Original Research Article

A study of thyroid hormones in alcoholic liver diseases

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Abstract

Background and objectives: Alcohol is a common cause of cirrhosis all over the world including India and alcoholic liver disease is among the ten most common causes of death worldwide. Alcoholic liver diseases affect most of the organs in our body. The study of thyroid hormone function tests will throw a light on the functional aspects of liver diseases and gives some better understanding of the alcoholic liver disease and their interrelationship with thyroid function and thus helps in the management of alcoholic liver diseases. Methods: 30 male cases diagnosed with alcoholic liver disease were compared with 30 male normal subjects as controls. The diagnosis was based on interview and questionnaire, clinical signs of liver disease and supporting laboratory test [bilirubin, total protein, serum albumin, A:G, AST, ALT, ALP and GGT] and ultrasound and their T3, T4, TSH were evaluated. Results: In alcoholic liver disease patients, there was reduction in T3 and T4. Though the TSH was high, the patients were clinically euthyroid. The assay of thyroid hormone levels helps in the management of the patients with alcoholic liver diseases. Conclusion: One of the more severe consequences of alcohol abuse is alcoholic liver disease characterized by tissue injury through hepatocytic dysfunction. Alcoholic liver disease is manifested by elevated transaminases, decrease in protein synthesis, increased bilirubin etc. In the present study, the majority of patients with ALD were presented with altered serum thyroid hormone levels. Mean of T3 decreases in cases compared to control due to the impaired liver conversion of T4 to T3 in the peripheral tissues. Mean of T4 decreases in cases compared to control due to the decrease in thyroid hormone binding proteins. Mean of TSH increases in cases compared to control. Patients are clinically euthyroid. The altered levels of thyroid profile in the patients of alcoholic liver disease will be helpful in their management

Keywords: Alcohol, TSH, Transaminases, Bilirubin, Total protein

Introduction

Alcoholic liver disease is a term that encompasses the hepatic manifestations of alcohol over consumption including fatty liver alcoholic hepatitis and chronic hepatitis with hepatic fibrosis or cirrhosis[1].

Alcohol is a common cause of cirrhosis all over the world including India and alcoholic liver disease is among the ten most common causes of death worldwide. The consumption of alcohol has been steadily increasing in India during the last decade due to socio economic status. Chronic and excessive alcohol ingestion is one of the major causesof liver disease[2].

Liver cirrhosis is most commonly caused by alcoholism and hepatitis B or C but has many other possible causes. Epidemiology of liver cirrhosis varies gender, ethnic groups and geographical distribution[3].

Quantity and duration of alcohol intake are the most important risk factor involved in the development of alcoholic liver disease. The threshold of developing alcoholic liver disease in men is an intake of > 60 to 80 g/d of alcohol for 10 years while in women are at increased risk of developing similar degrees of liver injury by consuming 20-40 g/d. Ingestion of 160g/d is associated with 25 fold increased risk of developing alcoholic cirrhosis.

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Gender dependent differences results from poorly understood effects of estrogen and the metabolism of alcohol. Social, immunologic and heritable factors have also been postulated to play a part in the development of the pathogenic process.

Chronic infection with hepatitis C is an important co-morbidity in the progression of alcoholic liver disease to cirrhosis in chronic excessive drinkers[2].

Alcoholic liver disease has a wide spectrum, varying from asymptomatic liver enlargement to severe liver failure and /or portal hypertension with high mortality rate.

The three main types of liver involvement are:

- Alcoholic fatty liver
- Alcoholic hepatitis
- Alcoholic cirrhosis

In men, 40-80 g/day of ethanol produces fatty liver, 160g/day for 10 years causes hepatitis or cirrhosis. Only 15% of alcoholics developed alcoholic liver disease. HCV infection concurrent with alcoholic liver disease is associated with younger age of severity, more advanced histology, decreased survival[2].

In the early phase inflammation cell products, proteinases and reactive oxygen radicals may initiate hepatocellular necrosis with consecutive releasing of numerouscytokines. Following hepatic injury there is the increase in extracellular matrix, the activation of stellate cells, the increase in rough endoplasmic reticulum and expression of smooth muscle specific alpha actin[4]. Activated stellate cells are influenced by numerous cytokines. Some of them have proliferative effect on stellate cells while other stimulate fibrogenesis[5-8].

