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Biomarkers In Alcoholic Liver Disease

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ABSTRACT

Extreme alcohol ingesting is a major health problem in the universal leading to both severe morbidity and mortality. Prolonged and undue alcohol ingestion is one of the major causes of Liver diseases. Alcohol is considered as a direct hepatotoxin. Progressive firosis and cirrhosis, clinically presenting as end-stage liver disease are common outcomes in alcoholic Liver disease patients.

The aim of this study is to identify potential novel biomarkers for progression of cirrhosis to end-stage liver cirrhosis. The different subjects were evaluated based in the age group. Blood samples were analysed for the analysis of different enzymatic levels. The urea, creatinine, albumin, total bilirubin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyltransferase (GGT) are observed for the any rise or decline in it. The alcohol is responsible for abnormal haematological, renal and liver chemistries.

Key-words: Liver diseases, biomarkers, biological markers, alcohol liver diseases.

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Introduction:

A biomarker, or biological marker, generally refers to a measurable indicator of some biological state or condition. The term is also occasionally used to refer to a substance the presence of which indicates the existence of a living organism. Further, life forms are known to shed unique chemicals, including DNA, into the environment as evidence of their presence in a particular location[1].

Biomarkers are often measured and evaluated to examine normal biological processes, pathogenic processes, or pharmacologic responses to a therapeutic intervention. Biomarkers are used in many scientific fields**.** A Biochemical marker can be a hormone, enzyme, antibody or protein that is detected in bodily fluids. These markers may be a sign of disease or other abnormalities in research areas such as Cancer, Cardiology, Immunology, Neuroscience and Metabolic.

In medicine, a biomarker can be a traceable substance that is introduced into an organism as a means to examine organ function or other aspects of health.

Alcoholic liver disease is a term that encompasses the liver manifestations of alcohol overconsumption, including fatty liver, alcoholic hepatitis, and chronic hepatitis with liver fibrosis or cirrhosis[2].

It is the major cause of liver disease. Although steatosis (fatty liver) will develop in any individual who consumes a large quantity of alcoholic beverages over a long period of time, this process is transient and reversible[2]. Of all chronic heavy drinkers, only 15–20% develop hepatitis or cirrhosis, which can occur concomitantly or in succession[3].

The mechanism behind this is not completely understood. 80% of alcohol passes through the liver to be detoxified. Chronic consumption of alcohol results in the secretion of pro-inflammatory cytokines (TNF-alpha, Interleukin 6 [IL6] and Interleukin 8 [IL8]), oxidative stress, lipid peroxidation, and acetaldehyde toxicity. These factors cause inflammation, apoptosis and eventually fibrosis of liver cells. Why this occurs in only a few individuals is still unclear. Additionally, the liver has tremendous capacity to regenerate and even when 75% of hepatocytes are dead, it continues to function as normal[4].

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[5] . 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 blood, renal and hepatic biomarkers against worsening child pugh criteria.

Study Population

A study was carried out in 50 cirrhotic patients with chronic alcoholism of 30-55 years of age, and consuming ethanol for past few years and without additional diseases.

Group I of Alcohol Liver Cirrhosis Patients

Group II Control Patients.

Biochemical Analyses

Patients were obtained from ward of hospital 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. These tests were used as screening measurements for diagnosis of liver injury. Blood samples containing heparin were analyzed using complete hemoglobin test. The serum obtained from samples was subjected to the following tests: urea, creatinine, albumin, total bilirubin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyltransferase (GGT).

Results

Effect on Liver Enzymes

The serum concentration of bilirubin was found to be significantly altered in patients with group 1 and controls (group 2). The serum bilirubin levels were significantly elevated in patients consuming alcohol for the past 10 years Group 2 as compared to Group 1 and the control subjects. The albumin concentration was significantly altered in group 1 & 2. The serum concentration of albumin was significantly decreased and the serum GGT Levels was significantly elevated and gradually declined with progression of cirrhosis. Also the serum levels of ALT, AST and AST/ALT ratio was significantly altered in patients consuming alcohol with more pronounced in decompensated subjects (Group 2) as compared to control subjects.

