



## A STUDY OF BIOCHEMICAL MARKERS IN ALCOHOLIC LIVER DISEASE

### KEYWORDS

alcohol, Biochemical marker,  $\gamma$ -Glutamyltransferase, Aminotransferases

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### ABSTRACT

*Chronic and excessive alcohol ingestion is one of the major causes of Liver diseases in the western world. Now alcohol consumption is increasing in modern India. Fatty Liver is present in 90% of chronic alcoholics. Alcohol is considered as a direct hepatotoxin. Progressive fibrosis and cirrhosis, clinically presenting as end-stage liver disease are common outcomes in alcoholic Liver disease (ALD) patients. A variety of laboratory tests are available to assist in the progression and diagnosis of cirrhosis to end stage liver disease. The aim of this study is to identify potential novel biomarkers for progression of cirrhosis to end-stage liver cirrhosis. A total of 150 subjects were participated in this study. 100 were diagnosed as alcoholic liver cirrhosis and 50 were normal health subjects. The biomarkers evaluated in this study included liver function indicators including serum albumin, total bilirubin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyltransferase (GGT) and renal parameters (urea and creatinine). The AST, ALT, GGT, ALT/AST Ratio and Bilirubin are significantly elevated in alcoholic liver cirrhosis compared to healthy controls. Serum albumin is decreased in alcoholic liver disease patients than in healthy controls.*

### Introduction

Liver is the versatile organ in the body. Due to changes in the life style, dietary habits and personal habits hepatic disorders are increasing in trend. These hepatic disorders continued to be important cause of morbidity and mortality in adult population. Hence early detection of hepatic disorders are important to prevent and reduce mortality and morbidity. By estimating serum enzymes serum bilirubin, serum proteins, prothrombin time we can diagnose the hepatic disorders. Alcoholism is condition resulting from excess drinking of beverages that contain alcohol. The major health risk of alcoholism includes liver disease, heart disease, pancreatitis, central nervous system disorders and certain forms of cancer [1]. Alcohol can be manifested in liver damage from fibrosis to end stage of cirrhosis and may eventually lead to carcinoma of liver. The liver is particularly vulnerable to disease related to heavy drinking, most commonly termed as alcoholic hepatitis or cirrhosis. The progression of alcoholic liver disease is characterized by steatosis, inflammation, necrosis and cirrhosis. When severe Cirrhosis occurs, death is the outcome [2]. Chronic consumption of alcoholic beverages is a primary cause of liver injury. Chronic and excessive consumption of alcoholic beverages provokes membrane lipid-peroxidation due to triglyceride accumulation in hepatocytes [3]. The study underway can serve as potential diagnostic tools for more specific biomarkers of ethanol-induced diseases. Hence, an attempt has been made to evaluate the effect of chronic alcohol consumption on renal and hepatic biomarkers.

### 2. Materials and Methods

#### 2.1. Design and Subjects

The present study was carried out in Department of Biochemistry, Kurnool Medical College, Kurnool. 100 cases of alcoholic liver cirrhotic patients were studied. 50 sub-

jects who were clinically healthy were taken as controls. The study was conducted with approval of Institutional Ethical Committee. A comparative study was carried out in a sample of 100 cirrhotic patients with chronic alcoholism of 40-60 years of age, and a mean consumption of ethanol  $150.7 \pm 35.5$  g/d during the past 10 years (without alcohol ingestion in the past 30 days) and without additional diseases. Patients who were having with clinical, biochemical and ultrasonographic evidence of cirrhosis of liver were taken as cases. 50 subjects of age matched of normal healthy adults with a mean age of  $40 \pm 9.6$  without alcoholism were taken as controls.

#### 2.2. Blood and Biochemical Analysis

Patients were obtained from gastroenterology ward of Government General Hospital, Kurnool with proven history of liver cirrhosis on the basis of clinical, biochemical and imaging methods and endoscopic signs. Cirrhosis was related to chronic alcohol intake. The severity of the disease was evaluated according to the Child-Pugh classification [4]. The serum obtained from samples containing no anti-coagulant agent was subjected to the following tests: urea, creatinine, albumin, total bilirubin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyltransferase (GGT) [5-12]. These tests were used as screening measurements for diagnosis of liver injury prevalent in different stages of cirrhotic patients.

#### 2.3. Statistical Analysis

Data were processed by use of standard statistical software Open epi. The results are presented as mean  $\pm$  SD. The exact measures of associations in results between patients and control were compared using chi square test and fisher statistics. The significance was taken at  $P < 0.001$ .

