

**Original Research Article****Assessment of enzymatic markers in patients of chronic alcoholic liver disease attending OPD of a tertiary health care level Institute of North India**

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Dr Rajju TiwariPost Graduate Resident 3rd Year, Department of Medical Biochemistry PGIMS Rohtak (Haryana) ,INDIAEmail: drriwari85@gmail.com**ABSTRACT**

Background: Alcoholic Liver disease (ALD), is a term that encompasses the hepatic manifestations of alcohol over consumption that includes- fatty liver, alcoholic hepatitis and chronic hepatitis with cirrhosis. Although Only 15% alcoholics develop liver disease even than alcohol is strong morbidity agent among alcoholics. As a markers of liver damage in case of alcoholic Liver disease, enzymes which are mainly important are- ALP- Alkaline Phosphatase, GLD- Glutamate Dehydrogenase and 5 NTP-5' Nucleotidase etc

Objective: To evaluate the status of enzymatic markers in alcoholic liver disease & to compare the enzymatic markers of alcoholic liver disease among the cases and control. **Materials and Methods:** Total 100 participants were enrolled as sample size among of them 50 patients attending OPD of Rama Medical college of Rama University, Kanpur were enrolled as cases and remaining 50 healthy individuals of same profiles were enrolled as controls in this study. 5 ml fasting Venous samples was taken for serum measurement of enzymatic markers of ALD patients and normal healthy individuals and samples were analysed in auto analysers.

Results: In the present study the mean age of cases was 48.06±10.07 yrs and in control group it was found 46.36±9.61yrs. ($p = 0.390$) and the mean weight of cases was 64.52± 6.08 kgs and in control group it was found 64.30± 6.03 kgs. ($p=0.856$) and the enzymatic markers i. e. SGOT,SGPT ALP and GGT were found to be significantly higher in cases than control, ($p<0.05$)

Conclusion: In the present study the status of enzymatic markers (AST,ALP,ALT,GGT) were evaluated in alcoholics liver disease. A significant association was obtained in the enzymatic markers between the alcoholics and non-alcoholics. It can be concluded that the level of enzymatic markers like AST,ALP,ALT and GGT are raised in alcoholics as compared to non-alcoholics.

Keywords: Alcoholic Liver Disease(ALD), AST,ALT,GGT.

Introduction

Alcoholic Liver disease is a term that encompasses the hepatic manifestations of alcohol over consumption that includes- fatty liver, alcoholic hepatitis and chronic hepatitis with cirrhosis. As per reports 15% alcoholics develop liver disease ^[1].

This issue of Alcohol alerts examiners the diagnosis and treatment of alcoholic liver disease (ALD), a serious and potentially fatal consequence of drinking alcohol. Another disorder, hepatitis C, also featured here, often is found in patients with ALD ^[2].

However, levels and patterns of alcohol consumption do not fully explain the cause of alcoholic liver disease mortality ^[3]. The global burden of disease project estimated alcohol to be responsible for 1.5% of all deaths and 3.5% of those who live life with disability ^[4]. Now a days,

it is a common substance abused in India. Alcoholism is a chronic, progressive disease and is one of the potential causes of liver disease ^[5].

Although alcoholism is more common in men, women are much more susceptible to the toxic effects of alcohol ^[6]. Recent evidence has shown that estrogen may increase the susceptibility of the liver to alcohol-related damage, rendering women more vulnerable to its toxic effects ^[7].

Cirrhosis mortality rates are very low in the younger population, but rise with increasing age. In fact, the rate of cirrhosis among people of 75–84 years of age is as high as 31.1 per 100,000 individuals and contribution of cirrhosis to total deaths peak between 45- 54 years of age, becoming the fourth leading cause of death in the US within this age group ^[7].

The prevalence of ALD, particularly cirrhosis, varies significantly with socioeconomic status and social class. Numerous studies have shown that individuals who are unemployed, having low income, or have low educational background exhibit higher rates of cirrhosis mortality ^[8].

Severity of liver damage is often associated with the amount of heavy alcohol consumption with a history of alcohol abuse ^[9].

However, the magnitude of ALD depends on the

total amount of alcohol consumed drinking patterns and type of alcoholic beverage intake ^[10].

Physicians have long sought an accurate and inexpensive means of identifying persons who consume excessive amounts of ethyl alcohol. It has been reported that medically diagnosed alcoholics can be differentiated reliably from non-alcoholics using clinical laboratory tests.

