

# Evaluation of hepatitis A, B, and C serology in patients with cirrhosis and intensive alcohol consumption

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## ABSTRACT

**OBJECTIVE:** The objective of this study was to evaluate the serology of hepatitis A, B, and C in patients with cirrhosis and intensive alcohol consumption.

**METHODS:** We retrospectively reviewed the viral serology results of 817 patients with cirrhosis and intensive alcohol consumption who presented to the Gastroenterology Clinic of Atatürk Training and Research Hospital of İzmir Katip Çelebi University between April 2008 and December 2017. The diagnosis of cirrhosis was based on clinical and biochemical evaluations and imaging results. Patients consuming absolute alcohol 40 g/day for >10 years were included and those who quit drinking ≥15 years ago were excluded.

**RESULTS:** Of all the patients, 806 (98.7%) were positive for anti-HAV IgG, 159 (19.5%) for HBsAg, and 32 (3.9%) for anti-HCV. Genotyping was performed in 13 patients. Genotype 1 was detected in 10 patients (1a, one patient; 1b, nine patients) and genotype 3 in three patients. Of the patients with HBV, 10.0% had HBeAg and 7.6% had anti-delta. One-hundred and two (12.5%) patients had HCC, and of these, six (5.9%) were HCV-positive and 53 (52.0%) were HBsAg-positive.

**CONCLUSION:** Patients with cirrhosis and intensive alcohol consumption have an increased hepatitis B and C prevalence. Patients with chronic viral hepatitis with alcohol habit are at a higher risk for HCC. Therefore, patients with cirrhosis and intensive alcohol consumption should be screened for hepatitis B and C.

*Keywords:* Alcohol, cirrhosis, Hepatitis A, Hepatitis B, Hepatitis C.

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Alcohol-related mortality and morbidity is an important public health problem worldwide. In the USA half of the liver-related deaths are due to alcohol [1]. In Europe, the most common cause of advanced hepatic disease is alcohol [2]. In Germany, 18% of the population aged >18 years consumes >20–30 g of alcohol per day [3]. Alcohol is responsible for 5.9% of all deaths world-

wide [4]. Intensive alcohol consumption is prevalent in alcoholic chronic HCV infection, with high seroprevalence of HCV detected in alcoholic individuals [5-8]. Alcohol consumption combined with hepatitis B presence results in the progression of chronic liver disease [9, 10]. Alcohol combined with hepatitis B or C presence has a synergistic effect for developing HCC [11].

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The present study aimed to determine hepatitis A, B, and C seroprevalence in patients with cirrhosis and intensive alcohol consumption.

## MATERIALS AND METHODS

### Patients

We retrospectively reviewed 817 patients with cirrhosis and intensive alcohol consumption who presented to our clinic between April 2008 and December 2017. Clinically, cirrhosis was defined as the presence of jaundice, ascites, and hepatic encephalopathy. Regarding the laboratory findings, PT prolongation and the presence of decreased albumin indicated cirrhosis. Radiologically, the presence of nodular liver, splenomegaly, and ascites indicated chronic liver disease. Patients consuming alcohol 40 g/day for >10 years were included in the study (>80 g/day in 800 patients). Individuals who quit drinking  $\geq 15$  years ago were excluded from the study. Patients were asked about the amount and type of alcohol they consumed and the duration (years) of their alcohol habit. The time and amount of smoking were expressed as daily number of packs multiplied by the duration. The height and weight of the patients were measured. For patients in whom HBV and HCV were detected, HCV-RNA or HBV-DNA was investigated using the real-time PCR method. The assessment was based on the serologic profile at the time of admission to the hepatology outpatient clinic. HBsAg was measured using the chemiluminescence method with the fully automated Johnson & Johnson macro ELISA instrument.

HCC diagnosis was made using dynamic imaging methods (MRI and CT) for patients with early arterial staining and venous washout.

### Statistical analysis

Statistical analyses were performed using the IBM SPSS Statistics 22 program. Statistics are reported as means, ranges, and percentages. The normal distribution suitability of the variables was studied using analytical methods. Patient distribution was done using Pearson's chi-square test and Fisher's exact test for categorical variables and Student's t test for independent samples. Kruskal-Wallis and Mann-Whitney U tests were used for samples with non-normal distribution. One-way ANOVA was used to assess multiple groups for normal distributions in continuous variables. Bonferroni correction was used to determine p value in post-hoc tests. When the

ANOVA results were evaluated post-hoc, the Scheffe test was used for homogenous distribution and Dunnett's C test for nonhomogeneous data. Statistical significance was set at  $p < 0.05$ .

## RESULTS

We evaluated 817 patients with cirrhosis and intensive alcohol consumption. Table 1 summarizes the demographic and clinical data of the patients.

