2 to 3 mg/ml = 2 points, over 3 mg/ml = 3 points
- Albumin: greater than 3.5mg/ml = 1 point, 2.8 to 3.5mg/ml = 2 points, less than 2.8mg/ml = 3 points
- Prothrombin Time* (sec prolonged): less than 4 sec = 1 point, 4 to 6 sec = 2 points, over 6 sec = 3 points

3. STATISTICAL ANALYSIS

The information collected regarding all selected patients was recorded in the master chart**.** Data analysis was done using computerizing Microsoft Excel and SPSS 22.0 (Trail version). This software calculated frequency, mean, median, and standard. The Student's t-test determines the significant mean difference between the two groups for all normally distributed variables. Karl-Pearson's correlation and p values were calculated, and values less than 0.05 was shown to have a significant correlation. The correlation was assessed by Pearson's method.

4. RESULTS

CHRONIC LIVER DISEASE: Demography of study population

Table 1: Age-wise distribution of Chronic liver disease patients in the study group

Age in years	Number of cases	Percentage
31 – 40	5	16.60%
41 – 50	9	30%
51 – 60	8	26.66%
61 – 70	6	20%
71 – 80	2	6.70 %
Total	30	100%

Table 1 shows the Age of the study population of 30 patients, which ranged from 31-80 years. 5 patients (16.6%) were aged between 31-40 years, 9 (30%) patients were aged between 41-50 years, 8 (26.66%) patients were aged between 51-60 years, 6 (20%) patients were aged between 61-70 years, 2 (6.70%) patients were aged between 71-80 years, the distribution of various groups depicted in Table 1 above. The mean age is 53.4 years (+/-10.8).

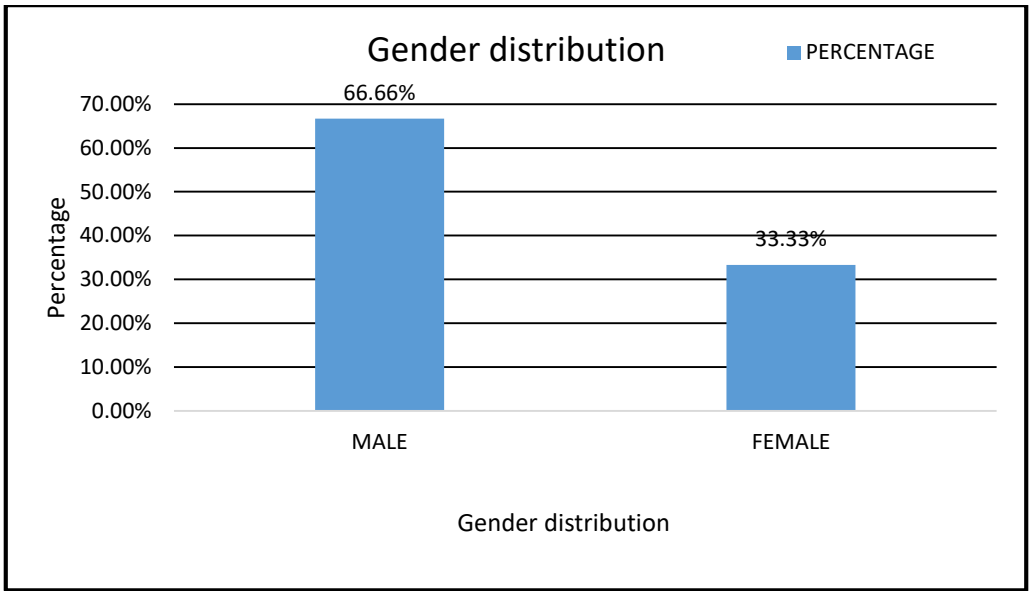

Fig 1: Gender-Wise Distribution of Study Population

Figure 1: Out of 30 patients with chronic liver disease, 20 (66.66%) were males and 10 (33.33%) were females.

