Journal of Cardiovascular Disease Research
ISSN: 0975-3583,0976-2833 VOL 15, ISSUE 11, 2024

Original Research

A Study of thyroid profile in Alcoholic Liver Diseases

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Received Date:24 September 2024 Accepted Date: 28 October 2024

ABSTRACT
AIM: The study aimed to find the correlation between thyroid function and severity of alcoholic liver disease.
METHODOLOGY: It was a case control study. 50 alcoholic patients with ultrasound proven liver disease were enrolled. The control included 50 non-alcoholic patients with ultrasound proven liver disease. The thyroid function tests were done in all the patients and its relation with severity of liver disease was determined.
RESULTS: The most common thyroid abnormality noted in alcoholic liver disease patient was sub clinical hypothyroidism and was seen in 40% of the patients. However, the most common finding in patients with non-alcoholic liver disease was euthyroid status seen in 54% of patients, which was followed by sub clinical hypothyroid status seen 40% of patients.
CONCLUSION: Thyroid dysfunction is common in Alcoholics, and correspond to the degree of liver disease in the patients. Early detection of these changes and treating them can prevent further complications and reduce mortality in these patients.
KEYWORDS: Alcoholic Liver Disease, Thyroid Function**,** Hypothyroidism

INTRODUCTION

Alcohol addiction has been characterised as an individual's dependence on alcohol, alcohol abuse or uncontrolled drinking propensity, which adversely interferes with his biological, social and mental well-being.[1] Alcohol acts as a direct toxin to the lining of the gut, the most widely recognized physical problems of the alcoholic patient are gastrointestinal. The early alcoholic may present with morning sickness and vomiting, dyspepsia, and oesophageal reflux. Heavy consumption can worsen existing peptic ulcers.[2] Other intestinal complaints include vague abdominal discomfort, anorexia, or recurrent diarrhoea, which may be a result of alcohol-induced duodenitis, ileitis, pancreatitis, fatty liver or irritable bowel syndrome.[3,4] Chronic heavy (>40g of alcohol per day) alcohol drinking over a long period of time (months or years) causes alcoholic fatty liver in 90–100% of people. Only 10–35 percent of those with alcoholic fatty liver who continue to drink heavily for a long time develop alcoholic steatohepatitis, which is a liver inflammation with particular histological abnormalities. Furthermore, alcoholic liver cirrhosis affects only 8–20 percent of persistent heavy drinkers. Cirrhosis patients develop hepatocellular carcinoma at a rate of 2% each year. Acute alcoholic hepatitis, a condition marked by jaundice and liver failure, can develop in patients with severe alcoholic steatohepatitis. Cirrhosis will occur in 70% of people who survive alcoholic hepatitis. Patients with alcoholic liver cirrhosis, on the other hand, are more likely to develop alcoholic hepatitis (acuteon-chronic illness), which has a high death.[5] The effect of alcohol on thyroid depends on the duration and amount of alcohol consumed, this may in turn correlate to the degree of hepatic dysfunction. But alteration in hypothalamo-pituitary-thyroid (HPT) axis or direct damage to the thyroid gland are also considered to play an important role in dysfunction of thyroid due to alcohol. Also, the liver diseases may affect the function of thyroid gland.[6] Alcohol-dependent individuals can also present with a “euthyroid sick syndrome,” evidenced by low levels of T3, high levels of reverse T3 (rT3), and normal levels of T4.[7-9] The present study aimed to study the thyroid function in patients with alcoholic liver disease and find the correlation between thyroid function and severity of alcoholic liver disease.

MATERIALS AND METHODS

The present study was case control study conducted in the Department of General Medicine, Guru Nanak Dev Hospital, Government Medical College, Amritsar. A total of 50 patients with alcoholic liver disease admitted to the hospital were enrolled in the study. 50 subjects with non-alcoholic liver disease were also selected as control group. The patients and controls were subjected to medical examination as per the proforma and their vitals such as blood pressure, height, weight, BMI was recorded in both groups

INCLUSION CRITERIA:

- Age ranging from 30-60 years of alcoholic liver diseases
- no history of diabetes mellitus, hypertension, non-alcoholic liver diseases, renal diseases, thyroid disorders
- Control subjects with age ranges from 30-60 years who were non-alcoholics liver disease.

EXCLUSION CRITERIA:

- Patients with clinical evidence of diabetes mellitus, renal diseases, hypertension and thyroid disorders.