Objectives

- Estimation of thyroid hormone levels i.e., T3, T4 and TSH in male patients ofalcoholic lever disease.
- Estimation of total bilirubin,
- Total protein, serum albumin, A;G ratio,
- Serum AST,
- Serum ALT,
- Serum ALP,
- Serum GGT, for the selection of test subjects.

To study the thyroid dysfunctions in male patients with alcoholic liver disease.

Materials and methods

Place and Duration

The study is done at Rohini Diagnostic Center, LB Nagar, Hyderabd. Study period January 2019 to January 2020.

Inclusion Criteria

Test subjects

30 males who are diagnosed with alcoholic liver disease between the age group of 40-60 years from Rohini Diagnostic Center, LB Nagar, Hyderabd.

Control subjects

30 males of age 40-60 years who were non-alcoholicS.

Exclusion Criteria

- Patient with clinical evidence of hypertension, diabetes mellitus, pancreatitis,renal failure.
- Malnutrition.
- Individuals belonging to other age group and female subjects.
- Subject on drugs affecting mineral metabolism.
- Primary biliary cirrhosis.
- Other causes of cirrhosis.

Data collection

Test subject are male patient with ALD between the age group of 40-60 years and control subject are healthy males with no history of ALD between the age group of 40-60 years from Shadan Institute of Medical Sciences and Hospital, Hyderabad.

The diagnosis of alcoholic liver disease is based on history of chronic significant alcohol abuse, clinical signs of liver disease and supporting laboratory test which are Total protein, serum albumin, A;G ratio, AST, ALT ALP and total bilirubin level, and gamma glutamyl transferase and ultrasonographic features.

Alcohol drinking history was assessed by interview and questionnaire. Data from the questionnaire are used to establish consumed duration type and pattern of alcohol intake.

The height, weight, BP and BMI were recorded in both the groups:

Height

Height was measured by vertical board with an attached metric scale. The subjects were made to stand on bare foot on a flat surface with heels together was brought in contact with the head to compress the hair and their reading recorded to the nearest 0.1cm.

Weight

Weight was recorded by making the patient stand on dial type weighing machine with body weight distributed between the feet.

Blood Pressure

BP was recorded using a sphygmomanometer with subject in sitting position. Those with SBP > 140 and DBP > 90 mmHg are considered

Fasting blood samples are collected and investigated for total protein, serum albumin, A:G ratio, total bilirubin, aspartate aminotransferase, alanine amino transferase, alkaline phosphatase, gamma glutamyl transferase, SerumT3, T4 and TSH. The samples were compared with controls.

Observations and results

Study design

A comparative two group case-control study.

Table 1: Age distribution of patients studied

Age in years	Cases		Controls	
	No.	%	No.	%
41-50	5	16.67	7	23.30
51-60	25	83.33	23	76.70
Total	30	100.0	30	100.0
Mean ± SD	56.10±3.89		55.21±4.62	

In the cases, studied 83.33% were in the age group of 51 to 60 years, 16.67%were in the age group of 41 to 50years.
In controls, studied 76.70% were in the age group of 51 to 60 years, 23.30% werein the age group of 41 to 50years.

Table 2: Total protein (g/dl) distribution of patients studied

Total Protein (g/dl)	Cases		Controls	
	No.	%	No.	%
<6.0	18	60.0	0	0.0
6.0-7.8	12	40.0	28	93.3
>7.8	0	0.0	2	6.7
Total	30	100.0	30	100.0

In 60% of cases, the total protein was less than 6g/dl and 40% varied between of6.0-7.8g/dl. In controls, the total protein was less than 6g/dl.

Table 3: Serum albumin (g/dl) distribution of patients studied

Serum Albumin (g/dl)	Cases		Controls	
	No.	%	No.	%
<3.5	23	76.7	2	6.7
3.5-5.2	7	23.3	28	93.3

>5.2	0	0.0	0	0.0
Total	30	100.0	30	100.0

In 76.7% of cases, serum albumin was less than3.5g/dl and 23.3% varied between 3.5-5.2g/dl. In controls, serum albumins 93.3% were in the range of 3.5-5.2g/dl.