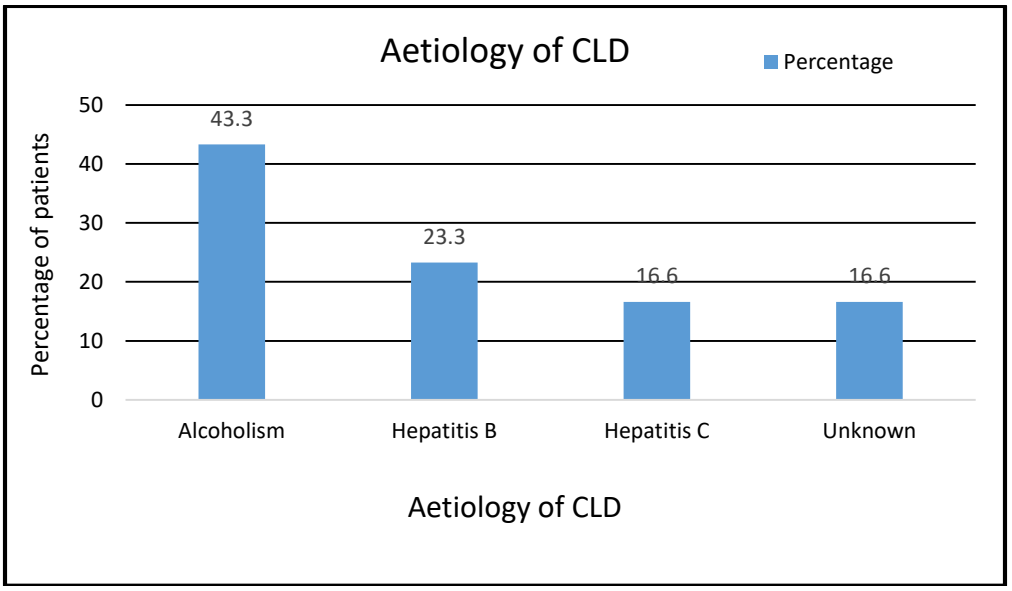

Fig 2: Aetiology of chronic liver disease (CLD)

Figure 2; Among etiology, alcoholism 13(43.33%) is observed mostly in chronic liver disease groups, 7 (23.3%) was hepatitis B,5(16.6%) was hepatitis C, and the cause is unknown in 5(16.6%) patients.

4.1. CHARACTERISTICS OF THE STUDY POPULATION

The present study included 30 patients with CLD and 15 patients with ALD. Overall 30 patients were males, and 15 patients were females. 27 patients were below 50 years, and 18 were over 50 years.

Table 2: Characteristics of the study population

Parameters	CLD(n=30)	ALD(n=15)	P value
Mean age	53.4±3.2 years	37.5±9.5	0.0001
Gender (no of males)	20	10	0.73

Table 2 shows the characteristics of the study population. There is a significant difference in the mean age between patients of CLD and ALD. There is no significant difference in gender between patients of ALD and CLD.

Table 3: TSH values among patients as per gender				
Parameters	**Males**	**Females**	**Total(n=30)**	**Percentage**
High TSH	6	2	8	26.6%
Low T4	6	2	8	26.6%
Low T3	8	4	12	40%
Free total T4 low	7	1	8	26.6%

Table 3 shows TSH levels in patients with CLD. Of 30 cases, TSH values were high in 8 (26.6%) cases; 6 were males, and 2 were females. Out of 30 cases, total T4 values were low in 8 (26.6%) cases; 6 were males and 2 were females. Out of 30 patients, a low total T3 was seen in 12 (40%), out of which 8 were males and 4 were females. Out of 30 cases, free total T4 values were low in 8 (26.6%) cases; 7 were males and 1 female.

Table 4: Distribution of Thyroid Abnormalities Among Various Child Pugh Classes					
Thyroid Abnormalities	**CTP A**	**CTP B**	**CTP C**	**TOTAL**	**Percentage**
Overt Hypothyroid	0	1	7	8	26.66%
Low T3 Syndrome	0	0	4	4	13.33%
Normal	2	4	12	18	60%
Total	2	5	23	30	100%

Table 4 shows Overt hypothyroidism in 26.6% of patients and low T3 syndrome in 13.3%. Thyroid profile was normal in 60% of patients among 30 patients with chronic liver disease.

