

# PREVALENCE OF HEPATITIS C VIRUS IN ALCOHOLIC PATIENTS: role of parenteral risk factors

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**ABSTRACT – Background** - The prevalence of hepatitis C virus (HCV) infection is elevated in alcoholic patients, but the risk factors are unclear. The role of parenteral risk factors are indetermined in this population. **Aims** - To determine the prevalence of hepatitis C virus infection in alcoholic patients admitted to a detoxification unit and to evaluate the presence of underlying parenteral risk factors. **Methods** - A total of 114 consecutive unselected alcoholic patients admitted to a single chemical dependency unit during 14 month were included. Epidemiological data and history of parenteral risk factors for hepatitis C virus infection were obtained with a standardized questionnaire. Blood was collected for determination of aminotransferases and anti-hepatitis C virus antibodies (ELISA-3). Positive samples were confirmed by polymerase chain reaction and tested for genotype. **Results** - Among the 114 alcoholics, 17 (15%) were anti-hepatitis C virus positive. Of these, 12 (71%) had detectable serum HCV-RNA by PCR. Genotype 1 was found in six cases and genotype 3 in five (one patient was undetermined). Forty-nine (43%) patients had elevated serum ALT and/or AST at baseline. The comparison between the 17 positive and the 97 negative patients showed significant differences in mean serum ALT levels ( $42 \pm 41$  IU/L vs.  $22 \pm 20$  IU/L), rate of elevated ALT (65% vs. 34%), and presence of parenteral risk factors (94% vs. 10%). Comparison between alcoholic patients with and without elevated aminotransferases showed significant difference only in the rate of positive anti-hepatitis C virus antibodies (24% vs. 7%). Furthermore, among the 17 anti-hepatitis C virus positive patients, the rate of detectable HCV-RNA was significantly higher in the 12 with elevated aminotransferases versus the 5 with normal aminotransferases (92% vs. 20%). **Conclusions** - There was a high prevalence of anti-hepatitis C virus antibodies in alcoholics and the majority was confirmed by the presence of detectable HCV-RNA. Intravenous drug use was the main risk factor for hepatitis C virus infection in this population.

**HEADINGS** – Hepatitis C. Alcoholism. Substance abuse, intravenous.

## INTRODUCTION

Hepatitis C virus (HCV) infects approximately 200 million people worldwide and is presently considered one of the main causes of chronic liver disease in most parts of the world<sup>(18)</sup>. HCV is known to be transmitted primarily by the parenteral route, mainly through exposure to contaminated blood and/or blood products<sup>(9)</sup>. The main risk factor for HCV infection is currently intravenous

drug use (IVDU), which accounts for 60% of cases<sup>(9)</sup>.

Several studies have demonstrated a high prevalence of anti-HCV among alcohol-dependent individuals but the mode of transmission is not clearly understood<sup>(4, 7, 10, 13, 20, 21, 22, 23, 24, 26, 27, 30, 33)</sup>.

The purpose of this study was to determine the prevalence of HCV infection in alcoholic patients admitted to a detoxification unit, and to evaluate the role of underlying parenteral risk factors.

The present study was performed at the Chemical Dependency Unit, "Hospital Mãe de Deus", Porto Alegre, RS, Brazil.

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## PATIENTS AND METHODS

### Patient selection and study design

All patients were recruited from a single chemical dependency unit located at "Hospital Mãe de Deus", a tertiary general hospital in the city of Porto Alegre, RS, southern Brazil. A total of 114 alcoholic patients were consecutively admitted to this unit for treatment of alcoholic dependency during 14 month. All patients were prospectively interviewed by the same investigator, who was blinded to the HCV test results and used a standardized questionnaire designed to obtain epidemiological data, such as mean alcohol intake, history of intravenous drug use anytime, blood transfusion prior to 1992, and/or transfusion of blood products before 1987.

Informed consent was obtained from each patient, and approval for the study protocol was granted by the Ethics Committee of the institution. Inclusion criteria were defined as a diagnosis of alcohol dependency according to ICD-10<sup>(34)</sup>, signed informed consent and availability of a blood sample for biochemical and serological tests. The only exclusion criterion was inability to answer the questionnaire. No patient was excluded from the study.