Table 4: A: G ratio distribution of patients studied

A: G Ratio	Cases		Controls	
	No.	%	No.	%
<1	11	36.7	0	0.0
1-1.5	19	63.3	23	76.7
>1.5	0	0.0	7	23.3
Total	30	100.0	30	100.0

In 63.3% of the cases, A:G was varying between 1 and 1.5 and 36.7% it was less than 1. In 76.7% of the controls, A:G varied between of 1 and 1.5 and 23.3% it was more than 1.5:1.

Table 5: AST (U/L) distribution of patients studied

AST (U/L)	Cases		Controls	
	No.	%	No.	%
0	0	0.0	0	0.0
0-42	0	0.0	30	100.0
>42	30	100.0	0	0.0
Total	30	100.0	30	100.0

In cases, AST was more than 42 U/L. In controls, it was less than 42U/L.

Table 6: ALT (U/L) distribution of patients studied

ALT (U/L)	Cases		Controls	
	No.	%	No.	%
0	0	0.0	0	0.0
0-48	7	23.3	30	100.0
>48	23	76.7	0	0.0
Total	30	100.0	30	100.0

In 76.7% of cases, ALT was more than 48U/L, and 23.3% it was less than 48U/LIn controls, ALT was less than 48U/L

Table 7: ALP (U/L) distribution of patients studied

ALP (U/L)	Cases		Controls	
	No.	%	No.	%
<100	3	10.0	16	53.3
100-200	10	33.3	14	46.7
>20	17	56.7	0	0.0
Total	30	100.0	30	100.0

In 56.7% of cases, ALP was more than 200 U/L, 33.3% varied between 100-200 U/L and 10% was less than 100U/L. In 53.3% of the controls, ALP was less than 100U/L whereas in 46.7% it was between 100-200 U/L.

Table 8: GGT (U/L) distribution of patients studied

GGT (U/L)	Cases		Controls	
	No.	%	No.	%
<50	0	0.0	30	100.0
50-150	23	76.7	0	0.0
>150	7	23.3	0	0.0
Total	30	100.0	30	100.0

In 76.7% of the cases, GGT was between 50-150U/L and it was more than150 U/L in 23.3%. In controls, GGT was less than 50 U/L.

Table 9: Thyroid function distribution of patients studied

Thyroid function	Cases (n=30)		Controls (n=30)		p value
	No.	%	No.	%	
T3 (ng/dl)					
<50	16	53.3	0	0.0	<0.001**
50-200	14	46.7	30	100.0	
>200	0	0.0	0	0.0	
T4 (microgram/dl)					
<4	10	33.3	0	0.0	
4-12	20	66.7	30	100.0	<0.001**

>12	0	0.0	0	0.0	
TSH (micro IU/l)					
<5	7	23.3	29	96.7	
5-6	12	40.0	1	3.3	
>6	11	36.7	0	0.0	0.009**

In 46.7% of the cases, T3 was between 50-200 ng/dl and in 53.3% it was less than 50ng/dl.In controls, T3 was between 50-200ng/dl. In 66.7% of the cases, T4 was between 4-12 microg/dl and in 33.3% was less than 4 microg/dl. In controls, T4 was between4-12 microg/dl. In 23.3% of the cases, TSH was less than 5 microIU/L, 40% it was between 5-6 micro IU/L and in 36.7% it was more than 6micro IU/L. In 96.7% of the controls, TSH was less than 5 microIU/L and 3.3% it wasbetween 5-6 micro IU/L.

Table 10: Bilirubin levels in two groups studied

Bilirubin(mg/dl)	Cases		Controls	
	No.	%	No.	%
<1.2	4	3.3	29	96.7
>1.2	26	86.7	1	3.3
Total	30	100.0	30	100.0

In 86.7% of the cases, bilirubin was more than 1.2mg/dl and in 13.3% it was less than 1.2mg/dl. In 96.7% of the controls, bilirubin was less than 1.2mg/dl and in 3.3% it was more than 1.2mg/dl.