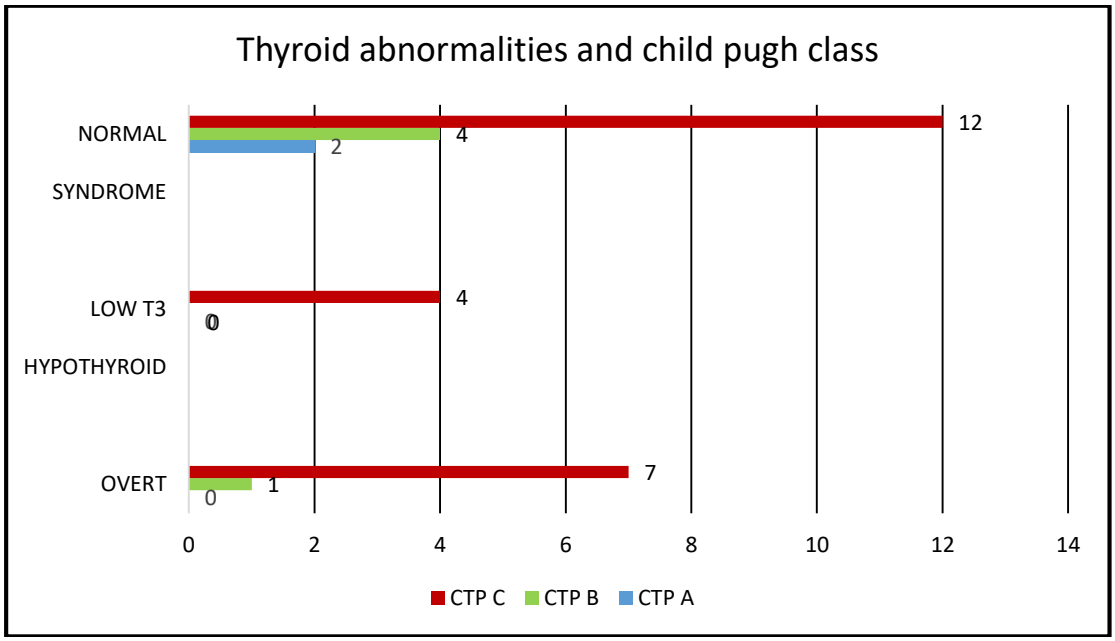

Fig 3: Thyroid abnormalities and child-pugh class

Figure 3 shows thyroid abnormalities and child-pugh class. 12 normal patients, 4 patients with low T3, and 7 patients with overt hypothyroidism belonged to CTP class C. 2 normal patients belonged to CTP Class A.

TABLE 5: Correlation Coefficient Between Thyroid Hormone Variables and Prognostic Indices					
Parameters	**Total Bilirubin**	**Direct Bilirubin**	**Albumin**	**Prothrombin Time**	**Cpt Score**
TSH	+0.506*	+0.578	-0.378	+0.402*	+0.399*
TT4	-0.605	-0.608	+0.653*	-0.388*	-0.623*
TT3	-0.465*	-0.439*	+0.558*	-0.443*	-0.524*
FREE T4	-0.615*	-0.622*	+0.511*	-0.413*	-0.446*
FREE T3	-0.648*	-0.645*	+0.613*	-0.314*	-0.584*

Pearson Correlation significant at 0.001 level

Table 5 showed a significant positive correlation between TSH and prothrombin time, child-pugh score, and total bilirubin. Total T3, free T3, and free T4 showed a significant positive correlation with albumin and a significant negative correlation with

prothrombin time and child-pugh score. Total T3, free T3, and free T4 significantly negatively correlated with total and direct bilirubin.

4.2. Patients with Acute Liver Disease

4.2.1. Demographic characteristics

A total of 15 acute liver disease (ALD) patients were included in the study population.

