

# To Study the Biochemical Aspect and Dependence in Alcoholic Liver Disease (ALD)

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## ABSTRACT

**Background:** Geographical variations exists regarding intake of alcohol, highest burden of alcohol-related disease is in developed world with subgroups who drinks excessively or are alcohol abusers and problem. Studies have shown that dependence severity is associated with young age and family drinking history with early neural attention biases to alcohol cues. The definitive diagnosis of any form of alcohol-related hepatic disorders needs to take evidence of alcohol consumption into account hence this study was designed, to study the biochemical aspects and dependence in alcoholic liver disease.

**Methodology:** This prospective, cross sectional study was conducted in patients suffering from Alcoholic Liver Disease. Patients who fulfilled the inclusion and exclusion criteria were enrolled in the study if they are willing to give written informed consent. The patients were also subjected to Severity of Alcohol Dependence Questionnaire (SADQ).

**Results:** A total of 30 patients were enrolled in the study, 17 patients were suffering from cirrhosis and 13 patients had fatty liver. The mean SDAQ score was  $23.83 \pm 2.6$  suggesting moderate dependence as per SADQ scores. The patients with fatty liver had lower levels of various biochemical tests but it was not statistically significant. Patients with fatty liver also had

a higher SADQ scores but it was not statistically significant. There was no statistically significant correlation with the various biochemical parameters.

**Conclusions:** To conclude our study demonstrated that patients with manifestation of fatty liver and cirrhosis had moderate dependence on alcohol, and this was more in patients with fatty liver.


**Key Words:** Fatty Liver, Cirrhosis, Alcohol, Dependence, Alcoholic Liver Disease.

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## INTRODUCTION

ALD (alcoholic liver disease) occurs due to years of heavy drinking as alcohol causes inflammation in liver,<sup>1</sup> varying from simple steatosis to cirrhosis, and are multiple stages that may be present simultaneously in a given individual.<sup>2</sup> Estimates by National Institute on Alcohol Abuse and Alcoholism demonstrated that liver cirrhosis was 12th leading cause of deaths in United States, with total of 29,925 deaths in 2007<sup>3</sup> and is the second leading indication for liver transplantation in United States and Europe.<sup>4</sup> Almost of the death related in alcohol were related with drinking alcohol outside mealtimes which leads to increase in ALD by 2.7 fold.<sup>3</sup>

Geographical variations exists regarding intake of alcohol, highest burden of alcohol-related disease is in developed world accounting for much as 9.2 % of all disability-adjusted life years. The developing regions of the world are also experiencing an

increase in disease burden as alcohol accounts for a major portion of the global disease burden, and are projected to take on increasing importance over time.<sup>5,6</sup> An aspartate transaminase/alanine transaminase (AST/ALT) ratio >3 is highly suggestive of ALD<sup>7</sup> and abstinence being the most important therapeutic intervention for patients with ALD<sup>8</sup> which has shown to improve the outcome of hepatic injury: reduced portal pressure, decreased progression to cirrhosis, and improved survival at all stages in patients with ALD.<sup>8-11</sup> There are subgroups of alcohol consumers who drinks excessively so to develop physical tolerance and withdrawal; and are diagnosed with alcohol dependence.<sup>12</sup> Another subset of people are alcohol abusers and problem drinkers as they engage in harmful use of alcohol, which is defined by the development of negative social and health consequences of drinking (e.g., unemployment, loss of family,

organ damage, accidental injury, or death).<sup>13</sup> The problem in the management of patients with ALD is failure to recognize alcoholism and thus impairs efforts at both the prevention and the management of patients with ALD.<sup>14,15</sup>

According to a study<sup>16</sup> conducted by a group, clinical, biochemical and histological findings were recorded of 282 males with alcohol-induced liver disease showed that proportion of persons under 50 years of age was significantly greater with alcoholic hepatitis than cirrhosis. The mean daily alcohol consumption was clearly lower among those with fatty liver than hepatitis or cirrhosis and duration of alcohol abuse was on average shorter in patients with fatty liver and hepatitis.

Another study done to compare alcohol dependence severity in patients with severe alcoholic liver disease with that in heavy drinkers without liver disease demonstrated that dependence severity in patients varies and tends to be lower than that in heavy drinkers seeking treatment at alcohol treatment centres. Alcohol dependence severity is associated with young age and family drinking history but is not specifically associated with the development of liver disease.<sup>17</sup> One more study done examine whether alcohol dependence and escape drinking were associated with early neural attention biases to alcohol cues showed that while alcohol dependence is associated with enhanced automatic attention biases early in processing, escape drinking is associated with more controlled attention biases to active alcohol cues during a relatively later stage in processing.<sup>18</sup> The definitive diagnosis of any form of alcohol-related hepatic disorders needs to take evidence of alcohol consumption into account.<sup>19</sup> Hence this study was designed, to study the biochemical aspects and dependence in alcoholic liver disease.

