

Alcoholics and Viral Markers from a Hospital in North India

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Abstract:

Introduction: Viral hepatitis with alcohol consumption is associated with accelerated progression of liver injury and with a higher frequency of cirrhosis. In different geographical areas alcoholics may have higher prevalence of infections by hepatitis B virus (HBV) and hepatitis C virus (HCV) than non alcoholics.

Objectives: The objective was to determine the prevalence of HBV and HCV infections in alcoholic patients, and to evaluate the presence of underlying risk factors.

Methodology: A prospective study was done on one hundred three alcoholic patients with or without liver disease and a control group of one hundred patients not consuming alcohol, all attending Department of Gastroenterology and Department of Hepatology, Nehru Hospital, PGIMER, Chandigarh for various ailments. A questionnaire based direct interview was used to collect various informations. Routine investigations including Ultrasound abdomen were done. All patients in the study group were uniformly tested for HBsAg and anti HCV by ELISA.

Results: Among alcoholics 102 (99 %) were male and 1 (1 %) female patient while in control group 65 (65 %) were male and 35 (35 %) female. The mean age of alcoholic patients was 44.11 yrs. \pm 10.695 and the mean age of control group was 32.55yrs. \pm 11.878. The mean daily intake of alcohol was 108.35 \pm 66.88 g/day with mean duration of drinking being 17.27 yrs. \pm 8.79. The most commonly consumed alcoholic beverage was whisky. 77.6% alcoholics (80/103) had liver disease in form of fatty liver disease (16.5%), acute hepatitis (4.8%), decompensated cirrhosis (44.6%) and acute on chronic liver failure (ACLF, 11.6%). Alcoholics with liver cirrhosis had higher mean daily intake of alcohol (122.1 g/day) . 3.7% alcoholics were HBsAg reactive while 9.7% alcoholics had Hepatitis C Virus (anti HCV reactive) infection. The factors significantly associated with presence of HBV and HCV infection was history of blood transfusion and intravenous drug abuse.

Conclusion: 77.6% chronic alcoholics have liver disease in various form as fatty liver, hepatitis, cirrhosis or acute on chronic liver failure. 3.7 % of alcoholics had Hepatitis B virus infection while 9.7% alcoholic had Hepatitis C virus infection.

Keywords: Alcoholics, Alcoholic liver disease, Cirrhosis, HBV, HCV.

I. Introduction

Viral hepatitis with alcohol consumption is associated with accelerated progression of liver injury, as well as with a higher frequency of cirrhosis and a higher incidence of hepatocellular carcinoma (HCC) than that observed with viral hepatitis alone or with alcohol consumption alone.¹ In different geographical areas it has been reported that alcoholics may have higher prevalence of infections by hepatitis B virus (HBV) and hepatitis C virus (HCV) than nonalcoholics.²⁻¹⁸ Patients with HCV infection and alcohol abuse develop more severe fibrosis with higher rate of cirrhosis and hepatocellular cancer (HCC) compared with nondrinkers.¹⁹ The purpose of this study is to determine the prevalence of HBV and HCV infections in alcoholic patients, and to evaluate the presence of underlying risk factors.

II. Methodology

A prospective study was done on one hundred three alcoholic patients with or without liver disease and a control group of one hundred patients not consuming alcohol, all attending Department of Gastroenterology and Department of Hepatology, Nehru Hospital, PGIMER, Chandigarh for various ailments. A questionnaire based direct interview was used to collect information on type, quantity, duration and pattern of alcohol consumption, demographic variables, disease profile and medications used. Particular attention was paid to possible risk factors for infection with HBV or HCV such as blood transfusions, hospital admissions, intravenous drug abuse (IVDA) or multiple unprotected sexual intercourse (MUSIC). Routine blood tests including serum alanine and aspartate aminotransferases (ALT and AST), alkaline phosphatase (ALP), direct and total serum bilirubin, total protein and albumin, prothrombin time and other hematological parameters including hemoglobin, platelets, white blood cell counts, red blood cell indices and peripheral blood film were obtained from PGIMER laboratories. Ultrasound abdomen was used to detect status of the liver.