### Biochemical and serological investigations

Blood was collected within the first 24 hours of admission for determination of serum levels of alanine aminotransferase (ALT; standard method), aspartate aminotransferase (AST; standard method) and antibodies to anti-HCV (COBAS CORE Anti-HCV EIA II; Roche Diagnostics). Patients with detectable anti-HCV antibodies underwent a second blood collection during admission to assess the presence of HCV RNA by polymerase chain reaction (PCR; COBAS AMPLICOR; Roche Diagnostics). Determination of HCV genotype was performed on PCR-positive samples using restriction fragment length polymorphism as previously described<sup>(29)</sup>.

### Data processing and statistical methods

Descriptive methods were used in the univariate analysis. A bivariate analysis was also performed and yielded odds ratio (OR) and a 95% confidence interval (CI). Stratified analyzes were used to assess the independent contribution of each exposure factor studied. In this analysis, the chi-square and the Mantel-Haenszel tests were used. The chi-square test was used for categorical variables (Fisher's exact test was used for values below 5). In regard to continuous variables, the analysis of variance (ANOVA) was used for data presenting normal distribution, and the Kruskal-Wallis test was used for nonparametric data<sup>(2, 12)</sup>. Statistical significance was set at  $P < 0.05$ .

## RESULTS

### Patient characteristics

A total of 114 alcoholic patients met inclusion criteria and were enrolled in the study. Of these, 97 (85%) were male. Mean age was  $41 \pm 13$  years (range: 15 to 72). All patients were white. Mean daily alcohol consumption was  $206 \pm 171$  g (range: 105 to 900) for a mean duration of  $9 \pm 10$  years (range: 1 to 45). Regarding the presence of parenteral risk factors for HCV

infection, 26 (23%) of the 114 patients had either a history of intravenous drug use (13 cases), blood transfusion prior to 1992 (11 cases), or both factors associated (2 cases).

### Laboratory characteristics

Among 114 alcoholics studied, a total of 17 (15%) were found to be anti-HCV positive. Of these, 12 (71%) also had detectable serum HCV-RNA by PCR. Genotype 1 was found in six cases and genotype 3 in five cases. One patient had an undetermined genotype. Forty-nine (43%) of 114 patients had elevated serum ALT and/or AST at baseline.

### Comparison between alcoholic patients with and without anti-HCV antibodies

When anti-HCV positive patients ( $n = 17$ ) were compared to anti-HCV negative patients ( $n = 97$ ), significant differences were observed in mean serum ALT values ( $42 \pm 41$  IU/L vs.  $22 \pm 20$  IU/L, respectively;  $P = 0.02$ ), number of patients with elevated ALT (65% vs. 34%, respectively;  $P = 0.02$ ), and presence of parenteral risk factors (94% vs. 10% respectively;  $P < 0.001$ ), (OR = 139.2, 95% CI: 16-3129). There was no significant difference between both groups regarding the following variables: sex, mean age, mean daily alcohol consumption, mean duration of alcohol and AST/ALT ratio (Table 1).

TABLE 1 – Comparison between 114 alcoholics with and without anti-HCV antibodies

	Anti-HCV positive	Anti-HCV negative	P	OR (95% CI)
n (%)	17 (15)	97 (85)		
Males	15 (88)	82 (84)	0.51	
Mean age (years $\pm$ SD)	$38.4 \pm 8.9$	$41.7 \pm 13.6$	0.96	
Mean daily AI (g $\pm$ SD)	$276 \pm 268$	$195 \pm 155$	0.62	
Mean AI duration (years $\pm$ SD)	$12.3 \pm 11.2$	$8.7 \pm 10.5$	0.21	
Mean ALT (IU/L)	$42 \pm 41$	$22 \pm 20$	0.02	
Elevated ALT [n (%)]	11 (65)	33 (34)	0.02	
AST/ALT ratio	$1.05 \pm 0.4$	$1.19 \pm 0.6$	0.26	
Parenteral risk factors [n (%)]	16 (94)	10 (10)	<0.001	139.2 (16-3129)
Intravenous drug use	13/16 (81)*	2/10 (20)	<0.001	154.4 (21-1535)
Blood transfusion only**	3/16 (18)	8/10 (80)	0.021	2.38 (0.4-11.7)