Investigations:

- Thyroid function tests (ELISA Method):
- Serum T3 • Serum T4 • Free T3 • Free T4 • Serum TSH ,
- Liver Function Tests (Routine methods using Auto Analysers)
- Total bilirubin
- Total protein
- Serum albumin
- Serum AST (SGOT) •Serum ALT (SGPT)
- Serum ALP
- Serum GGT
- USG

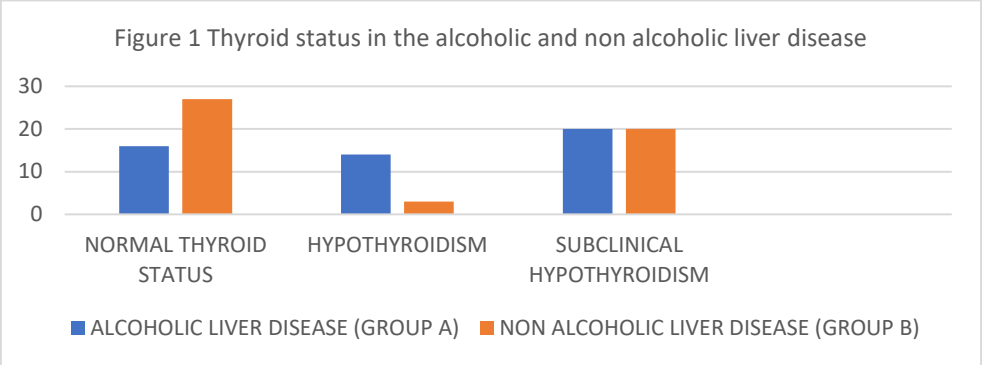
STASTICAL ANALYSIS:

Sample size was calculated keeping in view at most 5% risk, with minimum 80% power and 5 % significance level (significant at 95% confidence interval). Raw data was recorded in a Microsoft excel spread sheet and analysed using Statistical Package for the Social Sciences (SPSS version 21.00). Continuous data was presented as mean with standard deviation. Categorical data was expressed as percentages. Numerical variables were normally distributed and were compared using Chi Square test for non parametric data and Student's 't' test for parametric data. The p value was then determined to evaluate the level of significance. The results were analysed and compared to previous studies to draw relevant conclusions.

RESULTS

In our study 50 alcoholic patients (GROUP A) with ultrasound proven liver disease were enrolled. The control included 50 non-alcoholic patients (GROUP B) with ultrasound proven liver disease. The age group of study ranged from 30 to 60 years. In our study maximum number of alcoholics were between 51-60years of age(40%), followed by between 41-50years(32%), this was followed by those in the age group of 30-40years(28%). There was no difference in the age group between the two groups. Gender wise distribution of the study subjects was not studied as all the subjects involved in our study were males. In our study maximum patients had Cirrhosis as an Ultrasound finding (42%), it was followed by the patients with Liver parenchymal Disease (34%), whereas 24% patients with fatty liver had enrolled. There was no difference in Ultrasound findings between the two comparison groups.

Figure: 1 shows the thyroid status in the study patients.



Subclinical hypothyroidism (40%) was the most prevalent finding in the patients of Group A i.e. those with alcoholics liver disease, which was followed by Normal thyroid status (32%), and Hypothyroidism was seen in 28% of the patients of Group A. Whereas among the patients of Group B - Normal thyroid status was seen in 54% of the patients, which was followed by Subclinical hypothyroidism seen in 40% of the patients, Hypothyroidism was seen in 6% of the patients of Group B. There was a statistically significant difference (p=0.007) in between both the comparison groups.

Table :1 shows the correlation of lab parameters in alcoholic liver disease

GROUP A	Cirrhosis	Fatty liver	LPD	p value
T3 (ng/dl)	74.524±33.579	111.917±25.217	105±23.241	0.001
FT3(ng/dl)	0.223±.100	0.336±0.076	0.315±0.098	0.001
T4(µg/dl)	5.067±1.619	5.592±0.430	5.871±1.036	0.137
FT4(ng/dl)	0.796±0.229	0.896±0.073	0.938±0.189	0.054
TSH(µIU/L)	9.5±2.386	5.4±1.861	6.265±2.161	0.001

Table: 2 shows the correlation of lab parameters in non-alcoholic liver disease

GROUP B	Cirrhosis	Fatty liver	LPD	p value
T3 (ng/dl)	116.952±15.696	123.417±13.345	119.824±12.131	0.447
FT3(ng/dl)	0.351±0.047	0.370±0.040	0.365±0.033	0.033
T4(µg/dl)	8.040±1.404	8.210±0.460	8.411±0.463	0.514
FT4(ng/dl)	1.286±0.225	1.313±0.074	1.346±0.074	0.514
TSH(µIU/L)	6.464±1.732	3.869±2.164	4.178±2.083	0.001

Table: 3 shows the comparison of MEAN ±SD values of thyroid function tests and liver function tests between two groups

