

Prevalence of hepatitis A in Iranian patients with chronic liver disease

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ABSTRACT

Background: Acute hepatitis A in patients with chronic liver diseases (CLD) may lead to a more severe outcome for which routine vaccination is recommended in many regions. Nevertheless, studies of HAV seroprevalence and exposure predictors in populations with CLD are scanty in our region.

Patients and methods: We studied 200 patients with CLD between September 2005 and September 2006. Patients were stratified on the basis of age, gender, size of family, place of residency and etiology of liver disease. The HAV seroprevalence in patients with CLD was compared with age- and sex-matched controls. Independent predictors of HAV exposure were identified by logistic regression analysis.

Results: Of 200 patients, HAV seroprevalence was available for 190 (96.5%). Hepatitis B and C, alcohol, autoimmune hepatitis and Wilson's disease were the causes of CLD. Most of the seronegative patients aged 10-20 years. The overall HAV seroprevalence was 97.3% in controls. None of the risk factors were identified as independent predictors.

Conclusion: Age stratified seroprevalence of HAV in patients with CLD is close to that of the general population. High prevalence of HAV must be considered in vulnerable travelers to our country.

Keywords: *Hepatitis A, Seroprevalence, Chronic liver disease.*
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INTRODUCTION

Hepatitis A virus (HAV), identified in 1973, cause a self-limited disease seen worldwide and mostly in developing countries. It is principally transmitted through fecal-oral method (1,2). Hepatitis A occurs in epidemic and sporadic forms especially in developing countries (3). According to some studies Africa, India, Middle East and Asia have high seroprevalence rates (4) which is closely related to standards of hygiene and sanitation.

Asymptomatic infection of hepatitis A is mostly seen in children but more serious disease and fulminant liver failure after acute HAV infection

may occur in elderly and in patients with chronic liver disease (CLD) (5,6). Most people in hyperendemic areas for HAV have acquired the protective anti-HAV antibody through subclinical infection during their childhood, which provides lifelong immunity against further exposure (6). High prevalence of HAV infection in developing countries necessitates vaccination in these areas(7).

However, during recent years several reports from developing populations have suggested a shift in the HAV epidemiology (from high to intermediate or low endemicity), presumably because of improved life circumstances. Such observations have led to a recommendation for mass vaccination of all children and patients with chronic liver disease in those countries (6). Some

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190 Hepatitis A in patients with chronic liver disease

studies demonstrate a progressive reduction in spread of HAV infection in children, teenagers and young adults. Therefore, changing the average age of first infection with the virus from childhood to adolescence is not unexpected (1,2).

Scanty data are available on prevalence of HAV antibody among CLD patients in Iran. The aim of the present study was to compare the seroepidemiology of HAV infection in CLD patients with healthy controls in order to evaluate the necessity of vaccination for these patients.

PATIENTS and METHODS

A total of 200 CLD patients were continuously recruited from Gastroenterology clinic in Imam hospital in Tabriz during September 2005 and September 2006. IgG anti-HAV antibody was evaluated using Diagnostic BioProbes. Age- and sex-matched healthy controls were also studied (n=188).

Data were collected on patient's age, gender, marital status, number of children, literacy, place of birth, place of residency, etiology of liver disease, IgG anti-HAV, viral hepatitis serum markers, and serum protein electrophoresis. Then, they were analyzed using the SPSS package (version 13, SPSS Inc., USA). Student's t test and chi-square (or Fisher's exact test) were used, when appropriate. A logistic regression model was constructed to identify independent predictors for prior exposure to HAV. The outcome variable HAV was set as a binary variable and coded zero for negative and one for positive. Potential predictor variables used in the logistic regression analysis included race, etiology of liver disease, patient's age and risk factors for viral hepatitis transmission. Statistical testing was done at the 2-tailed level of 0.05.

RESULTS

The case group included 125 (62.5%) males and 75 (37.5%) females with the mean age (\pm standard

deviation) of 48.2 ± 18.1 years (a range, 10-87 years), however, 188 healthy individuals with the mean age of 43.5 ± 18.7 years (a range, 11-87 years) comprised our control group. None of the patients were immunized against hepatitis A. Seroprevalence and etiology of chronic liver disease are shown in table 1.