### 3. Results

#### 3.1. Effect of Alcohol on Serum Levels of Liver Chemistries.

Table 1 indicates the levels of serum bilirubin, albumin, GGT and ALT/AST ratio of alcoholic cirrhotic groups were altered as compared to that of control. The serum concentration of bilirubin was found to be significantly elevated in cases as compared to controls. The serum bilirubin levels were significantly elevated in patients consuming alcohol for the past 10 years. ( $P < 0.001$ ). The serum concentration of albumin was significantly decreased ( $P < 0.001$ ) and the serum GGT Levels was significantly elevated ( $P < 0.001$ ). Also the serum levels of ALT, AST and AST/ALT ratio was significantly altered in patients consuming alcohol.

#### 3.2. Effect of Alcohol Intake on Renal Markers

Table 2 shows the activities of serum urea and creatinine compared to control subjects respectively. The serum levels of urea and creatinine showed pronounced elevation in alcoholic cirrhotic patients as compared to healthy controls.

**Table 1. Serum ALT, AST, T.Bilirubin, Albumin, GTT levels of patients**

Patients	ALT (mean $\pm$ SD)	AST (mean $\pm$ SD)	T.Bilirubin (mean $\pm$ SD)	Albumin (mean $\pm$ SD)	GGT (mean $\pm$ SD)
Control	13.66 $\pm$ 2.58	25.1 $\pm$ 4.17	0.56 $\pm$ 0.16	3.40 $\pm$ 0.35	17.8 $\pm$ 3.06
Alcoholic cirrhosis	65.60 $\pm$ 12.50	126.34 $\pm$ 30.39	4.67 $\pm$ 2.24	2.80 $\pm$ 0.20	84.26 $\pm$ 4.36

ALT=Alanine aminotransferase; AST=Aspartate aminotransferase; GGT=gamma glutamyl transpeptidase

**Table 2. Values of serum urea, creatinine in cirrhosis groups**

KIDNEY FUNCTION TESTS	CONTROLS	ALCOHOLIC CIRRHOSIS
UREA	23.43 $\pm$ 7.27	44.17 $\pm$ 9.61
CREATININE	0.90 $\pm$ 0.22	1.80 $\pm$ 1.24

### 4. Discussion

The Threshold for developing severe alcoholic liver disease in men is an intake of more than 60-80gm/day of alcohol for 10 years. In women 10-40gm/day for 10 years causes similar degree of liver injury. Excessive chronic consumption of alcohol results in profound alterations in the blood chemistries which may be associated with alterations in metabolic activities of cell resulting in several clinical and/or biochemical changes. **4.1. Effect of Chronic Alcohol Consumption on Liver Chemistries**

Table 1 indicates that

The serum gamma glutamyl transferase ( $\gamma$ GT), aspartate aminotransferase, bilirubin and albumin are considered to be well known markers of cirrhosis [13].

**SERUM BILURIBIN:** Serum Bilurubin levels are directly associated with hepatic damage. In alcoholic cirrhosis mean serum bilirubin levels are 4.67mg/dl. Hence there is increase in bilirubin levels in alcoholic cirrhosis ( $p < 0.001$ ).

**ALT:** Mean ALT levels in alcoholic cirrhosis are 65.60 IU/L. This shows an increase when compared to normal controls. ( $p < 0.001$ ). Similar finding were reported by Shimanaka, K. tsutsumi M et al.

**AST:** Mean AST levels in alcoholic cirrhosis were 126.34 IU/L. This shows increase levels when compared with normal levels. ( $p < 0.001$ ).

**ALBUMIN:** Mean albumin levels in alcoholic cirrhosis were 2.80gm/dl. There is significant decrease in serum albumin in alcoholic cirrhosis when compared to normal controls. ( $p < 0.001$ ).

**GGT:** In alcoholic cirrhosis mean value of GGT were 84.26 IU/L. This shows a highly significant increase when compared to controls. ( $p < 0.001$ ).

#### 4.2. Effect of Chronic Alcohol Consumption on Renal Chemistries

Our present findings of kidney profile comprising slightly elevated blood urea and serum creatinine in alcoholic cirrhosis when compared to controls and compensated cirrhosis are quite similar to earlier reports of Das et al [13]. The values of bilirubin are associated with urea and creatinine as observed by us may be used as markers in combination for diagnosis for ALD. It has been reported that liver disease has been associated with renal disorders [14].

### 5. Conclusion

In conclusion, it is evident from the results of this study and the existing literature that there was a compromise of Liver function system with variation in other related biomarkers of injury with respect to different organs and body systems. Highly elevated serum bilirubin and transaminases were observed in alcoholic cirrhosis. GGT is highly increased in alcoholic cirrhosis compared to controls. This shows that alcohol consumption provokes release of GGT from liver into the plasma to a significant increase in enzyme level in plasma. Albumin is decreased in alcoholic cirrhosis showing synthetic capacity of hepatocytes has decreased. Regular monitoring of these markers in alcoholic patients is necessary for better patient management and to minimize the morbidity and mortality related to liver injuries.

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