Moreover, distinguishing alcoholic from non-alcoholic liver disease has important implications for treatment and management ^[11]. The most widely used tests for this purpose are standard liver function tests, gammaglutamyl transferase (GGT), and mean cell volume (MCV) using an electronic cell counter.

Although GGT is a sensitive indicator of excessive alcohol intake, it is also raised in a variety of non-alcoholic liver diseases ^[12]. Other Liver enzymes which are mainly important in case of alcoholic damages are- ALP- Alkaline Phosphatase, GLD- Glutamate Dehydrogenase and 5 NTP-5' Nucleotidase etc ^[13].

By taking all these facts the present study was carried out among alcoholic liver disease patients and healthy individuals, along with base line parameters mainly ALT, AST, ALP and GGT were analysed among both of the group so that elevation of these enzymatic markers among ALD patients can be seen clearly.

U.P. Sample size was a total of 100 subject divided into two, group cases and control. In Cases – About 50 patient was diagnosis of alcoholic liver disease and in Control- 50 healthy patient without any history of alcoholic liver disease were enrolled in the both of the group age was between 30 to 70 yrs old. The adopted

Inclusion criterias were -

I) For test group -30 to 70 yrs of age group having diagnosed alcoholic liver disease and will give the consent to participate will be the included in the present study.

II) For the control group- same age group of healthy participants and willing to participate in the present study and non alcoholic. A semi structured quationarre based proforma was used to collect the data.

Diagnosis of Alcoholic Liver Disease-Based upon history of long use of alcohol, clinical features, biochemical markers of Alcoholic Liver Disease and ultra sono graphic features of patients , these all evidences were used to confirm a case of Alcoholic Liver Disease.

Ethical consideration-All the study process was started only after obtaining ethical approval from the institutional ethical committee. All the information about the participants was also kept confidential.

Blood Sample- Over night fasting blood sample of 5ml was collected from the each participants for estimation of AST,ALT,ALP,and GGT.

Methods of estimation- The estimation of various enzymatic markers was done as per following-

Estimation of AST &ALT- It was done by using the fasting blood sample based upon the spectrophotometric principle and with the help of Auto analyzer machine.

Normal value AST- Women <31U/L and for males it is <35U/L and

Normal value for ALT- for woman is <34U/L and it is <45U/L for males.

Estimation of ALP- It was done by using the fasting blood sample based upon the

spectrophotometric principle and with the help of Auto analyzer machine.

Normal value of ALP- womens: 42-98U/L, males:53-128U/L

Estimation of GGT- It was also estimated in fasting samples with the spectrophotometric principle based kit used auto analyzer machine.

Normal value of GGT-male; 55U/L, female;38U/L

Results

All the subjects were subjected to detailed history-taking as per proforma. Test parameters were tabulated as per the master chart. The results were expressed in terms of mean \pm SD. The p value <0.05 was considered as significant. In the present study the mean age of case was 48.06 ± 10.07 yrs and in control group it was found 46.36 ± 9.61 yrs. ($p = 0.390$, Table No. 1) In the present study the mean wt of case was 64.52 ± 6.08 kgs and in control group it was found 64.30 ± 6.03 kgs. $p=0.856$, Table No. 2) In the present study SGOT,SGPT ALP and GGT were found to be significantly higher in cases than control, ($p < 0.05$, Table No 3).

Table no. 1 Age wise distribution of study subjects

Age (in year)	cases	control
31-35	2	8
36-40	11	7
41-45	8	3
46-50	14	10
51-55	4	12
56-60	3	8
61-65	3	1
66-70	5	1
Total	50	50
Mean \pm SD	48.06 ± 10.07	46.36 ± 9.61

$p = 0.390$

Table no. 2 Distribution of weight (kg) of patients studied

Weight (in kgs)	case	control
Mean \pm SD	64.52 ± 6.08	64.30 ± 6.03

$p = 0.856$

Table no. 3 Comparison of enzymatic markers in cases and control

Parameter		Cases	Control	p value
SGOT(U/L)	Mean ± SD	86.64 ± 17.52	31.78 ± 11.71	<0.05
SGPT (U/L)	Mean ± SD	46.60 ± 18.38	30.98 ± 13.55	<0.05
ALP (U/L)	Mean ± SD	97.49 ± 39.55	80.58 ± 24.47	0.008
GGT	Mean ± SD	97.49 ± 39.55	50.04 ± 26.23	<0.05