Tests for HBsAg and anti-HCV were carried out in sera (stored at -20°C) by commercially available Enzyme Immunoassay (Erba Lisa Hepatitis B, Erba Lisa Hepatitis C). Evidence for alcoholic liver disease was evaluated clinically, biochemically and by ultrasound. (i) Alcoholic hepatitis was suspected in patients who were continuing their drinking habit, developed jaundice with raised transaminases with or without hepatocellular failure in the form of ascites and/or encephalopathy. (ii) Alcoholic cirrhosis was suspected in patients with clinical evidence of decompensation in the form of ascites or encephalopathy or variceal bleed, firm, irregular, nodular liver with or without enlargement along with or without splenic enlargement, Ultrasound evidence of cirrhosis in the form of heterogenous echotexture, irregular margin, irregular portal vein radicles with or without change in the span of liver along with or without portal hypertension having portal vein diameter greater than 12mm or splenic vein diameter greater than 7 mm or with presence of collaterals at splenic hilum. (iii) Alcoholic fatty liver was suspected in patients with ultrasound evidence of fatty liver with or without enlarged liver in the absence of alcoholic cirrhosis or alcoholic hepatitis. (iv) Acute on chronic liver failure (ACLF) was defined as an acute hepatic insult manifesting as jaundice (serum bilirubin >5 mg/dl) & coagulopathy (INR >1.5 or prothrombin activity $<40\%$) and complicated within 4 weeks by ascites and/or encephalopathy in a patient with previously diagnosed or undiagnosed chronic liver disease. Alcoholics with no liver disease was suspected in the patients without clinical features of liver disease (history and physical examination), normal biochemical tests including serum alanine and aspartate aminotransferases (ALT and AST), alkaline phosphatase (ALP), direct and total serum bilirubin, total protein and albumin, prothrombin time and other hematological parameters including hemoglobin, platelets, white blood cell counts, red blood cell indices and peripheral blood film and a normal liver in ultrasound. Data was analysed with SPSS 21 trial version. The effect of the intervention within the group was checked using Student's t-test (paired). The various parameters at each point of time or changes (before and after Intervention) for two groups were compared by Student's t-tests or Mann Whitney U test. Qualitative or categorical data were described as frequencies and proportions and were analyzed for its association with the groups using Chi-square test or Fisher's exact test, whichever was applicable. 'p' value of <0.05 was considered significant in all the tests.

III. Results

There were 102 (99 %) male and 1 (1 %) female patients among alcoholics as study group and 65 (65 %) male and 35 (35 %) female in the screened patients in the control group. The mean age of alcoholic patients was 44.11 yrs. \pm 10.695 and the mean age of control group was 32.55yrs. \pm 11.878. 20(19.4%) out of 103 alcoholics started consuming alcohol below 21 years. 51 alcoholics (49.5 %) had history of alcoholism in the family. Mean daily intake (g/day) of alcohol was 108.35 ± 66.88 g/day and mean duration (years) of drinking was 17.27 ± 8.79 . Binge drinking was observed in 71 (68.9 %) cases. 37 (35.9 %) alcoholics had history of a drink first thing in the morning to steady nerves or get rid of a hangover (eye opener). The most commonly consumed drink among 55 (53.4%) alcoholics was foreign liquor, 34 (33 %) consumed locally-made liquor, and 14 (13.6 %) consumed both the types of liquor. The most common type of alcoholic beverage was whisky, followed by locally-made liquor. On the basis of clinical, biochemical and radiological evidence 80 out of 103 alcoholics (77.6%) were found to have liver disease. Out of 80 alcoholic patients 17 (21.2 %) had fatty liver disease, 5 (6.2%) had acute hepatitis, 46 (57.5 %) patients with liver cirrhosis had decompensation and 12 (15 %) patients had acute on chronic liver failure (ACLF). All patients with ACLF had alcoholic cirrhosis as underlying CLD. Overall among 103 alcoholics, 17 patients (16.5%) were of fatty liver disease, 5 patients (4.8%) had acute hepatitis, 46 patients (44.6%) were of decompensated cirrhosis and 12 patients (11.6%) of ACLF. Mean daily intake (g/day) in alcoholics with liver disease was higher as compared to alcoholics without liver disease (114.37g/day and 87.39 g/day respectively). Alcoholics with liver cirrhosis had mean daily intake of 122.1g/day which was significantly higher when compared to alcoholics with no liver disease ($p=0.005$). In patients with hepatitis, ACLF and decompensated cirrhosis daily amount of consumption was higher than alcoholics without liver disease but was not found to be statistically significant. Mean duration of consumption was similar in alcoholics with and without liver disease (17.5 years and 16.4 years respectively) ($p=0.588$). In other stages of liver disease (hepatitis, ACLF and decompensated cirrhosis) duration of intake was higher than alcoholics without liver disease, however not statistically significant. Age at first use was similar in alcoholics with and without liver disease (27.5 years and 24.8 years respectively) ($p=0.122$). In patients with decompensated cirrhosis the age of first drink was significantly higher than alcoholics without liver disease (29.1 years and 24.8 years respectively) ($p=0.006$). 60 (75 %) out of 80 alcoholics with liver disease had history of binge drinking as compared to 11 (47.8 %) out of 23 alcoholics without liver disease ($p=0.013$). However binge drinking was found similar in alcoholics with different stages of liver disease. 66 (64 %) out of 103 alcoholics had raised serum bilirubin. Serum alanine and aspartate aminotransferases (ALT and AST) were found elevated in 46 (44.6%) and 20 (20.4%) alcoholics respectively. Low serum albumin (<3.4 g/dl) was observed in 71 (68.9%) alcoholics and 55 (53.4%) had low prothrombin time index (PTI).

