

Sensitivity, Specificity and Diagnostic Efficiency of Serum Sialic Acid as a Biochemical Marker in Alcohol Abuse

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ABSTRACT

Background: Many biochemical markers have been used for detection of alcohol abuse, but each of them has clinical limitations. Sialic acid (SA) has been suggested as a new potential marker of excessive alcohol consumption.

Aim: To compare the sensitivity, specificity and diagnostic efficiency of serum Sialic acid with other traditional markers like AST (Aspartate amino transaminase), ALT (Alanine amino transaminase), GGT (Gamma Glutamyl Transferase), as a marker of alcohol abuse.

Methods: This was a case-control study conducted on 100 subjects. Alcohol dependent subjects without liver disease (cases = 50) and healthy subjects (controls = 50) were considered for the study. Sera from the subjects were analyzed for SA manually by modified Warren's Colorimetric assay and AST, ALT, GGT were estimated by auto analyzer.

Statistical analysis: Student t test (two tailed, independent) has been used to find the significance of study parameters between controls and cases. Receiving Operating Characteristics (ROC) tool has been used to find the diagnostic performance of study parameters.

Results: There was significant elevation ($p < 0.001$) of AST, ALT, GGT and SA in alcohol dependent subjects when compared to the controls. Diagnostic efficacy was more for GGT followed by AST and SA as a marker of alcohol abuse.

Conclusion: Sialic acid can be used as a biochemical marker in alcohol abuse, where secondary effects of liver disease hamper the use of traditional markers.

KEYWORDS : Sialic acid ; Alcoholism; GGT; AST; ALT; Sensitivity; Specificity.

INTRODUCTION:

The prevalence of current use of alcohol in India ranged from 7% in western states of Gujarat (officially under prohibition) to 75% in the North eastern state of Arunachal Pradesh¹. The prevalence of hazardous use of alcohol was 14.2% in rural south India². Thus, alcohol abuse has a major public, family and health related problems with impairment of social, legal, inter personal and occupational functioning in those individuals who have been addicted to alcoholism.

A wide variety of biochemical and haematological parameters are affected by regular excessive alcohol consumption. The blood tests traditionally used most commonly as markers of recent drinking are the liver enzymes, gamma glutamyltransferase (GGT), aspartate aminotransferase (AST) and alanine aminotransferase (ALT), and the mean volume of the red blood cells (mean corpuscular volume (MCV)). But they were not sensitive or specific enough for use as single tests³.

Elevated Gamma glutamyltransferase levels are an early indicator of liver disease; chronic heavy drinkers, especially those who also take certain other drugs, often have increased GGT levels. However, GGT is not a very sensitive marker, showing up in only 30–50 percent of excessive drinkers in the general population. It is not a specific marker of chronic heavy

alcohol use, because other digestive diseases, such as pancreatitis and prostate disease, also can raise GGT levels⁴.

AST and ALT are enzymes that help metabolize amino acids, the building blocks of proteins. They are an even less sensitive measure of alcoholism than GGT; indeed, they are more useful as an indication of liver disease than as a direct link to alcohol consumption. Nevertheless, research finds that when otherwise healthy people drink large amounts of alcohol, AST and ALT levels in the blood increase. Of the two enzymes, ALT is the more specific measure of alcohol-induced liver injury because it is found predominantly in the liver, whereas AST is found in several organs, including the liver, heart, muscle, kidney, and brain. Very high levels of these enzymes (e.g., 500 units per liter) may indicate alcoholic liver disease. Clinicians often use a patient's ratio of AST to ALT to confirm an impression of heavy alcohol consumption. However, because these markers are not as accurate in patients who are under age 30 or over age 70, they are less useful than some of the other more comprehensive markers⁵.

AST /ALT ratio of more than 1.5 strongly suggests and ratio > 2.0 is almost indicative of alcohol induced damaged to liver⁶. It has been suggested that an AST/ ALT ratio greater than 2 is highly suggestive or indicative of alcoholic etiology of liver disease. But extreme elevations of this ratio, with AST level

greater than five times the normal should suggest non-alcoholic cause of hepatocellular necrosis⁷.

Sialic acid, which is a derivative of acetyl neuraminic acid, attached to non-reducing residues of carbohydrate chain of glycoproteins and glycolipids is found to be elevated in alcohol abuse⁸.

In this study we compared sensitivity, specificity and diagnostic efficiency of serum Sialic acid with other traditional markers like AST (Aspartate amino transaminase), ALT (Alanine amino transaminase), GGT (Gamma Glutamyl Transferase), as a marker of alcohol abuse.

MATERIALS AND METHODS:

This was a case-control study which was conducted on 100 male subjects aged 20-60 years, 50 cases and 50 controls. Cases comprised of patients diagnosed to have Alcohol Dependant Syndrome (ADS) who were admitted in Psychiatry-ADS ward, at Mahathma Gandhi Memorial Hospital, Warangal. Study was approved by the Institutional ethical committee. Amount, duration and the type of alcohol in the form of Rum, Whisky, Brandy, Vodka, Gin, Arrack, etc consumed was enquired, those subjects who consumed more than half bottles of these spirits daily (or intermittently with abstinence of 2-3 days), for more than 5 years were chosen for this study. Dependence of their alcoholism was enquired in the form of CAGE questionnaire⁹.

- C : Cut down drinking,
- A : Annoyed others by drinking,
- G : Guilty feeling of drinking.
- E : Eye-opener

Those who satisfied two or more questions were taken as cases¹⁰ and their blood samples were collected for the study after their informed consent. Controls were selected from healthy subjects came for master health check up at MGMH health clinic, with no history of alcoholism.