SD = standard deviation; AI = alcohol intake;  
ALT = alanine aminotransferase; AST = aspartate aminotransferase  
\* two patients with intravenous drug use in this group also had blood transfusions;  
\*\* blood transfusion before 1992

### Comparison between alcoholic patients with and without elevated aminotransferases

When patients with elevated ALT and/or AST ( $n = 49$ ) were compared to those with normal ALT and AST ( $n = 65$ ), significant differences were found in the rate of patients with positive anti-HCV antibodies (24% vs. 7% respectively;  $P = 0.01$ ). Furthermore, a separate analysis of 17 anti-HCV positive patients showed a significantly higher rate of detectable HCV-RNA among the 12 patients with elevated aminotransferases when compared to the 5 patients with normal aminotransferase levels (92% vs. 20% respectively;  $P = 0.009$ ). There was no significant difference

between both groups regarding the following variables: sex, mean age, mean daily alcohol consumption, and mean duration of alcohol use (Table 2).

TABLE 2 – Comparison between alcoholic patients with and without elevated aminotransferases

	Elevated aminotransferases	Normal aminotransferases	P
n (%)	49 (43)	65 (57)	
Males	42 (87)	55 (85)	0.87
Mean age (years ±SD)	43.6 ± 10.3	39.3 ± 14.5	0.06
Mean daily AI (g ± SD)	201 ± 165	210 ± 184	0.76
Mean AI duration (years ± SD)	8.8 ± 10.4	9.6 ± 10.9	0.35
Anti-HCV positive [n (%)]	12 (24)	5 (7)	0.01
With positive HCV-RNA	11/12 (92)	1/5 (20)	0.009

SD = standard deviation; AI = alcohol intake

## DISCUSSION

The prevalence of anti-HCV antibodies among alcoholic patients is higher when compared to the general population and the rate seems to vary according to the presence or absence of co-existing liver disease<sup>(28)</sup>. Indeed, serum markers for HCV infection have been detected in 33% to 50% of alcoholic patients with evidence of liver injury, compared to only 2% to 10% in those without any sign of liver disease<sup>(4, 5, 7, 10, 13, 15, 21, 23, 24, 25, 26, 27, 30, 33, 35)</sup>.

In the present study, anti-HCV antibodies were detected in 17 (15%) of 114 unselected alcoholic patients admitted to our detoxification unit. This result is several-fold higher than the 1.7% prevalence of positive anti-HCV antibodies reported recently in a sample of almost 40,000 blood donors from the same area<sup>(1)</sup>. However, a very similar prevalence (16%) was found in a recent review of published data involving 799 unselected individuals with alcohol abuse<sup>(17)</sup>. Previous studies conducted in Brazil also found anti-HCV antibodies in 12% to 16% of unselected alcoholic patients<sup>(6, 8, 14)</sup>. In contrast, serum markers of HCV infection were detected in up to 36% of Brazilian patients with alcoholic cirrhosis<sup>(31)</sup>.

Most alcoholics with anti-HCV antibodies and evidence of liver disease also have HCV-RNA detectable in serum<sup>(28)</sup>. Several independent studies have showed that 56% to 86% of anti-HCV positive alcoholic patients were also HCV-RNA positive by PCR<sup>(4, 7, 10, 13, 17, 24, 32)</sup>. We found serum HCV-RNA in 12 (71%) of our 17 alcoholic patients with anti-HCV antibodies. Genotype 1 was observed in more than half of the cases and genotype 3 in the remaining. This profile is similar to that recently described in a study with unselected HCV-infected patients from the same geographical area<sup>(19)</sup>.

Ninety two percent of our anti-HCV positive patients with elevated aminotransferases also had HCV-RNA detectable in serum. In contrast, only 20% of the ones with normal aminotransferases had detectable HCV-RNA. The high positive predictive value for positive HCV-RNA among those patients with elevated aminotransferases renders PCR testing almost dispensable in this group. In this regard, HCV-RNA testing seems to be most valuable among alcoholics with anti-HCV antibodies and normal aminotransferases, because in this group there is a higher chance for a negative PCR result. The use of recombinant immunoblot assay (RIBA) test could contribute to distinguish individuals with true HCV infection in the past followed by spontaneous resolution from those with a false-positive enzyme-linked immunosorbent assay (ELISA) test, however, this methodology was not employed in our study.