Of the patients, 806 (98.7%) were positive for anti-HAV IgG, 159 (19.5%) for HBsAg, and 32 (3.9%) for anti-HCV. One patient was negative for HCV-RNA. Genotyping was performed in 13 patients. Genotype 1 was detected in 10 patients (1a, one patient; 1b, nine patients) and genotype 3 in three patients. One patient was positive for both hepatitis B and C.

Of the patients with HBV, delta antibody was detected in 7.2% and HBeAg was positive in 10.0%. Table 2 summarizes the characteristics of patients with hepatitis B and C infection.

**TABLE 1.** Demographic profiles and clinical characteristics of the study group

Patients characteristics n=817	
Age	55.8±9.9
Sex (F/M)	13/804
Alcohol consumption time (year)	27.6±9.4
Alcohol consumption (g/day)	149±62
Recent 10 year alcohol consumption (g/day)	165±83
Kind of alcohol	
Beer	22.4%
Raki	68.5%
Wine	7.6%
Whiskey	1.6%
Smoking rate (%)	90.0%
Smoking consumption time (year)	32 (5-62)
Smoking (packs*year)	35 (3-110)
BMI (kg/m <sup>2</sup> )	27.5±5.4
Serology	
Anti HAV IgG	806 (98.7%)
HBsAg	159 (19.5%)
Anti HbC IgG	448 (54.8%)
Isolated Anti HbC IgG	91 (11.1%)
Anti HBs	248 (30.4%)
Anti HCV	32 (%3.9)

**TABLE 2.** Comparison of HBV+alcohol, HCV+alcohol and alcohol groups

Patients characteristics	Alcohol+HBV n=159	Alcohol+HCV n=31	Alcohol n=628	p
Age	55±9	60±10	56±10	0.03
Age at the time of first drinking alcohol	29.4±9.8	32.5±13.5	28.1±9.0	0.071
Sex (F/M)	2/157	0/31	11/616	0.698
Alcohol consumption time (year)	26.3±8.9	29.1±10.7	27.8±9.4	0.236
Alcohol consumption (g/day)	136±56	154±57	152±63	0.049
Recent 10 year alcohol consumption (g/day)	137±59	156±58	172±87	<0.0001
Smoking rate (%)	93.5%	92.9%	89.2%	0.436
Smoking consumption time (year)*	35 (8-60)	40 (20-60)	32 (5-62)	0.007
Smoking (packs*year)*	32.5 (3-100)	50 (10-110)	35 (3-100)	0.039
BMI (kg/m <sup>2</sup> )	25.8±5.9	25.7±4.1	27.8±5.4	0.147
Presence of HCC at admission	53/159 (33.3%)	6/31 (19.4%)	41/627 (6.5%)	<0.0001
Anti HAV IgG	97.9%	100%	98.7%	0.833
Anti Delta	7.2%	-	-	
HBeAg	10.0%	-	-	
Log HBV-DNA	4.3±2.3	-	-	
Log HCV-RNA	-	5.5±1.6	-	

\*Smokers only

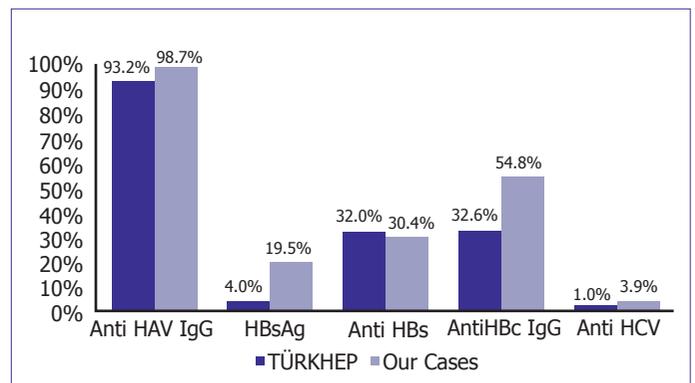
One-hundred and two (12.5%) patients had HCC on admission. Of these patients, six (5.9%) were HCV-positive and 53 (52.0%) were HBsAg-positive. Among anti-HBs positive patients, 12 (4.83%) had HCC on admission.

Multivariate regression analysis showed that age and HBV infection were independently related to HCC occurrence.

## DISCUSSION

A population-based multicenter study performed in Turkey found HBsAg, anti-HAV total, and anti-HCV seroprevalences of 4.0%, 93.2%, and 1%, respectively [12]. According to this data, hepatitis B and C seroprevalence was higher in our patients with cirrhosis and intensive alcohol consumption than in the Turkish population. Figure 1 presents a comparison of data from the normal population and subjects in our study.