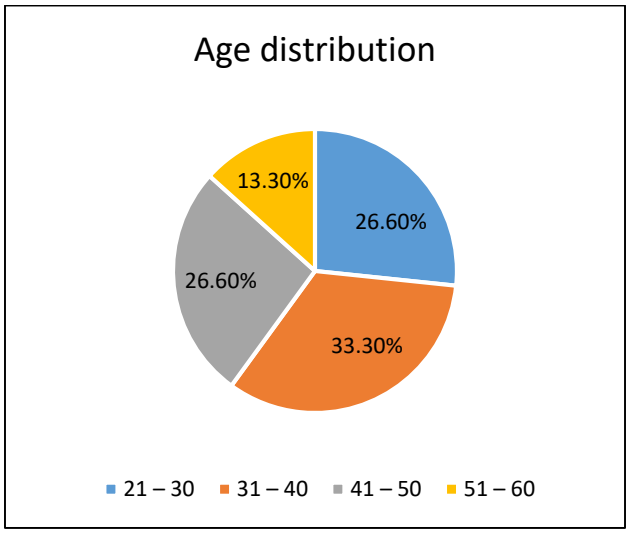

Fig 4: Age-wise distribution of ALD patients in the study group

Figure 4 showed Age of the study population ranged from 21-60 years, 4 (26.6%) patients were aged between 21-30 years,5 (33.3%) patients were aged between 31-40 years, 4 (26.6%) patients were aged between 41-50 years. The distribution of various groups is depicted in Table 1 above. The mean age is 37.5 years (+/-9.57).

TABLE 6: Gender-Wise Distribution of ALD Patients

Gender	Frequency	Percentage
Male	10	66.6%
Female	5	33.3%
Total	15	100%

Table 6 showed that out of 15 patients, 10(66.6%) were males, and 5 (33.3%) were females.

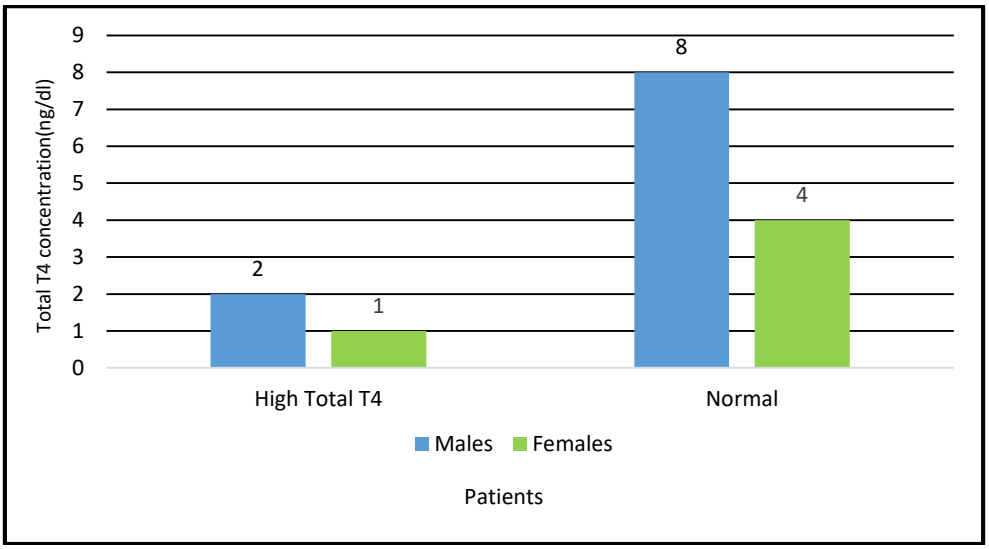

Fig 5: Thyroid abnormalities as per gender

Figure 5 shows that Total T4 is high in 3 (20%) patients, out of which 2 were males and 1 female. The remaining 12 (40%) showed a normal total T4 value- 8 subjects were males, and 4 were females.

Table 7: Thyroid hormone profile based on age			
Parameters	**Below 50 years(n=27)**	**Above 50 years(n=18)**	**P value**
TSH (mU/ml)	4.63±1.1	4.8±0.98	0.59
FT4(pg/ml)	1.67±0.52	1.8±0.65	0.46
FT3(pg/ml)	1.74±0.12	1.77±0.51	0.76

Mean± SD

Table 7 shows TSH levels in patients as per age. 27 patients were below 50 years, and 18 were above 50 years among 45 patients with CLD and ALD. As per the T-test, there is no significant difference in the mean TSH, Free T4, and Free T3 levels among patients aged above and below 50 years.

Table 8: Thyroid hormone profile as per gender			
Parameters	**Males(n=30)**	**Females(n=15)**	**P value**
TSH (mU/ml)	4.28±1.09	4.17±0.81	0.58
FT4(pg/ml)	1.71±0.54	1.81±0.78	0.61
FT3(pg/ml)	1.76±0.14	1.75±0.47	0.91

Mean± SD

Table 8 shows TSH levels in patients as per gender. 30 patients were males, and 15 were females among 45 patients with ALD and CLD. As per the T-test, there is no significant difference in the mean TSH, Free T4, and Free T3 levels among males and females.

