

Significance of Protein Bound Sialic Acid In Alcoholic Liver Disease

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ABSTRACT

Alcoholic liver disease is a term that encompasses the hepatic manifestations of alcohol overconsumption, including fatty liver, alcoholic hepatitis, and chronic hepatitis with hepatic fibrosis or cirrhosis. Fatty liver is present in >90% of binge and chronic drinkers. A much smaller percentage of heavy drinkers will progress to alcoholic hepatitis, thought to be a precursor to cirrhosis. The prognosis of severe alcoholic liver disease is dismal; the mortality of patients with alcoholic hepatitis concurrent with cirrhosis is nearly 60% at 4 years, although alcohol is considered a direct hepatotoxin, only between 10 and 20% of alcoholics will develop alcoholic hepatitis. Present study is done to evaluate the level of protein bound sialic acid in alcoholic liver disease and to assess the utility of this parameter as prognostic indices of liver function. The present study was conducted in the Department of Biochemistry in collaboration with department of Medicine, Pt. B.D. sharma, P.G.I.M.S, Rohtak. A total of 100 subjects were included in the present study. Subjects were divided into two groups. Group I was study group and Group II was control group. Study group included clinically diagnosed cases of alcoholic liver diseases supported with serological tests, ultrasonogram in the age group of 25-60 years. Control group included 50 age and sex matched healthy individual. On statistical comparison; we found highly significantly raised sialic acid in group I as compared to group II.

Keywords:Significance, Protein bound sialic acid, alcohol liver disease

INTRODUCTION

Alcoholic liver disease refers to alcohol induced disease of the hepatobiliary system with genetic, psycho-social and environmental factors influencing its development and having liver specific and systemic manifestations [1].The disease is often progressive and is considered to be a major cause of morbidity and mortality [2].Alcoholic liver disease represents a spectrum of clinical illness and morphological changes that range from fatty liver to hepatic inflammation and necrosis (alcoholic hepatitis) to progressive fibrosis (alcoholic cirrhosis)[3].

In the United state annual incidence of newly diagnosed chronic liver disease is 72.3%, of which 24% is alcohol induced[4]. Five year survival rate for alcoholic cirrhosis is between 23% and 50%. In India the prevalence rate is higher owing to consumption of illicit liquor. The development of cirrhosis is directly related to the duration and quantity of alcohol consumption [5].

Risk factors for developing ALD include

1. Liver disease is more common in subjects with the habits of daily drinking, volume of consumption > 200ml per day, and duration of drinking >14 years[6].
2. Sex (women may be more likely to develop cirrhosis).

3. Presence of co-infection with HBV or HCV (both of which increase risk of cirrhosis).
4. Nutritional status (poor nutrition increases risk of cirrhosis).

In addition, there is evidence for an immunological component in alcoholic liver disease, and there is evidence that modification of liver proteins by ethanol metabolites is involved in the pathogenesis. Alcoholic hepatitis is less likely to have increase aspartate amino transaminase (AST) or alanine amino transaminase (ALT) as compared to other causes of chronic hepatitis and more likely to have AST higher than ALT. Furthermore sustained excessive alcohol intake favours the progression of other liver diseases, such as virus-related chronic hepatitis, also increasing the risk of hepatocellular carcinoma (HCC).The prognosis of chronic ALD is better than that for other forms of liver disease, with only 10%-15% developing cirrhosis and a much smaller fraction developing HCC[7-8].

SIALIC ACID

Sialic acids are either N or O-acetyl derivatives of 9-carbon sugar neuraminic acid - an aldol condensation product of mannosamine and pyruvic acid. Sialic acids are terminal sugar components of the oligosaccharide chains of glycoproteins and glycolipids and sialic acid is localized at the end chain of many acute phase proteins. The majority of sialic acids are found in either protein (PBSA) or lipid – bounded (LBSA) forms, while little amounts is in the free forms[9]. Sialic acid participates in the stabilization of the conformation of glycoproteins, glycolipids various mucoproteins and cellular membranes. Lipid associated sialic acid (LASA) and protein associated sialic acid (PASA) are alkylated derivatives of neuraminic acid, the carbohydrate moiety characterized the cohesive, adhesive and antigenetic properties by its effect on cell-to-cell contacts[10].

Body fluids and tissues contain sialic acids. It is also present as constituent of membrane glycoproteins of erythrocytes, leucocytes and platelets[11]. N-Acetyl neuraminic acid is the most prominent sialic acid in eukaryotes. The structural diversity of sialic acid is exploited by viruses, bacteria and toxins and by the sialoglycoproteins and sialoglycolipids involved in cell to cell recognition in their highly specific recognition and binding to cellular receptors[9].

N-acetyl neuraminic acid has been isolated from human serum. The concentration of sialic acid in the human serum is higher in a number of pathological states where the indulging pathology is either of tissue destruction, tissue proliferation, depolymerization or inflammation[10]

MATERIALS AND METHODS

The present study was conducted in the department of Biochemistry in collaboration with Department of Medicine, Pt. B.D. SHARMA, P.G.I.M.S, Rohtak.