The mean serum bilirubin in alcoholics with acute hepatitis and ACLF was 11.8 mg/dl and 15.3 mg/dl respectively, a much higher figure in comparison to fatty liver disease and decompensated cirrhosis in whom it was 1.5mg/dl and 7.7 mg/dl respectively. Similarly serum AST value in acute hepatitis and ACLF (108.8 units/l and 151.9 units/l respectively) was much higher than patients with fatty liver disease and decompensated cirrhosis (56.1 units/l and 86.3 units/l respectively). Serum ALT value was much higher, 88.6 units/l in acute hepatitis in comparison to fatty liver disease (38.0 units/l), in cirrhosis and in ACLF it was 64.5 and 63.6 units/l respectively. Mean serum albumin value in fatty liver disease was 3.2 g/dl which was higher than in acute hepatitis and ACLF where it was 2.9 and 2.8g/dl respectively. Mean PTI value was lower in cirrhosis with decompensation and ACLF, 63.9% and 53.2 % respectively than alcoholics with fatty liver disease and hepatitis where it was 85.8% and 68.6 % respectively (Table I). Sera from 4 alcoholics (3.9 %) were positive for HBsAg and 10 (9.7 %) were positive for anti-HCV. Both HBsAg and anti-HCV was detected in a sample from 1 patient. Among controls HBsAg was detected in 2 (2%) and anti-HCV was found in 1 (1%) of the screened family members. No person was positive for both HBsAg and anti-HCV among controls. The difference between alcoholics and the control group was significant for the prevalence of anti-HCV (p = 0.006) . The difference for prevalence of HBsAg was not significant between the two groups (P=0.428) (Table II) .

The two factors that were significantly associated with the presence of anti-HCV and the combined presence of markers of HBsAg and anti-HCV were history of blood transfusion and intravenous drug abuse. History of blood transfusion was elicited in 6 of 10 (60 %) alcoholics with anti-HCV. Only 1 out of 4 (25 %) alcoholics with HBsAg had history of blood transfusion . Only one alcoholic had history of parenteral drug abuse which was found to have HCV infection. Mean serum bilirubin was higher in alcoholics with HBV infection (12.4mg/dl ± 11.0) compared to alcoholics without viral infection (6.5 mg/dl ± 9.2) . Low platelet count was associated with anti HCV reactive alcoholics (107 ± 54× 10³per ml) as compared to alcoholics without viral infection (193 ± 141× 10³per ml, p < 0.06) . However variations in other biochemical parameters were seen but it was not statistically significant (Table III).

There was no difference between the groups concerning other risk factors such as hospitalization, multiple unprotected sexual intercourse, duration and amount of alcohol consumption and alcoholism in family. No relationship could be observed to know whether the prevalence of virus B and C markers rises with increasing duration of excessive drinking. There was no significant difference between increasing mean daily alcohol intake and the presence of virus markers.

IV. Tables

Table I. Liver function tests' (LFT) and different stages of Liver Disease in Alcoholics.

Parameter	Fatty Liver Disease(n=17)	Hepatitis (n=5)	Decomp Cirrhosis (n=46)	ACLF (n=12)
Bilirubin(mg/dl)	1.5±2.7	11.8±3.1	7.7±10.0	15.3±10.8
AST(units/l)	56.1 ±27.5	108.8+34.4	86.3+64.1	151.9+92.8
ALT (units/l)	38.0+24.1	88.6+ 104.8	64.5+ 132.6	63.6+41.0
Albumin(g/dl)	3.2+0.76	2.9+0.8	2.9+0.65	2.8+0.8
PTI(%)	85.8+10.0	68.6±20	63.9+17.5	53.2+18.0

NB: Decomp Cirrhosis - Decompensated Cirrhosis;
ACLF - Acute on Chronic Liver Failure;

Table II. Prevalence of markers of HBV and for HCV in alcoholics

Virus Markers	Alcoholics (n=103)	Controls (n=100)	p value
HBsAg positive	4 (3.9%)	2 (2%)	0.428
Anti-HCV positive	10 (9.7%)	1 (1%)	0.006
At least one marker positive	13 (12.6%)	3 (3 %)	0.011

NB: One alcoholic had dual infection for HBV and HCV.