Table 9: Thyroid Hormone profile as per the duration of disease			
Parameters	**Less than 2 years(n=13)**	**More than 2 years(n=32)**	**P value**
TSH (mU/ml)	4.31±0.87	4.18±0.52	0.53
FT4(pg/ml)	1.69±0.32	1.61±0.79	0.72
FT3(pg/ml)	1.71±0.13	1.73±0.51	0.89

Mean± SD

Table 9 shows patients' TSH levels as per the liver disease duration. 13 patients had liver disease for less than 2 years, and 32 patients had liver disease for more than 2 years among 45 patients. There is no significant difference in the mean TSH, Free T4, and Free T3 levels among patients as per their disease duration and T-test.

Table 10: Thyroid hormone profile in the study population			
Parameters	**CLD(n=30)**	**ALD(n=15)**	**P value**
TSH (mU/ml)	3.09±2.11	2.37±1.08	0.22
FT4(pg/ml)	1.12±0.43	1.30±0.37	0.13
FT3(pg/ml)	1.93±0.49	2.34±0.17	0.002

Mean± SD

Table 10 showed mean TSH levels, free T3, and free T4 levels among patients with acute and chronic liver disease. There is no significant difference in mean TSH and free T4 levels between patients of ALD and CLD.

Table 11: Detailed Thyroid Hormone Levels in Two Groups.					
GROUP	**TSH MEAN**	**TT4 MEAN**	**TT3 MEAN**	**FT4 MEAN**	**FT3 MEAN**
Patients with CLD	3.09(+/-2.11)	6.05(+/-1.91)	67.5(+/-32.3)	1.126(+/-0.430)	1.930(+/-0.492)
Patients with ALD	2.37(+/-1.08)	8.67(+/-2.59)	78.86(+/-20.28)	1.306(+/-0.374)	2.34(+/-0.17)
P value	0.22	0.0003	0.21	0.13	0.002

Table 11 showed mean TSH levels, Total T4, total T3, free T3, and free T4 levels among patients with acute and chronic liver disease. Total T4 and free T3 levels were significantly lower in patients with CLD than in patients with ALD.

Table 12: Correlation Between Total T4 and Direct Bilirubin			
Total T4 Mean	**Direct Bilirubin**	**Correlation Coefficient**	**P Value**
8.672 (+/-2.59)	4.98(+/-1.64)	+0.109	0.001*

Table 12 shows a significant positive correlation between direct bilirubin and total T4. *Correlation significant at 0.001 level between total t4 and direct bilirubin.

Table 13: Correlation Between Total T4 with AST and Serum Albumin

Total T4	AST	Correlation Coefficient	P Value
8.672(+/-2.598)	397.5(+/-158.2)	+0.092	0.001*
	Albumin 3.44(+/-0.427)	-318	0.001*

Table 13 shows a significant positive correlation between total T4 and AST levels. *Correlation significant between total t4 and AST, albumin at 0.001 level.