## METHODOLOGY

This prospective, cross sectional study was conducted in patients suffering from Alcoholic Liver Disease from the outpatient and inpatient department of a tertiary care teaching hospital in North India. An assessment was done on the basis of AST/ALT from biochemical aspect and features of liver disease. Patients of both sexes, more than 18years with history of alcoholism, diagnosed with alcoholic liver disease and willing to give written informed consent were included in the study. Any patients with non-alcoholic fatty liver, chronic medical, surgical conditions, organic brain syndrome, and chronic mental illness were excluded from the study.

Prior to the enrolment of the patients in the study, approval was obtained from the Institutional Ethics Committee, the patients visiting the department of Internal Medicine and suffering from ALD underwent a thorough medical examination and then the severity of ALD was determined by radiological and biochemical findings. Patients who fulfilled the inclusion and exclusion criteria were enrolled in the study if they are willing to give written informed consent. The patients were also subjected to Severity of Alcohol Dependence Questionnaire (SADQ).<sup>20</sup>

## Severity of Alcohol Dependence Questionnaire (SADQ)

The Severity of Alcohol Dependence Questionnaire was developed by the Addiction Research Unit at the Maudsley Hospital which measures the severity of dependence. The SADQ questions cover the following aspects of dependency syndrome: physical withdrawal symptoms, affective withdrawal symptoms, relief drinking, frequency of alcohol consumption and speed of onset of withdrawal symptoms. A score of 31 or higher indicates "severe alcohol dependence". A score of 16 -30 indicates "moderate dependence" and a score of below 16 usually indicates only a mild physical dependency. A chlordiazepoxide detoxification regime is usually indicated for someone who scores 16 or over. It is essential to take account of the amount of alcohol that the patient reports drinking prior to admission as well as the result of the SADQ.<sup>20</sup>

## Statistical Analysis

The data was presented as mean  $\pm$  standard deviation (mean  $\pm$  SD). The results obtained from the scales were compared using appropriate parametric (Student's 't' test, ANOVA) and non-parametric tests (Chi-Square, Mann Whitney U, Wilcoxon Sign Rank test) wherever applicable. A  $p < 0.05$  was considered statistically significant.

## RESULTS

A total of 55 patients with alcoholic liver disease visited the department of medicine in a period of 6 months out of which 30 patients were enrolled in the study. 15 patients did not give consent to participate in the study and 10 patients were not fulfilling the inclusion and exclusion criteria. Out of 30 patients, 17 patients were suffering from cirrhosis and 13 patients had fatty liver. All patients enrolled in the study were males. The baseline parameters of the patients are shown in table 1. The mean SDAQ score was  $23.83 \pm 2.6$  suggesting moderate dependence as per SADQ scores.

Table 1: Baseline Characteristic of Patients

Parameter	n=30 (Mean $\pm$ SD)
Age (years)	50.83 $\pm$ 11.94
Total Bilirubin (mg/dL)	6.52 $\pm$ 9.29
Conjugated Bilirubin (mg/dL)	3.44 $\pm$ 4.84
Total Proteins (g/dL)	8.49 $\pm$ 11.97
Albumin (g/dL)	3.44 $\pm$ 0.96
Globulin (g/dL)	3.57 $\pm$ 0.56
AG Ratio	0.95 $\pm$ 0.31
Aspartate Aminotransferase (SGOT) (IU/L)	117.70 $\pm$ 93.16
Alanine Transaminase (SGPT) (IU/L)	52.50 $\pm$ 23.99
Alkaline Phosphatase (ALP) (IU/L)	178.40 $\pm$ 109.10
SADQ Scores	23.83 $\pm$ 2.60

Table 2: Characteristic of patients in both groups

Parameter	Group 1 (n=13)	Group 2 (n=17)	p value
Age (years)	53.00±10.91	48.29±11.63	>0.05*
Total Bilirubin (mg/dL)	5.40±9.05	7.42±9.61	>0.05*
Conjugated Bilirubin (mg/dL)	2.58±4.55	4.17±5.07	>0.05*
Total Proteins (g/dL)	6.96±0.89	9.89±16.18	>0.05*
Albumin (g/dL)	3.63±0.78	3.21±1.07	>0.05*
Globulin (g/dL)	3.41±0.39	3.74±0.57	>0.05*
AG Ratio	1.02±0.30	0.91±0.32	>0.05*
Aspartate Aminotransferase (SGOT) (IU/L)	99.77±79.10	133.94±101.63	>0.05*
Alanine Transaminase (SGPT) (IU/L)	48.62±25.85	52.12±22.85	>0.05*
Alkaline Phosphatase (ALP) (IU/L)	155.15±86.69	184.71±123.11	>0.05*
SADQ Scores	24.23±2.89	23.47±2.35	>0.05*

\*no statistically significant difference between groups using student 't' test.