Table III. Laboratory parameters in alcoholics with or without HBV and/or HCV infection

Parameter	Group A HBsAg + n=4	Group B anti-HCV + n=10	Group C n=90 Without HBV&HCV markers	p value
AST (units/l)	102+66	93+77	79+64	* 0.52 ** 0.55
ALT (units/l)	309+414	58+50	42+32	* 0.29 ** 0.88
AST/ALT (ratio)	1.08+1.14	1.63+0.66	1.99+0.94	* 0.06 ** 0.29
ALT (units/l)	122+67	110+36	150+156	* 0.74 ** 0.42
Bilirubin (mg/dl)	12.4+11.0	3.6+5.2	6.5+9.2	* 0.18 ** 0.29
Total Protein (g/dl)	6.9+0.5	6.2+1.2	6.4+0.8	* 0.26 ** 0.57
Albumin (g/dl)	3.6+1.1	2.7+0.6	3.0+0.7	* 0.11 ** 0.13
PTI (%)	63+25	64+24	70+17	* 0.44 ** 0.31
Hemoglobin (g/dl)	11.3+3.7	10.2+2.3	9.9+2.2	* 0.24 ** 0.74
Platelets (x10 ³)	125+65	107+54	193+141	* 0.38 ** 0.06
WBC count	7475+4606	9220+4156	10540+6110	* 0.33 ** 0.53

NB: * Group A vs. C, ** Group B vs. C, $p < 0.05$ = statistical significant.

V. Discussion

This study showed that about half of alcoholics had history of alcoholism in family and only one third alcoholics had education level above high school. Similar results have been reported in previous studies.¹⁴ In the present study, it was found that 55 (53.4%) took foreign liquor, 34 (33%) took only locally-made alcoholic beverages, and 14 (13.6%) took both. Whisky was the most preferred type of liquor in our patients (47.3%). This finding corroborates the findings of other studies from different urban areas of India^{22,23,24}. In contrast, one study from Arunachal Pradesh found local home-made beverages as preferred type of alcohol²⁵. The spectrum of alcohol-related liver injury varies from simple steatosis to cirrhosis. These are not necessarily distinct stages of evolution of disease, but rather, multiple stages that may be present simultaneously in a given individual^{27,28}. In present study, 80 out of 103 alcoholics (77.6 %) were found to have liver disease. Among these 103 alcoholic patients 16 (15.53 %) had fatty liver disease, 5 (4.85%) had hepatitis and 58 (56.31 %) had liver cirrhosis. 46 (44.6 %) patients with liver cirrhosis had decompensated cirrhosis and 12 (11.65 %) patients presented with acute on chronic liver failure (ACLF).

In this study all patients with ACLF had alcoholic cirrhosis as underlying chronic liver disease (CLD). In all patients the cause of acute insult was ongoing alcohol consumption. In addition one patient had sepsis and one patient had acute variceal bleed as contributory non-hepatic injury. In contrast, a study on 102 ACLF patients by Duseja et al. showed that all patients had cirrhosis as underlying CLD and alcohol was found in 62 (61 %) patients as a cause of cirrhosis. Daily intake in alcoholics with liver disease was higher as compared to alcoholics without liver disease (114.37 and 87.39 g/day respectively) but it was not statistically significant ($p = 0.141$). In patients with fatty liver disease mean amount of alcohol intake was significantly lower (73.4 g/day). In alcoholics with liver cirrhosis the mean daily intake was significantly higher (122.1g/day) as compared to alcoholics with no liver disease (87.4 g/day) (p value < 0.001 and 0.005 respectively). Mean duration (years) of consumption was not found statistically different between alcoholics with different stages of liver disease and alcoholics without liver disease. The fact that only small numbers of heavy drinkers develop advanced ALD indicates that other factors are involved in pathogenesis of ALD. Several risk factors are associated with ALD have been identified. These include sex, obesity, drinking patterns, dietary factors, non-sex-linked genetic factors, and cigarette smoking^{30,31,32}. In this study we found a significant increased prevalence of HCV infection and combined prevalence of HBV and HCV infection in alcoholics compared to the control group of family members of patients with HBV and/or HCV infection. The frequency of HBV infection was similar among alcoholics and the screened family members.