Table 1. Hepatitis A seroprevalence in patients with chronic liver disease in East Azerbaijan

	Number	HAV seroprevalence (%)
Age interval (years)		
10-20	21	71.4
21-30	17	100
31-40	32	96.9
41-50	31	100
51-60	45	100
61-70	35	100
>70	19	100
Cause of liver disease		
<u>Cirrhosis</u>		
Hepatitis B	61	100
Hepatitis C	7	100
Autoimmune	33	93.9
Cryptogenic	52	98.1
Primary billiary	4	100
Alcohol	1	100
<u>Chronic hepatitis</u>		
Hepatitis B	22	95.5
Hepatitis C	10	100
Autoimmune	6	83.3
Wilson's disease	4	50
Place of residence		
Rural	64	100
Urban	136	95.2

One hundred and ninety three (96.5%) patients were seropositive for HAV infection. Most of the seronegative patients aged 10-20 years (table 1). Mean level of serum albumin, SGOT and SGPT in cirrhotic patients were 3.7, 69.3 and 54.6 U/L, respectively that was not associated with HAV seropositivity. Among controls, 183 (97.3%) were IgG anti-HAV positive.

Multivariate analysis revealed insignificant association between seropositivity and etiology of chronic liver disease, gender, literacy, place of

residency (rural/urban), or family size between patients and controls. However, mean age of HAV-infected subjects was significantly higher when compared with seronegative subjects in both groups ($p < 0.005$). In contrary, family size was more or less the same in seronegative and seropositive subjects of both groups. There was a trend toward a higher incidence of HAV infection in rural inhabitants (table 1). In multivariate logistic regression model, variables were not independent predictor for hepatitis A seropositivity.

DISCUSSION

Viral hepatitis continues to be a major public health problem worldwide. Acute HAV is usually self-limited with an average case fatality rate of approximately 0.3%. However, acute HAV infection in patients with underlying chronic liver disease is associated with an increased case fatality rate (1,5,8-10). In United States, approximately 100 individuals expire from fulminant liver failure due to acute HAV annually (11). An epidemiological report from the Center for Disease Control and Prevention (CDC) in Atlanta, USA, estimated case fatality rate in patients with underlying chronic hepatitis B to be 11.7% (58-fold higher than in patients with no pre-existing liver disease) (2). Mortality is clearly associated with elder age. Even though patients with chronic liver disease are not at an increased risk for acquiring acute hepatitis A, they seem to be at high risk for death as a result of fulminant hepatic failure due to acute hepatitis A (10).

CDC recommends routine vaccination of chronic liver disease patients against HAV, because they are at increased risk of developing fulminant liver failure from acute HAV infection. Consequently, the HAV vaccine is now considered the standard of care in patients with CLD (5,8).

India, China, Nepal, Bangladesh, Pakistan, Myanmar and the Philippines are countries with high endemicity for HAV (9,12). Hepatitis A is

enteric transmitted viral disease occurring in epidemic forms especially in developing countries. The overall HAV seroprevalence described in our study (96.5%) is close to the HAV seroprevalence in patients (98%) with chronic liver disease in Shiraz, Iran as well India (95.7%) (6,7). In our study, seroepidemiology of IgG anti HAV in two groups (case and control) were almost equal.

Recently many reports have been published indicating a global change in the seroepidemiology of hepatitis A infection in the world (13). Similarly, studies from Italy (2), USA (5) and Shiraz (7) indicated that patients aged 51-70 years are more likely to be exposed to HAV than younger adults.

Additionally, improvement of socioeconomic status of population, water sources, hygiene and sanitation decrease HAV infection in some areas such as Turkey, Italy, Greece, India and Poland. Therefore, it is not surprising that the average age of first infection with the virus is changing from childhood to adolescence (1,2,6). As a result, increasing seronegativity for HAV infection in adolescence should be taken into consideration and an appropriate vaccination program should be planned.

In the USA and some other countries, HAV vaccine is included in routine vaccination programs since 2000 (1). Decreasing prevalence of HAV infection in India has led to the recommendation of HAV vaccination for school children as well as adults (6).

Seroprevalence data on HAV infection among patients with established chronic liver disease in our country has not been yet assessed and there are scanty data on possible changes in HAV infection epidemiology. A large sample study on children in Tehran (2002) stated that HAV infection is not highly endemic in Iran (seroprevalence of 22.3%) (14). A study from Zanjan province shows a higher prevalence (44.3%), during the same period, in 7-10 years old children (15). This rate markedly decreases in a recent report from general population of Isfahan to 8.1% (16). However,

192 Hepatitis A in patients with chronic liver disease

another recent study from Mazandaran province shows high prevalence of hepatitis A in patients with chronic liver disease (more than 90%) which is in agreement with ours (17).

As described earlier, vaccination against HAV is not routinely achieved among CLD patients in our region, however, further studies should be conducted to draw a firm decision on how to approach these patients.

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