Inclusion Criteria

Group-I: This group included 50 clinically diagnosed cases of Alcoholic Liver diseases (ALD) supported with serological tests, ultrasonogram in the age group of 25-60 years.

Group-II: This group included 50 age and sex matched healthy individuals.

Exclusions Criteria

Patients with following disease were excluded from the study

- Any patient with history of drug intake that are known to be hepatotoxic
- Diabetes, hypertension and any other long term systemic illness
- Tuberculosis
- Acute lymphoid leukemia

- Chronic viral hepatitis
- Wilson's disease
- Hemochromatosis
- Any malignant disease
- Infectious mononucleosis

Sample collection Under all aseptic precautions 10ml of venous blood sample was collected in Red topped vacutainer. Samples were allowed to stand at room temperature until clotted. Clotted Samples were centrifuged at 3000rpm and serum separated. The samples were stored at -20°C . Analysis of Protein bound Sialic acid was done.

Protein Bound Sialic acid was estimated by modified Aminoff's method[12]

Principle:

The bound sialic acid is released by sulfuric acid and reacts with thiobarbituric acid (TBA) to form TBA-sialic acid complex. On boiling in water bath, this gives a pink colour. This colour is further extracted using acid-butanol mixture and then measured at 549nm spectrophotometrically against blank.

RESULTS

Sialic acid

Table 1 Comparison of Protein bound sialic acid level between Group I and Group II

Investigation	Group I (n=50)	Group II (n=50)	p value
Protein bound Sialic acid (mg/dL)	4.90±1.01	1.46±0.51	<0.001 Highly significant

Mean protein bound sialic acid was 4.90±1.01 mg/dL in group I and 1.46±0.51 mg/dL in group II. On statistical comparison; we found highly significantly raised sialic acid in group I as compared to group II (p<0.001).

Table 2 USG findings in study group

USG findings	No. of patients n (%)
Cirrhosis	20 (40%)
Fatty liver	8 (16%)
Hepatitis	22 (44%)

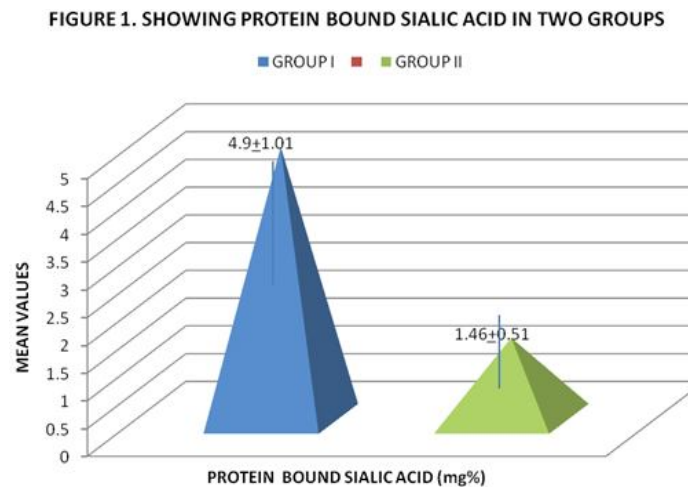
Table II shows that in the present study majority of patients suffered from hepatitis i.e.22patients (44%) followed by 20 patients (40%) of cirrhosis. Only 8 patients (16%) were found to be suffering from fatty liver disease.

Table 3 Protein bound sialic acid in patients of liver cirrhosis, fatty liver and hepatitis

USG findings	No. of patients	Protein bound sialic acid(mg/dL)
Cirrhosis	20 (40%)	4.62±0.93
Fatty liver	8 (16%)	4.87±1.09
Hepatitis	22 (44%)	5.17±1.02

Protein bound sialic acid in patients of hepatitis was 5.17±1.02mg/dL; in patients of cirrhosis was 4.62±0.93mg/dL and in patients of fatty liver was 4.87±1.09mg/dL.

Figure.1



DISCUSSION

The increased Protein bound sialic acid levels in alcoholic liver disease indicated that the deformation has been occurred in the cells, and an amount of sialic acid containing glycolipid or glycoprotein, (mainly acute phase proteins, such as alpha acid glycoprotein and alpha antitrypsin) were released from vascular cells into blood stream[13]. Further various studies suggested that inflammatory neutrophils undergo a interleukin-8- inducible recruitment of intracellular sialidase to the cell surface, where the release of bound sialic acid from surface molecules in the surrounding environment is responsible for raised sialic acid concentration[14].

Present study also showed a significant increase in protein bound sialic acid in subjects with ALD when compared with control subjects.

CONCLUSION

Alcohol consumption is associated with a number of changes in hepatic cell functions. In the present study, we have analysed protein bound sialic acid in alcoholic liver disease patients as well as controls. It is concluded that the estimation of protein bound sialic acid in serum is an important non invasive prognostic tool which may be helpful in the management of patients, before they develop the complications of the disease. Nature of alteration in the sialic acid may provide a basis for better understanding of pathogenesis and mechanism responsible in the patients of alcoholic liver disease.

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