Regarding the epidemiology of HCV among alcoholic patients, several studies found a strong association between serum markers for HCV infection and the presence of parenteral risk factors.^{16,19,20,21,33,34} Among our 103 alcoholic patients, 10 were anti-HCV positive and 6 of those had history of blood transfusion and one had history of intravenous drug use. These two factors were found significantly associated with the prevalence of anti-HCV antibodies in alcoholic patients.

Other risk factors such as amount and duration of alcohol consumption, hospitalization, multiple unprotected sexual intercourse (MUSIC), alcoholism in family were not associated with increased prevalence of virus markers in alcoholic patients. In our study, out of 103 alcoholic patients only one patient had history of MUSIC. It is possible that some of our alcoholics may actually have had a history of risky sexual behavior - a risk factor that is difficult to exclude objectively. In the present study we observed that all the 13 alcoholic patients with positive virus markers in their sera had liver disease. This result clearly indicate an association between the presence of liver disease and the presence of at least one marker of HBV or HCV ($p = 0.039$). These data suggest that viral infection plays a significant role in development of liver disease in alcoholic patients. As to our alcoholic cirrhotic patients with and without virus infection, it was not possible to differentiate them as to the severity of disease.

Out of 58 alcoholic patients with liver cirrhosis, 47 were not HBsAg positive or anti-HCV positive, showing that in these patients alcohol seems to be the only cause of cirrhosis. However we cannot rule out the possibility that undetectable hepatotropic viruses are involved in the pathogenesis of cirrhosis in the alcoholic patients. The fact that some alcoholics developed liver cirrhosis and the others did not seems to be also related to factors like genetic predisposition, nutrition, environmental and immunologic factors, or comorbidity.

Some studies showed levels of serum aminotransferases (ALT and AST) and ALT/AST ratio significantly higher in alcoholics with superadded viral infection.^{6, 10} In present study levels of serum aminotransferases (ALT and AST) and ALT/AST ratio was higher in patients with dual pathology (alcohol + virus) but was not found statistically significant. Other laboratory tests including alkaline phosphatase (ALP), serum bilirubin, albumin and prothrombin index (PTI) were essentially similar in alcoholics with and without virus markers. Thus, the presence of virus infection in an alcoholic patient cannot be inferred on the basis of routine liver tests. Only one hematological parameter, values of platelets were significantly lower in alcoholics with positive anti-HCV antibody as compared to uninfected alcoholics ($p = 0.001$).

The two main causes of liver disease (alcohol and virus) are partially preventable as they both depend on risky behaviors. Avoidance of alcohol intake is required for the prevention of virus infection and development of liver disease in alcoholics. This is best achieved by using educational and social programs to convince patients and their caretakers of the great necessity to eliminate alcohol intake.

VI. Conclusion

In present study mean age of alcoholic patient was 44.11 yrs. \pm 10.695. The mean daily intake of alcohol was 108.35 \pm 66.88 g/day with mean duration of drinking being 17.27 yrs. \pm 8.79. The most commonly consumed alcoholic beverage was whisky.

77.6% alcoholics (80/103) had liver disease in form of fatty liver disease (16.5%), acute hepatitis (4.8%), decompensated cirrhosis (44.6%) and acute on chronic liver failure (ACLF, 11.6%). Alcoholics with liver cirrhosis had higher mean daily intake of alcohol (122.1 g/day). The mean serum bilirubin, serum AST and serum ALT was much higher in alcoholics with acute hepatitis and ACLF compared to alcoholics with fatty liver disease and decompensated cirrhosis.

3.7% alcoholics were HBsAg reactive while 9.7% alcoholics had Hepatitis C Virus (anti HCV reactive) infection. The factors significantly associated with presence of HBV and HCV infection was history of blood transfusion and intravenous drug abuse.

The presence of virus infection in an alcoholic patient cannot be inferred on the basis of routine blood tests used for initial assessment of liver disease including levels of serum alanine and aspartate aminotransferases (ALT and AST), AST/ALT ratio, alkaline phosphatase (ALP), serum bilirubin, albumin and prothrombin index (PTI). Only low platelet counts were significantly associated with anti-HCV reactivity in alcoholics as compared to uninfected alcoholics ($p = 0.001$).

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