The reason for admission among patients with cirrhosis is the symptoms emerging as a result of progressing cirrhosis. The HBV group, despite less alcohol use (p=0.0001), had earlier onset of symptoms (p=0.03) and higher probability of presenting with HCC (p=0.0001). There are many studies evaluating hepatitis B and C sero-



**FIGURE 1.** Comparison of viral hepatitis seroprevalences between alcoholic cirrhotic patients and normal population.

prevalences in subjects with alcohol intake. The results of 25 studies publishing HCV prevalence in patients with HCV were pooled and resulted in a mean prevalence of 16.3% [13]. However, this study found a higher result as it involved European subjects. In a study by Tekin et al. in 2015, anti-HAV total, HBsAg, and anti-HCV positivity for patients with alcoholic cirrhosis were 91.5%, 16.3%, and 8.2%, respectively. Bruno et al. determined hepatitis C seroprevalence of 15% in alcoholic individuals [14]. In a further study, anti-HCV and HBsAg were found to be 55.6% and 15.7 %, respectively [15]. Although varying

numbers have been reported across studies, all had higher hepatitis B and hepatitis C seroprevalences in subjects with alcohol intake than in the normal population. In our study, the results were high, similar to those reported in previous studies. In the HBV group, anti-delta and HBeAg frequency were comparable with that in the normal population in Turkey. Among HCV patients, genotype 3 was detected in 3/13 (23.1%) patients. Genotype 3 is more common in some geographical regions and is more frequent among IV drug abusers. In Turkey, genotype 1B (about 90%) is the dominant HCV genotype. The result may be incidental.

A meta-analysis by Hutchinson et al. demonstrated in 15,000 patients with chronic HCV infection [16] that heavy alcohol intake (210–260 g/week) increased the risk of advanced fibrosis and cirrhosis. Another study found an increased cirrhosis risk in patients with hepatitis B and C and alcohol intake [17].

Alcohol intake increased hepatic necroinflammatory activity and fibrosis in HBsAg-positive patients. A study by Larkin et al. in transgenic mice in 2001 demonstrated that alcohol intake combined with hepatitis B increased the risk of developing cirrhosis and HCC [18].

HCV-related hepatic disease progression and HCC risk were evaluated in a study in Japanese moderate (<80 g/day) and heavy (>80 g/day) drinkers. Compared with nonalcohol drinkers, the risk of developing cirrhosis and HCC was 1.5–2.5 times higher [19]. There are other studies showing an increased HCC risk in patients with viral hepatitis and alcohol intake [18, 20, 21].

A study by Cortes et al. in 2013 found a high risk of developing HCC in patients with hepatitis B and heavy alcohol consumption [15].

A study in Turkey investigating the risk factors for HCC determined HBV and HCV infections with alcohol intake in 18 (8.6%) of 207 patients with HCC. The proportion of those taking alcohol only was 7.2% [22]. In our study, 102 (12.5%) patients had HCC at the time of admission. Of these patients, 52.0% were positive for HBsAg and 5.9% for HCV.

In this study, the clinical, laboratory, and radiological findings indicated cirrhosis in all patients. The increased risk of HCC and cirrhosis associated with alcohol intake combined with hepatitis B or hepatitis C is also described in the literature. Therefore, viral hepatitis serology should be checked in all patients with cirrhosis and intensive alcohol consumption, and a closer monitoring of patients with positive results may be appropriate.

The limitation of our study was its retrospective and cross-sectional design. Thus, it is not conclusively known whether the risk of developing HCC remains high following the cessation of drinking, particularly in patients with chronic viral hepatitis. It may be more appropriate to seek the answer to this question in cohort studies. The other limitation is that we were unable to distinguish alcoholic cirrhosis from alcoholic steatohepatitis. Although laboratory and clinical findings are similar in these situations, determining fibrosis with biopsy is helpful for discrimination. We were unable to obtain biopsies because of the laboratory findings of the patients.

In conclusion, both the risk of encountering chronic viral hepatitis and the prevalence of chronic viral hepatitis is higher in patients with cirrhosis and alcohol intake. There is a higher risk of progressing to advanced liver disease and developing HCC in chronic viral hepatitis.

## CONCLUSION

Hepatitis C and B seroprevalences in patients with cirrhosis and intensive alcoholic consumption were higher than that in the normal population. The proportion of our patients with HCC at the time of first admission was also high. Our data is consistent with other results in the literature. Therefore, serologic tests for hepatitis B and C should be performed in patients with cirrhosis and intensive alcohol consumption, and they should be vaccinated as necessary. Studies should be performed to determine whether the risk of HCC remains high even after quitting alcohol.

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