

## Seroprevalence of Hepatitis A in Patients with Chronic Hepatitis C in Isfahan Province

Parisa Shoaie<sup>1</sup>, Laleh Zeidabadinejad<sup>1</sup>, Razieh Hassannejad<sup>1</sup>, Behrooz Ataei<sup>1</sup>, Majid Yaran<sup>1</sup>,  
Nazila Kassaian<sup>1</sup>, Zary Nokhodian<sup>1</sup>, Maryam Foroughifar<sup>1</sup>

<sup>1</sup> Infectious Diseases and Tropical Medicine Research center, Isfahan University of Medical Sciences, Isfahan, Iran.

### Correspondence to:

Behrooz Ataei  
Infectious Diseases and Tropical Medicine  
Research center, Isfahan University of  
Medical Sciences, Isfahan, Iran.  
Email: ataei@med.mui.ac.ir

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### ABSTRACT

**Objectives:** Patients with Hepatitis C Virus infection are at high risk of getting hepatitis A virus. Hepatitis A virus is an important widespread virus that usually causes more severe medical consequences in patients with chronic liver disease. The purpose of this study was to evaluate prevalence of Hepatitis A Virus antibody in patients with chronic HCV in Isfahan province, Iran.

**Methods:** A cross-sectional study was carried out on 117 patients with chronic hepatitis C virus from spring 2010 to spring 2011. Subject's characteristics such as age, gender, education, genotype of HCV infection and history of intravenous drug use were collected by questionnaire and studied. Statistical analysis was done by SPSS software (version 19.0. 2010, SPSS) using Chi-square test, Fisher Exact tests and Cochran-Armitage trend test.

**Results:** The mean age of the subjects was  $33.18 \pm 10.97$  years. The seroprevalence of HAV was 94.9% in patients with chronic HCV. The prevalence of anti-HAV increased nearly as age increased. But, there was no statistically significant difference in HAV positive rate according to the age groups ( $P = 0.242$ ) and other patient's characteristics.

**Conclusions:** According to the high HAV immunity in our study and less severe form of HAV infection, vaccination was not required in these patients. However, hepatitis A vaccination program should be performed in HAV seronegative patients with HCV to produce an adequate immune response.

**Keywords:** Chronic liver diseases, Hepatitis A virus, Hepatitis C virus.

### INTRODUCTION

Hepatitis C virus is one of the serious public health problems and is prevalent worldwide. Acute HCV infection leads to chronic infection in 55% to 85% of individuals.<sup>[1]</sup> Hepatitis C virus infection causes serious medical outcomes such as cirrhosis and liver diseases and is the most prevalent reason for liver transplantation in adults.<sup>[2,3]</sup> Hepatitis C virus infection is transmitted through exposure to blood or blood products and many routes including intravenous drug use, sharing injection equipments,

transfusions and unprotected sexual activity with infected individuals. However, there is no accessible vaccine for prevention of HCV infection.<sup>[1]</sup>

Patients with HCV infection are at high risk of getting HAV. Hepatitis A virus is an important widespread virus that usually acquires by closed personal or sexual contact, oral-fecal contact, household contact, during travel and intravenous drug use.<sup>[1,4]</sup> Hepatitis A virus is a benign and asymptomatic disease, however when it happens in super infection with hepatitis C, it leads to more severe consequences such as liver diseases, acute liver failure and even fulminant hepatitis or death.<sup>[1]</sup> In addition, it can be related with noticeable morbidity due to its complications in patients underlying chronic liver diseases caused by HCV infection.<sup>[4,5]</sup> Therefore, vaccination against HAV may prevent co-infection phenomena in patients already infected with HCV. Vaccination against HAV in patients with HCV was suggested by the centers for disease control and prevention (CDC), national Institutes of Health and U.S. and veteran Health Administration.<sup>[3,6,7]</sup>

According to the appropriate decision-making for national vaccination against HAV to prevent its fatal outcome in patients with HCV, depends on the right information concerning prevalence and incidence of HAV infection. Epidemiological study for this infection should be considered. It needs more investigations, whether the consequence of HAV coinfection is related to the hepatitis injury resulted by HCV.

Therefore, the aim of this study was to assess seroprevalence of HAV antibody in patients with chronic hepatitis C infection in Isfahan province, Iran.

## METHODS

### *Design and Patients:*

A descriptive cross-sectional study was conducted from spring 2010 to spring 2011. Patients with chronic hepatitis C infection who had referred to Infectious diseases and Tropical Medicine Research Center of Isfahan, Iran were investigated. The inclusion criteria consisted of

hepatitis C virus (HCV) antibodies (anti-HCV) and HCV RNA positivity in more than two tests for at least 6 months. The exclusion criteria consisted of patients with human immunodeficiency virus infection and a past medical history of HAV vaccination.

Subject's characteristics were gathered by a questionnaire and some of information such as age, gender, education, genotype of HCV infection and history of intravenous drug use were studied.

Individuals took part in the study voluntary and filled out consent form. This study was approved by the ethical committee of Isfahan University of Medical Sciences, Isfahan, Iran.

### *Laboratory Procedures:*

Five milliliter of intravenous blood was obtained from each participants and separated serum was stored at  $-20^{\circ}\text{C}$ .