Discussion

In present study, 50 subjects who are diagnosed with alcoholic liver disease were enrolled as cases and 50 normal healthy individuals were enrolled as controls and compared. when both cases and controls were matched age wise then it was found that the difference was with p value of 0.390 (Table 1) which shows no statistically significant difference was observed in case of age wise distribution similarly in case of weight wise distribution among cases and controls, shows no statistically significant difference was observed (Table 2- p value of 0.856). The slight elevated weight in cases may be due to that alcohol influence hunger via several central mechanisms. The effects of alcohol on opioid, serotonergic, and GABAergic pathways in the brain all suggest the potential to increase appetite. Given the complexity of the interplay between central and peripheral signals of satiety, more research needs to be performed in order to elucidate the precise biochemical mechanism driving food intake following alcohol consumption.^[14]

In case of enzymatic marker evaluation among cases and controls, AST is increased in cases with mean value of 86.64 ± 17.52 U/L when compared with controls with mean of 31.78 ± 11.71 U/L. p value is < 0.05 which is significant. ALT is increased in cases with mean value of 46.60 ± 18.38 U/L when compared to controls with mean value of 30.98 ± 13.55 U/L. p value is 0.05 which is significant. Gamma glutamyltransferase is increased in cases with mean value of 111.88 ± 31.72 U/L when compared with controls with mean of 26.88 ± 13.01 U/L, p value is < 0.05 which is significant. ALP in cases was found to be 97.49 ± 39.55 and in control it was 80.58 ± 24.47. This result is consistent with study conducted by

H. Nyblom, U. Berggren^[15]. et al showed increase in aminotransferases in alcoholic cirrhosis. Another study conducted by Anil Batta^[16]. also showed increase AST and ALT in alcoholic liver disease. Similarly a study conducted by Selinger MJ, Matloff DS^[17]. et al showed that patients with alcoholic liver disease the serum gamma glutamyltransferase is increased sevenfold. This increase in liver enzymes was may be due to CYP 2E1, which is upregulated in chronic alcohol use, generates free radicals through the oxidation of nicotinamide adenine dinucleotide phosphate (NADPH) to NADP. Alcohol metabolism appears to increase oxygen utilization by liver cells, thereby reducing the availability of oxygen for other important cellular functions (see sidebar). This phenomenon is most important in zone 3 of the liver lobules, which normally is exposed to lower concentrations of oxygen than zone 1 or zone 2. The tendency of hypoxia to occur in zone 3, together with the fact that free radicals are more likely to be formed in this region, may account for the observation that alcoholic liver damage tends to concentrate in zone 3. Cells lining the liver sinusoids also may contribute to hypoxia by secreting endothelin, a potent agent that induces narrowing of blood vessels. The resulting narrowing of the sinusoids may decrease the delivery of oxygen-containing blood to zone 3. Zone 3 of the hepatic acinus has a higher concentration of AST and damage to this zone, may result in greater alteration to AST levels. Chronic alcohol exposure also activates hepatic macrophages, which then produce tumor necrosis factor-alpha (TNF-alpha). TNF-alpha induces mitochondria to increase the production of reactive oxygen species. This oxidative stress promotes hepatocyte necrosis and apoptosis, which is exaggerated in the alcoholic who is deficient in antioxidants such as glutathione and vitamin E^[18].

Injury to the liver, whether acute or chronic, eventually results in an increase in serum concentrations of aminotransferases, AST and ALT. stimulus to alcoholic liver fibrosis is a cytokine called transforming growth factor beta

(TGF- β). In the presence of this cytokine, stellate cells grown in culture begin to synthesize collagen. Increased serum levels of GGT was observed in alcoholic liver disease can be the result of enzyme induction and decreased clearance. In these patients, GGT serum levels can be markedly altered (>10 times the upper reference value), whereas ALP levels may be normal or only slightly altered. Alkaline phosphatase (ALP) levels above the upper reference value and increased glutamyl-transpeptidase levels interpret the hepatic source of GGT, which is shown in alcoholic liver disease. Alcohol might increase GGT production by inducing hepatic microsomal production, or it might cause the leakage of GGT from hepatocytes [20].

However some studies showed that determination of high levels of total serum GGT activity is not specific to alcoholic intoxication. [20].

Conclusion

In the present study the status of enzymatic markers (AST,ALP,ALT,GGT) were evaluated in alcoholics liver disease. A significant association was obtained in the enzymatic markers between the alcoholics and non-alcoholics. It can be concluded that the level of enzymatic markers like AST,ALP,ALT and GGT are raised in alcoholics as compared to non-alcoholics.

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