Parameter	Group A Alcoholic Liver Disease	Group B Non Alcoholic Liver Disease	p value
T3 (ng/dl)	93.860±32.596	119.48±13.97	0.001
FT3(ng/dl)	0.281±0.098	0.360±0.041	0.001
T4(µg/dl)	5.466±1.261	8.207±0.974	0.001
FT4(ng/dl)	0.869±0.189	1.313±0.156	0.001
TSH(µIU/L)	7.416±2.818	5.064±2.083	0.001
Bilirubin(mg/dl)	2.248±0.861	1.604±0.689	0.001
Total protein levels(g/dl)	5.701±0.869	5.894±1.028	0.336
Serum albumin level(g/dl)	2.906±0.651	3.188±8.824	0.061
AST(U/L)	157.374±55.702	102.260±41.045	0.001
ALT(U/L)	78.082±29.880	85.920±33.375	0.219
ALP(U/L)	184.322±95.284	162.5±47.615	0.151
GGT(U/L)	126.448±44.323	116.920±38.125	0.252

DISCUSSION

Alcoholic liver disease is major cause of mortality and morbidity, with increasing incidence day by day especially in developing countries like India.The findings of the present study reveal important insights into the thyroid profile variations among different types of alcoholic liver disease (ALD), highlighting significant

differences in T3, FT3, and TSH levels across cirrhosis, fatty liver, and liver parenchymal disease (LPD) groups. In cirrhotic patients, both total T3 and free T3 (FT3) levels are markedly lower as compared to those with fatty liver and LPD, with a statistically significant p-value of 0.001. This decrease in T3 and FT3 in cirrhotic patients aligns with previous research suggesting that hepatic dysfunction impairs the conversion of thyroxine (T4) to triiodothyronine (T3), leading to lower active thyroid hormone levels in patients with advanced liver disease.[10, 11] Reduced hepatic deiodinase activity, which converts T4 to T3, is thought to be the main driver behind these findings.[12]Thyroid-stimulating hormone (TSH) levels also vary significantly among the groups, with cirrhotic patients exhibiting higher levelsthan those with fatty liver and LPD, with a significant p-value of 0.001. Elevated TSH in cirrhotic patients may indicate a compensatory response to the low T3 and FT3 levels, as the hypothalamic-pituitary axis attempts to stimulate thyroid function to counterbalance the diminished thyroid hormone levels.[13] Some studies also suggest that chronic liver disease might lead to a resistance to TSH in peripheral tissues, possibly explaining the higher circulating TSH despite low thyroid hormones in cirrhosis.[14]Punekar et al also showed that level of TSH increases with MELD score.[10]This pattern highlights the complexity of thyroid dysfunction in advanced liver disease, where the hypothalamic-pituitary-thyroid (HPT) axis appears disrupted by both impaired hormone conversion and altered feedback mechanisms.

Other parameters, including T4 and FT4, show non-significant variations across groups, with p-values of 0.137 and 0.054, respectively. The slight increase in these parameters in fatty liver and LPD compared to cirrhosis suggests that while early stages of ALD (like fatty liver) may have minimal impact on thyroid function, advanced liver disease (cirrhosis) affects thyroid hormones more extensively. This trend is consistent with findings that T4 and FT4 levels may remain stable or undergo mild changes in liver disease, unlike T3 and FT3, which are more sensitive to hepatic dysfunction.[15] These results emphasize the importance of thyroid hormone evaluation in ALD patients, particularly in those with cirrhosis, where thyroid hormone deficiencies may contribute to the disease burden and affect prognosis.In a study conducted in 2017 by Verma et al.,[16] it was concluded that low free T3 and free T4 was found in 72.5% and 26.47% of patients with cirrhosis of liver respectively. TSH towards the upper limit of normal range was observed in 52.3% of patients. Low free T3 and free T4 was found to be inversely related to the severity of liver disease.[17] Similarly in 2019, Patira NK et al.,[18] showed that prevalence of subclinical hypothyroidism with cirrhosis was 62%. The prevalence of hypothyroidism in cirrhosis patients increases as the severity of cirrhosis increases and findings were statistically significant.