Table 11: Comparison of study variables in cases and controls studied

Variables	Cases	Controls	p value
Total protein (g/dl)	5.67±0.87	6.95±0.62	<0.001**
Serum albumin (g/dl)	2.90±0.64	4.11±0.49	<0.001**
A:G	1.04±0.18	1.42±0.14	<0.001**
AST (U/L)	153.94±54.33	20.81±6.64	<0.001**
ALT (U/L)	77.62±28.57	18.24±5.98	<0.001**
ALP (U/L)	215.47±85.18	93.87±17.31	<0.001**
GGT (U/L)	130.77±47.49	24.60±8.20	<0.001**
T3 (ng/dl)	68.75±27.81	111.97±10.17	<0.001**
T4 (micro gram/dl)	4.76±0.89	8.36±0.45	<0.001**
TSH (micro IU/l)	7.22±8.49	3.02±0.80	0.009**
Bilirubin	1.72±0.67	0.62±0.30	<0.001**

Total protein in cases was low when compared with control with a p value of <0.001 which is significant. Serum albumin in cases was low when compared with control with a p value of <0.001 which is significant. A: G in in cases was low when compared with control with a p value of <0.001 which is significant. AST in cases was more when compared with control with a p value of <0.001 which is significant. ALT in cases was more when compared with control with a p value of <0.001which is significant.

ALP in cases was more when compared with control with a p value of <0.001 which is significant. GGT in cases was more when compared with control with a p value of <0.001 which is significant. T3 in cases was low when compared with control with a p value of <0.001 which is significant. T4 in cases was low when compared with control with a p value of <0.001 which is significant. TSH in cases was more when compared with control with a p value of 0.009 which is significant. Bilirubin in cases was more when compared with control with a p value of <0.001which is significant.

Discussion

Alcoholic liver disease is considered to be a major cause of morbidity and mortality, with increasing incidence day by day especially in developing countries like India. Alcohol intake remains the major cause of cirrhosis. Excessive consumption of alcohol by large section of population is still a medical and social problem in many countries.

The present study has shown that in cases when compared with the controls the total protein was found to be low, serum albumin decreased, A:G ratio decreased, bilirubin has increased, AST, ALT, ALP, GGT have increased.

In the present study, in the cases when compared with the controls the mean of T3, T4 has decreased whereas the mean of TSH increased.The formation of T4 to T3 is catalyzed by iodothyronine 5-deiodinase.This enzyme is located predominantly in the microsomes and plasma membrane of the liver and kidney. In patients with alcoholic liver disease, due to the deficiency of hepatic iodothyronine 5-deiodinase activity, the peripheral conversion of T4 to T3 decreases results in decreased serum T3.

The liver synthesizes the protein which transports thyroxine [T4] in the circulation: T4 binding globulin, T4-binding prealbumin and albumin

The decrease in serum T4 is due to the reduction in plasma thyroid hormone binding proteins in these patients. The findings in this study are comparable with the previous studies[9,10].

Study conducted by Hepner GW, Chopra IJ, et al showed that serum T3 were decreased significantly in patients with alcoholic cirrhosis. Serum T3, T4 were lower in cirrhotic patients who died within three months of study compared with those whosurvived[9].

Study conducted by Geurts J, Demeester-Mirkine N et al showed that there was a significant reduction in total serum T4 with an accompanying in circulating TBG in chronic alcoholics. During alcohol withdrawal there was a rapid increase in T4 and TBG into the normal range[11].

Thus, the noxious substance ethanol in alcohol causing the liver damage is responsible for altered thyroid function which will be useful in the management of the patients with alcoholic liver disease.

Conclusion

One of the more severe consequences of alcohol abuse is alcoholic liver disease characterized by tissue injury through hepatocytic dysfunction. Alcoholic liver disease is manifested by elevated transaminases, decrease inprotein synthesis, increased bilirubin etc. In the present study, the majority of patients with ALD were presented with altered serum thyroid hormone levels. Mean of T3 decreases in cases compared to control due to the impaired liver conversion of T4 to T3 in the peripheral tissues. Mean of T4

decreases in cases compared to control due to the decrease in thyroid hormone binding proteins. Mean of TSH increases in cases compared to control. Patients are clinically euthyroid. The altered levels of thyroid profile in the patients of alcoholic liver disease will be helpful in their management.

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