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

Patients	ALT	AST	Bilurubin	Albumin	GGT
Group I (Liver Cirrhotic)	66.98±1.8	127.60±25.8	4.91± 0.4	2.90 ± 0.35	81.5 ± 3.8
Group II (Control)	12.86±2.8	24.8±3.6	0.68 ± 0.3	3.60± 0.2	19.2 ± 4.5

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

Effect on Renal Markers

The serum levels of urea and creatinine showed pronounced elevation in cirrhotic patient and control subjects.

Table 2 : Values of serum urea, creatinine in cirrhosis groups

Biomarkers	Urea	Creatinine
Group I (Liver Cirrhotic)	43.58± 8.90	2.50±0.50
Group II (Control)	22.45± 6.90	0.85±0.15

Effect on Haemoglobin RBC Count and Serum Ferritin

The levels of total RBC count, Hb content showed depleted values against serum ferritin levels which showed steep elevation in cirrhotic patient and control groups. The prothrombin time was significantly altered in cirrhotic patient and control groups. The serum concentrations of cirrhotic patients were reflected according to progression and gradation of cirrhosis and significantly elevated as compared to control subjects.

Table 3 : Values of Blood Contents

Patients	Group I (Liver Cirrhotic)	Group II (Control)
RBC Count	4.1±0.4	5.2 ±1.5

Ferritin	154.8±19.5	68.8±19.2
Hb (g/ml)	14.11±0.4	15.1±0.5
PT	14.0±0.5	12.60±0.7

Discussion

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.

Effect of Chronic Alcohol Consumption on Liver Chemistries

The serum gamma glutamyl transferase (γGT), aspartate aminotransferase, bilirubin and albumin are considered to be well known markers of cirrhosis[6]. We have measured liver function tests, albumin and gamma glutamyl transferase, considering γGT as the most sensitive markers for acute hepatocellular damage. Our results revealed that levels of γGT were high in patients with severe alcoholic liver[7]. However some researches depicted controversial results[8]. The rise in the levels of γGT as also concluded by certain other studies[7] in alcoholic liver diseases may probably be due to inductive action of alcohol. Hyperbilirubinemia and hypoalbuminemia were also observed to be common features with alcoholics in our study. Albumin has been known as a potential subject for the formation of adduct by acetaldehyde, an alcohol metabolite. Ethanol consumption also slows down the rate of hepatic protein catabolism and may be related to degree of ethanol-induced Liver injury[6]. The serum transaminases viz, aspartate aminotransferase (AST) and alanine amino-transferase (ALT) are significantly elevated in cirrhotic patient and control groups. The ratio of AST to ALT may help in the differential diagnosis of alcoholic liver disease. The ratio is generally 1 or less with acute liver injury[5]. The Bilirubin levels observed by us were high in cirrhotic patient and low in control groups.

Effect of Chronic Alcohol Consumption on Renal Chemistries and Glucose Levels

The kidney profile comprising slightly elevated blood urea and serum creatinine in later stages of decompensation as compared to controls. 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[9].

Effect of Chronic Alcohol Consumption on Haematological Values

Alcohol has a variety of pathologic effects[9] in general including hematolological abnormalities. On hematopoiesis, it has been found that alcohol has direct action on erythroid precursors, thereby contributing to macrocytosis and the anemic state of chronic alcoholics[10]. Ethanol induces sideroblastic anemia due to interference with heme synthesis. The hematological study in the present work showed Prothrombin time (PT). The percentage of hemoglobin and the total number of RBC were found to be significantly decreased with heavy alcohol intake as a result of hemodilution. The degree of liver impairment showed direct relation with decrease in RBC count.

In our study we also made it a point to note that with the increase in consumption of alcohol and the level of liver injury in cirrhotic patients was profoundly more severe which was evident with elevated serum transaminases levels and other biomarkers.

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. The two groups also suggested compromise of liver function with increase in alcohol consumption. Regular monitoring of these markers and iron overload indicators in alcoholic patients is necessary for better patient management and to minimize the morbidity and mortality related to liver injury.

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