The data on thyroid hormone levels across different types of non-alcoholic liver disease (NALD)—cirrhosis, fatty liver, and liver parenchymal disease (LPD). Notably, T3 levels do not differ significantly among the groups ($p = 0.447$), suggesting that, unlike in alcoholic liver disease (ALD), liver function impairment in NALD has less impact on T3 levels. The mean T3 level remains relatively consistent across cirrhosis, fatty liver, and LPD. Studies suggest that metabolic factors associated with NALD, such as insulin resistance and obesity, may help preserve T3 levels to some extent, as T3 has a role in metabolic regulation that might counterbalance mild liver dysfunction.[19] This finding contrasts with ALD, where liver dysfunction severely impairs T3 synthesis, indicating different underlying mechanisms of liver disease pathology in relation to thyroid function.[10]Free T3 (FT3) shows a statistically significant difference across groups ($p = 0.033$), with levels slightly lower in cirrhotic patients compared to those with fatty liver and LPD. This subtle decline in FT3 among cirrhotic patients aligns with evidence suggesting that, even in non-alcoholic cirrhosis, advanced liver impairment can affect thyroid hormone conversion, albeit to a lesser degree than in ALD.[12] However, the relatively preserved FT3 levels in NALD patients reflect a milder hepatic deiodinase dysfunction, possibly due to a lack of direct hepatotoxic effects seen in ALD. FT4 and T4 levels remain stable across groups with non-significant p-values (0.514), reinforcing the notion that thyroid hormone disturbances in NALD are often less severe and predominantly affect free hormone levels rather than total hormone reserves.[20]TSH levels show a significant difference ($p = 0.001$) among the groups, with higher levels observed in cirrhotic patients compared to those with fatty liver and LPD. Elevated TSH in NALD cirrhosis may indicate a compensatory mechanism responding to marginally lower FT3 levels, suggesting an altered hypothalamic-pituitary-thyroid (HPT) feedback loop, similar to what is observed in ALD but to a lesser degree.[14] The disparity in TSH among NALD subgroups might also reflect varying degrees of metabolic dysfunction, with higher TSH associated with more severe liver damage.[21] These results underscore the complexity of thyroid-liver interactions in NALD, where thyroid function remains relatively stable across disease types, yet advanced disease still exerts some impact on TSH and FT3 levels.

The thyroid function tests and liver function tests between two groups: patients with alcoholic liver disease (ALD) and those with non-alcoholic liver disease (NALD). Thyroid hormone levels, including T3, FT3, T4, and FT4, are significantly lower in the ALD group than in the NALD group, with p-values of 0.001 for each parameter. These findings align with previous studies, which have demonstrated that alcohol-related liver damage can disrupt the conversion of T4 to T3 due to impaired hepatic deiodinase function, resulting in reduced T3 and FT3 levels (Malik et al., 2020). In contrast, NALD patients, particularly those with less severe liver impairment, often maintain closer-to-normal thyroid hormone levels, possibly due to the different pathophysiology underlying metabolic dysfunction in non-alcoholic fatty liver disease (NAFLD).[12]

In terms of liver function, several parameters are significantly different between the two groups. Bilirubin levels are notably higher in ALD compared to NALD, with a p-value of 0.001. This elevation in bilirubin in ALD is consistent with the extensive liver cell damage and impaired bilirubin clearance commonly associated with alcohol-related liver injury.[22]Similarly, aspartate aminotransferase (AST) levels are significantly higher in ALD (157.374 ± 55.702 U/L) than in NALD (102.260 ± 41.045 U/L), with a p-value of 0.001. Elevated AST, along with the characteristic AST/ALT ratio > 2 often seen in ALD, is a hallmark of alcoholic liver injury, reflecting mitochondrial damage in hepatocytes due to chronic alcohol exposure. [23] Alanine aminotransferase (ALT), alkaline phosphatase (ALP), and gamma-glutamyl transferase (GGT) levels, however, do not show statistically significant differences, suggesting that while liver enzymes are elevated in both types of liver disease, the degree of elevation may vary depending on the underlying cause and extent of liver damage.

Thyroid-stimulating hormone (TSH) levels differ significantly between the groups, with higher levels observed in ALD compared to NALD, with a p-value of 0.001. This elevation in TSH in ALD may indicate a compensatory response to the low T3 and FT3 levels or a possible disruption in the hypothalamic-pituitary-thyroid (HPT) axis due to chronic alcohol use, which has been shown to interfere with TSH secretion.[24] Interestingly, while total protein and serum albumin levels are slightly lower in ALD than NALD, these differences are not statistically significant (p-values of 0.336 and 0.061, respectively), suggesting that both ALD and NALD may impact protein synthesis, albeit to varying extents. The findings emphasize how ALD and NALD affect thyroid and liver function differently, underlining the need for distinct clinical approaches in managing these conditions.

There are few limitations in the study. The sample size is small therefore large cohort studies are required to confirm these findings. No females were included in this study, therefore, these results can not be applied to the population.

CONCLUSION

Thyroid dysfunction is common in Alcoholics, and correspond to the degree of liver disease in the patients. Early detection of these changes and treating them can prevent further complications and reduce mortality in these patients.

DECLARATION

Funding : No funding resources
Conflict of interest :None
Ethical Approval : The study was approved by Institutional Ethical Committee.

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