IgG anti-HAV antibody was evaluated by Enzyme-linked Immunosorbent Assay (DIA-PRO Kit, Diagnostic Bio probes s. r.j) according to the manufacturer recommendations.

### *Statistical Analysis:*

Statistical analysis was done by SPSS software (version 19.0. 2010, SPSS). Chi-square and Fisher Exact tests were applied to assess association between patient's characteristics and HAV seroprevalence. The Cochran-Armitage trend test was used to evaluate the relationship between age and seroprevalence of HAV.

## RESULTS

### *Search Results*

One hundred and seventeen patients with chronic hepatitis C enrolled in the study. The mean age of the subjects was  $33.18 \pm 10.97$  years. The majority of the participants were male (93.2%). Ninety nine (88.4%) patients had history of intravenous drug use. The Laboratory test showed that 111 (94.9%) of the subjects had super infection with HAV.

The prevalence of IgG anti-HAV, according to the age groups was shown in Table 1. The anti-HAV seropositivity was 93.1% and 93.3%

**Table 1.** Prevalence of IgG anti-hepatitis A virus in patients with hepatitis C virus according to the age groups

Age (year)	No. of Subjects		Anti-HAV +	
	N	%	N	%
≤30	58	49.6	54	93.1
31-40	30	25.6	28	93.3
41-50	20	17.1	20	100
51-60	6	5.1	6	100
≥61	3	2.6	3	100

P-value = 0.242 for Cochran-Armitage trend test

in the subjects in their 20s and 30s, respectively. In patients in their 40s, 50s and patients more than 60-years old, seroprevalence of anti-HAV was 100%. Therefore, the prevalence of anti-HAV rise nearly as age increased. There was no statistically significant difference in HAV seropositivity rate, according to the age groups ( $P = 0.242$ ).

Table 2 describes HAV prevalence according to patient's characteristics. There was no statistically significant difference in HAV positive rate, according to patient's characteristics.

## DISCUSSION

Patients with chronic hepatitis C are at more high risk of acquiring complication after HAV

infection than healthily individuals. A number of studies have reported acute HAV co-infection resulted acute hepatic failure and death in patients undergoing chronic HCV infection.<sup>[1]</sup> Hepatitis A hardly ever causes fulminant hepatic failure in healthy people. However, in adults and in patients with chronic HCV infection and other chronic liver diseases, it may lead to more sever diseases and higher rate of fulminant hepatitis.<sup>[4,5]</sup> Hepatitis A virus infection is more serious in patients with HCV infection and mortality in those patients is higher than patients without HCV due to critical complication.<sup>[1,4]</sup>

The HAV seroprevalence in present study was estimated 94.9% that is in agreement with other studies.<sup>[5,8,9]</sup> According to the fact that Iran

**Table 2.** Prevalence of IgG anti-hepatitis A virus in Patients with hepatitis c virus according to patients' characteristics

	No. of Subjects		Anti-HAV +		P-value
	N	%	N	%	
<b>Sex</b>					0.353
Male	109	93.2	104	95.4	
Female	8	6.8	7	6.3	
<b>Education</b>					0.384
Illiterate	2	3.6	2	100	
Elementary school	6	10.9	6	100	
Secondary school	13	23.6	13	100	
High school	30	54.6	29	96.7	
university	4	7.3	3	75	
<b>IVDU</b>					0.102
Yes	99	88.4	96	97	
No	13	11.6	11	84.6	
<b>Genotype of HCV</b>					0.007
1	46	39.3	40	87	
3	38	32.5	38	100	

is an endemic country for HAV infection this frequency almost, as much as expectation. Therefore, HCV infected individuals are important group and should be considered regarding HCV status.

In accordance with previous studies,<sup>[4,8]</sup> our findings showed the anti-HAV prevalence was higher in older patients. Patients aged more than 40 years had higher prevalence than younger patients. Many recent studies have reported a worldwide change in the seroepidemiology of hepatitis A.<sup>[10]</sup> These findings show average age of infection is changing from childhood to adolescence.<sup>[9,11,12]</sup> Hygiene condition and sanitation status in each community affect the rate of transmission and prevalence of infection. According to the improvement of healthy situation and socioeconomic conditions it is expected that incidence of HCV infection and age-specific HAV prevalence in the general population have constantly reduced.<sup>[4,5]</sup> Therefore, increasing seronegativity for HAV infection in adolescence is considerable and proper vaccination program should be conducted.<sup>[5]</sup>

Available evidences have shown that HAV status super infection with HCV leads to more serious hepatic injuries and more severe clinical consequences than infection with HCV alone. Centers for Disease Control and Prevention have suggested vaccination program against HAV in patients with HCV infection should be conducted regularly.<sup>[7]</sup> Patients with chronic hepatitis C and other chronic liver diseases should be considered as a priority group for HAV vaccination, as soon as possible after diagnosis.<sup>[1]</sup>

It can be concluded that, according to the high HAV immunity (94.9%) in our study and less severe form of HAV infection, vaccination was not required in these patients. However, hepatitis A vaccination program should be performed in HAV seronegative patients with HCV to produce an adequate immune response<sup>[13]</sup>

Because of the immunogenicity of hepatitis A, vaccine in subjects with chronic HCV is less effective than other liver diseases.<sup>[14]</sup> These patients should be offered retesting to investigate

antibody response following a full course of vaccination.

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