Table 3: Correlation coefficients for age with biochemical parameters among patients in both groups

Variables	SADQ			
	Group 1 (n=13)		Group 2 (n=17)	
	R	p	r	p
Age	-0.02	0.96	0.02	0.94
Serum Bilirubin	0.20	0.52	0.11	0.71
Serum Bilirubin Direct	0.25	0.44	0.20	0.46
Total protein	0.06	0.85	0.22	0.40
Serum Albumin	-0.09	0.78	-0.18	0.49
Albumin: Globulin Ratio	-0.06	0.85	0.15	0.57
SGOT	0.22	0.48	-0.35	0.17
SGPT	0.12	0.69	-0.31	0.23
ALP	0.09	0.76	-0.17	0.52

p>0.05 and not statistically significant

The SADQ score of all patients were in the range of 18 to 28, suggesting moderate dependence of patients enrolled in the study. The patients on the basis of clinical findings were divided into two groups, Group1 were patients suffering from fatty liver, whereas, Group 2 were patients with a diagnosis of cirrhosis. As per criteria a total of 13 patients were in group 1 and 17 patients in group 2. The parameters of patients in both groups are compared in table 2.

The patients in Group 1 had lower levels of various biochemical tests as compared to Group2 but it was not statistically significant. Patients in Group 1 belonged to higher age group and they also had a higher SADQ scores, though it was not statistically significant.

#### Correlation

Estimates of correlation for SADQ with age and various biochemical parameters was calculated and it was seen that there was no statistically significant ( $p>0.05$ ) correlation with the various biochemical parameters (Table 3).

#### DISCUSSION

Excessive alcohol consumption is one of the leading causes of preventable morbidity and mortality worldwide and is associated with a multitude of adverse health consequences with a significant burden attributable to ALD. One of the top five risk factors with

2.5 million deaths and 69.4 million annual disability adjusted life years is excessive or harmful use of alcohol and results in approximately \$223.5 billion of societal costs annually in United States.<sup>21</sup> Individuals with severe alcoholic disease are severely dependent on alcohol and show physical and psychological withdrawal symptoms, relief drinking, impaired control of drinking, salience of drinking behavior and narrowing of drinking repertoire.<sup>17</sup>

Our study was done to assess the biochemical findings and dependence in Alcoholic liver disease. The results of our study demonstrated that patients with manifestation of fatty liver and cirrhosis had moderate dependence on alcohol, and this was more in patients with fatty liver. The biochemical aspects showed that patients with fatty liver had lowers reading as compared to cirrhosis though it was not significant. There was no correlation found with the SADQ questionnaire.

A study done to compare alcohol dependence severity in patients with severe alcoholic liver disease (ALD) with that in heavy drinkers without liver disease demonstrated that patients with ALD had slightly higher SADD alcohol dependence severity score. Alcohol dependence severity is associated with young age and family drinking history but is not specifically associated with the development of liver disease. The findings of this study are somewhat similar to our study where we found that patients with

fatty liver had slightly higher dependence as compared to patients with cirrhosis though both groups were having moderate dependence.<sup>17</sup>

Another study done to examine whether alcohol dependence and escape drinking were associated with early neural attention biases to alcohol cues demonstrated more neural attention bias to the active alcohol-related stimuli. Escape drinkers showed greater neural attention to the active alcohol, time-course of attention processing in problem drinkers have important implications. The results of our study also showed that patients whether with fatty liver or cirrhosis had moderate dependence though we did not focus on the escape drinking or alcoholic cues.<sup>18</sup>

One more study done to compare the scores of obsessive compulsive drinking scale with visual analogue scale, severity of alcohol dependence questionnaire and addiction severity index showed that craving was higher among those who relapsed and craving did predict high alcohol consumption and high index of severity. The results of our study have shown that moderate dependence is seen in patient with alcoholic liver disease though we did not study the craving phenomenon and its correlation.<sup>22</sup>

There are certain limitations to our study, firstly the sample size is small, our study was focused on a time duration hence we tried to enroll the patients within the given time span. Secondly an intervention could have been another option but due to time constraint we could not go for a follow up of patients. Thirdly, an intervention could have helped but due to financial constraints it could not be done.

To conclude our study demonstrated that patients with manifestation of fatty liver and cirrhosis had moderate dependence on alcohol, and this was more in patients with fatty liver. There was no correlation found with the SADQ questionnaire.

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