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<sup>(3, 4, 7, 10, 11, 13, 16, 21, 23, 27, 33)</sup>. Interestingly, other authors showed a remarkably low prevalence of parenteral risk factors among alcoholic patients with anti-HCV antibodies<sup>(7, 23, 30)</sup>. This controversy may be explained by the high false-positive rate of first generation anti-HCV tests employed in the earlier studies and also by the possibility of underreporting of intravenous drug use behaviour.

Among our 114 alcoholic patients, 15 (13%) revealed a history of intravenous drug use and 13 (87%) of those were anti-HCV positive. In contrast, among the 99 individuals without a history of intravenous drug use, only four (4%) were anti-HCV positive, and three (75%) of them had a blood transfusion prior to 1992. These results clearly demonstrate that in our experience, most alcoholic patients with evidence of HCV infection have a clearly identifiable parenteral risk factor, either intravenous drug use or blood transfusion prior to 1992. Indeed, among our 17 anti-HCV positive alcoholics, there was only one case in which we were not able to find an association between the positive HCV status and the history of a defined parenteral risk factor. Also, our findings suggest that parenteral exposure through the use of intravenous drugs is the main risk factor for HCV infection among alcoholic patients.

In conclusion, the present study showed a high prevalence (15%) of anti-HCV antibodies among unselected alcoholics consecutively admitted to a detoxification unit. Moreover, we found that most patients (71%) had serum HCV-RNA detectable by PCR, especially those with elevated aminotransferases (92%). In our population, there was a strong association between positive anti-HCV antibodies and a history of intravenous drug use (87%). We believe these findings can be useful to design future healthcare strategies aimed at improving the management of alcoholic patients admitted for detoxification.

Galperim B, Cheinquer H, Stein A, Fonseca A, Lunge V, Ikuta N. Prevalência do vírus da hepatite C em alcoolistas: a atuação dos fatores de risco parenterais. *Arq Gastroenterol.* 2006;43(2):81-4.

**RESUMO – Racional** - A prevalência da infecção pelo vírus da hepatite C (VHC) é elevada em pacientes alcoolistas, porém os fatores de risco não estão bem estabelecidos. O papel dos fatores de risco parenterais permanece ainda indefinido nessa população. **Objetivos** - Determinar a prevalência da infecção pelo VHC em alcoolistas internados em uma unidade de desintoxicação, e avaliar a presença de fatores de risco parenteral subjacentes. **Pacientes e Métodos** - Foram estudados 114 alcoolistas, não selecionados, consecutivamente admitidos em uma unidade de dependência química durante 14 meses. Através de questionário estruturado, obtiveram-se os dados epidemiológicos e história de fatores de risco parenteral para infecção pelo VHC. Foi coletado sangue para determinação de aminotransferases e anticorpos anti-VHC (ELISA-3). As amostras positivas foram confirmadas pela PCR e determinado o genótipo. **Resultados** - Entre os 114 alcoolistas, 17 (15%) eram anti-VHC positivos. Doze (71%) tinham RNA do VHC detectável por PCR no soro. O genótipo 1 foi encontrado em seis casos e o genótipo 3 em cinco (em um paciente foi indeterminado). Quarenta e quatro (43%) pacientes tinham ALT e/ou AST elevadas. A comparação entre os 17 pacientes positivos e os 97 negativos mostrou diferenças significativas na média do nível da ALT ( $42 \pm 41$  UI/L vs.  $22 \pm 20$  UI/L), na taxa de ALT elevada (65% vs. 34%), e na presença de fatores de risco parenteral (94% vs. 10%). A comparação entre alcoolistas com e sem aminotransferases elevadas mostrou diferença significativa apenas na taxa de anti-VHC positivo (24% vs. 7%). Entretanto, entre os 17 pacientes anti-VHC positivos, a taxa de RNA do VHC detectável no soro foi significativamente maior entre os 12 com aminotransferases elevadas do que entre os 5 com aminotransferases normais (92% vs. 20%). **Conclusão** - A prevalência de anti-VHC foi elevada em alcoolistas, sendo a maioria confirmada pela presença do RNA do VHC no soro. O uso de drogas injetáveis foi o principal fator de risco para infecção pelo VHC nesta população.

**DESCRITORES** – Hepatite C. Alcoolismo. Abuso de substâncias por via endovenosa.

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