5. DISCUSSION

Among 45 patients enrolled in this study who qualified for the inclusion and exclusion criteria,30 were patients diagnosed with chronic liver disease, and the remaining 15 were diagnosed with acute liver disease. In the present study mean age in the chronic liver disease group was 53.4 years (+/-10.8), and in the acute liver disease group, the mean age was 37.5 years (+/-9.75). The chronic liver disease group was considerably older than the acute liver disease group in this study. On analyzing the thyroid hormone variables in the study, the thyroid stimulating hormone in the chronic liver disease group was high in 8 patients (23.33%), and 8 patients (23.33 %) showed low total T4 and free T4 values. In a study done by Sandeep Kharb et al., the authors showed 4 (5.33%) patients out of 75 patients with liver disease to be hypothyroid, in which 3(3.5%) were subclinical and 1 (1.3%) the patient was overt hypothyroid.[25] Out of 30 patients with liver cirrhosis in a study conducted by Harikumar et al., results showed subclinical hypothyroidism in 10% (3 patients), central hypothyroidism in 6.66% (2 patients), and primary hypothyroidism in 3.3% (1 patient).[26] Study done by EL feki et al. showed high TSH values.[27] Study done by Kayacetin et al. showed no difference in TSH in liver cirrhosis patients. [28] According to G. Deepika et al., in a study done on 310 cirrhotic patients, results showed that cirrhotic patients were more prevalent thyroid abnormality, especially hypothyroidism, because of various reasons.[29] Joeimon et al. 30 reported that the prevalence of hypothyroidism was 21.6% (similar to our study). Still, this prevalence contradicted the study done by Patira et al., in which the prevalence of subclinical hypothyroidism was 62%.[31] In the present study, in chronic liver disease group, overt hypothyroidism was seen in 8 patients (26.6%) and low T3 syndrome in 4 (13.3%) patients, similar results to the above studies as the occurrence of hypothyroidism in chronic liver disease group. But hyperthyroidism is neither sub-clinical nor primary noted in this study. This difference may be due to varied etiology, sample size, and severity of the liver disease. In this study, total t4 decreased in 8 patients (23.3%) in the chronic liver disease group and increased in 3 (20%) patients in the acute liver disease group. An increase in total T4 has been observed in patients with acute liver disease group due to an increase in TBG levels, which is synthesized as an acute phase reactant. In the initial state of acute liver diseases, the total T4 production increases as liver function worsens. It would have reduced due to TBG's higher and lower concentrations. In this study, Total T3 is decreased in 40 % of patients in chronic liver disease groups. Free T3 decreased in 40% of patients in the chronic liver disease group. A study was done by D'costa and Dhume et al.,[32] Saleem and Wadea et al.,[33] El-Sawy and Tawfi,[34] the levels of FT3 were significantly lower in liver cirrhosis patients. This study assessing the correlation between TSH and the child-pugh score showed a significant positive correlation (p-value <0.001). whereas total T4, Total T3, free T3 and free T4 showed significant negative correlation with child pugh score. This study observed similar results as Sudhir Kumar Verma et al.,[35], which showed free T3 levels were inversely correlated with the Child-Pugh score. Israel et al. study found a significant inverse relationship between serum T3 concentrations and the severity of liver dysfunction, as well as a progressive T3 increase in those subjects who eventually had a good outcome, implying that T3 concentrations in patients with advanced liver disease could be used as a helpful prognostic indicator.[36] A study by Wang et al.[37] showed significantly reduced TSH in type A Hepatic encephalopathy compared to acute liver failure patients. However, no such findings were seen in our study as there is a difference in sample size, age, sex, and regional variations and not in encephalopathy. According to Takahashi et al., in chronic liver diseases, serum Free T3 declined according to the degree of liver dysfunction in conditions such as CAH, CPH, and LC, and it seemed to reflect the severity of damage to the liver.[38] Yamaba et al. reported that T3/T4 value decreased mostly in acute hepatitis and slightly decreased in chronic persistent hepatitis and chronic active hepatitis. At the same time, no significant difference was noted in liver cirrhosis compared with that of controls.[39] Ertugrul Kayacetina et al.[40] found no significant difference in functional thyroid parameters between patients surviving and not surviving with hepatic encephalopathy (p<0.375).

6. CONCLUSION

Thyroid hormone patterns may help assess the prognosis of patients with liver disorders as they show a significant correlation with established markers of prognosis of liver diseases. Total T3 and free T3 were found to be promising in CLD patients; given various undetected thyroid hormone patterns in patients with liver disease, thyroid function tests should be done in patients with liver disease and treated regularly if necessary.

7. ACKNOWLEDGMENTS

We want to express our sincere thanks to the Principal and Superintendent and Institutional ethics committee of Dr. Pinnamaneni Siddhartha Institute of Medical Sciences and Research Foundation, Vijayawada. We want to thank all our patients who participated in the study.

8. AUTHORS CONTRIBUTION STATEMENT

Dr. Uppala Bhaskar Rao designed and planned the entire study. Dr. Karri Anusha drafted the study. Dr. Venkat Nikhil collected patient data through a case record form. Dr.

Bhavani Mareedu did the statistical analysis. All the authors drafted and approved the final version of the manuscript.

9. CONFLICT OF INTEREST

Conflict of interest declared none.

10. REFERENCES

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