Exclusion criteria:

Patients with history of Diabetes mellitus, Cardiac disease, Viral/Bacterial Hepatitis, Alcoholic hepatitis, tumors, meningitis and history of current use of hepatotoxic and nephrotoxic drugs were excluded from the study.

4ml of blood was collected from each subject from median cubital vein by venipuncture, serum was separated and the different parameters were analyzed. Estimation of serum Sialic acid was done by modified thiobarbituric acid assay of warren¹¹ (Lorentz and Krass) by colorimetric method. Estimations of Aspartate transaminase^{12, 13, 14} Alanine transaminase^{13, 15, 16} Gamma glutamyl transferase^{17, 18} were done by IFCC recommended methods on Dimension Clinical chemistry system (auto analyzer).

Statistical analysis: Student t test (two tailed, independent) has been used to find the significance of study parameters between controls and cases. Receiving Operating Characteristics (ROC) tool (SPSS 17 version) has been used to find the diagnostic performance of study parameters.

RESULTS:

It was observed that all the study parameters were significantly increased (p value < 0.001) in subjects with alcohol abuse when compared to the controls as shown in the Table 1. The ROC analyses of the different parameters were shown in Fig 1 and Table 2. GGT was having highest Diagnostic efficacy followed by AST and SA as a marker of alcohol abuse.

Figure 1: ROC Curve analysis of different parameters

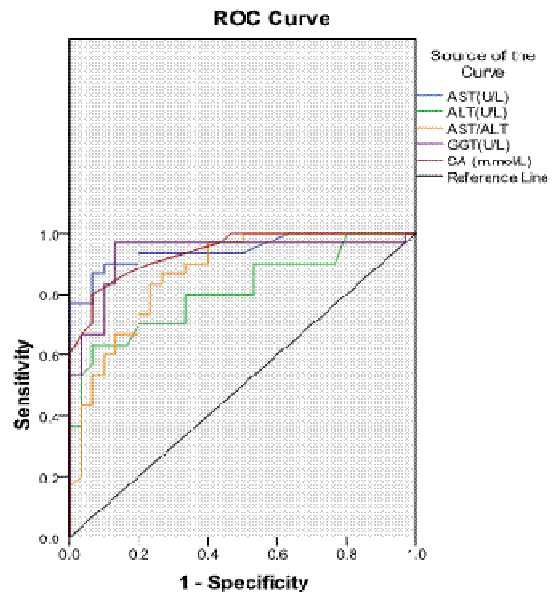


Table1: Comparison of study parameters between controls and cases

Parameters	controls	cases	P value
AST(U/L)	24.83±7.57	87.9 ±53.72	<0.001
ALT(U/L)	47.63 ±18.77	88.83± 46.53	<0.001
AST/ALT	0.58 ± 0.23	0.982 ± 0.29	<0.001
GGT(U/L)	39.36 ±v 20.23	264.13± 298.74	<0.001
SA(m mol/L)	1.81 ± 0.42	2.92±0.706	<0.001

Table 2: ROC Analysis of different study parameters

Parameters	Best-Cutoff value	Sensitivity	Specificity	Diagnostic efficacy	AUC
AST(U/L)	37.50	86.66 %	93.33%	90%	0.946
ALT(U/L)	71.00	63.33%	93.33%	78.33%	0.811
AST/ALT	0.732	83.33%	76.66%	80%	0.869
GGT(U/L)	55.50	96.66%	86.66%	91.66%	0.929
SA(m mol/L)	2.3	80%	93.33%	86.66%	0.939

DISCUSSION:

Alcoholism is a serious health issue with major socio-economic consequences. Significant morbidity is related to chronic heavy alcohol use and alcoholics seek advice only when a complication of drinking sets in. The diagnosis is often based on patients self-reporting of alcohol consumption, which is unreliable and requires high degree of clinical suspicion.

Clinical histories and questionnaires are the commonest initial means of detection of alcohol abuse. They are cheap, easily administered but are subjective. If the history remains uncertain and there is suspicion of alcohol abuse, biological markers provide objectivity. A combination of markers remains essential in detection. Liver is the prime target organ for alcohol-induced disease. Liver enzymes are also important indicators of liver dysfunction, possibly as markers of alcohol dependence. Commonly used markers are GGT, AST and ALT. Laboratory markers help clinicians to raise the issue of excessive drinking as the possible cause of health problem, unfortunately because of lack of sensitive and specific methods, the detection of problem drinking in clinical settings has remained difficult. Therefore, findings of increased serum SA concentrations in alcoholics have raised the possibility of developing new tools for such purpose.

In the present study on analyzing the results it was found that an increased concentration of Serum Sialic acid and other traditional biochemical markers GGT, AST, ALT was observed in cases compared to that of controls. Over all GGT had a good sensitivity and specificity. The other traditional markers used in alcohol abuse varied considerably in their specificities and sensitivities. The increase in serum Sialic acid concentration in alcohol abusers in our present study is in accordance with the studies conducted by other investigators^{8, 19, 20, 21}. The diagnostic accuracy of SA was in accordance with the study by Antilla P et al¹⁹. The increase in serum GGT, ALT and AST concentration in alcohol abusers were in accordance with the studies conducted by other investigators^{19, 22}.

CONCLUSION:

In our study, Sialic Acid proved to be a good test with sensitivity of 80% and specificity of 93.33% with a diagnostic accuracy of 86.66% showing that SA can be used as a biochemical marker in alcohol abuse where secondary effects of liver disease hamper the use of traditional markers.

Limitations of the study are as follows: This study was done in small group of people only; a larger study consisting of alcohol abusers with and without specific liver disease should be conducted to confirm the role of SA as a new marker for alcohol abuse where the traditional markers will be altered by the different liver diseases.

Competing Interests

None declared

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