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Seroprevalence and associated factors of hepatitis A IgG antibody among HIV-positive people in Tehran, Iran

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Abstract

Introduction: Hepatitis A is an acute viral infection involving hepatocytes, and it is transmitted through fecal-oral contacts. There is no difference between symptoms of hepatitis A in HIV-positive and HIV-negative people, but the duration of hepatitis A virus (HAV) viremia and stool shedding may be longer in HIV-positive patients. Also, HIV viral load could increase in co-infection with HAV. Therefore, HAV vaccination is suggested for people who are at higher risk of HIV infection in non-endemic countries. We aim to estimate the seroprevalence of anti-HAV IgG in Iranian HIV-positive population to evaluate the need for vaccination in this group.

Material and methods: A cross-sectional study was conducted with 72 HIV-positive people who referred to a voluntary counseling and testing center in a referral hospital during 2019-2020. Participants answered a questionnaire about their demographic data, history of drug use, and HIV risk behaviors. Blood for anti-HAV IgG was tested, and last laboratory results of CD4+ count, HIV viral load, and hepatitis B and C panels from electronic medical records were collected.

Results: The seroprevalence of anti-HAV IgG was 82.6%, and independently associated with older age and being married. The participants older than 45 years had significantly higher seropositivity among all age groups (89.7%).

Conclusions: Hepatitis A is an endemic viral infection among the Iranian population. Therefore, HAV vaccination does not seem necessary at present. However, we suggest further studies on hepatitis A panel to re-evaluate the need for HAV vaccination in HIV-positive people in the future. We recommend HAV vaccination for travelers from non-endemic countries to Iran.

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Introduction

Hepatitis A is a viral infection of hepatocytes caused by hepatitis A virus (HAV) that could be transmitted through fecal-oral contacts. The severity of symptoms increases with age. Hepatitis A in children is usually asymptomatic or presents mild gastro-intestinal symptoms. While in adults, it causes more severe symptoms, such as fever, malaise, loss of appetite, jaundice, nausea, vomiting, and abdominal pain [1]. It has always been a concern that immunocompromised patients, including HIV-positive people, are more susceptible to infections showing more severe illnesses. Previous studies found no difference in the severity of hepatitis A between HIV-positive and HIV-negative people, and HAV viral load, duration of HAV viremia, and the period of HAV stool shedding are shown longer in HIV-positive people [2, 3]. In addition, HIV-positive people are more likely to transmit HAV to others [2]. Therefore, there is a substantial risk of hepatitis A outbreaks in high-risk groups, such as men who have sex with men (MSM) [4]. It is reported that 37.5% of HIV-positive people experience a rise in HIV viral load in the course of co-infection with HAV [2]. As a result, some studies suggested vaccination against HAV in HIV-positive people, who have chronic liver diseases or are at higher risk for hepatitis A, including MSMs, injecting drug users (IDUs), travelers to endemic countries, and patients who routinely receive blood products [5].

The seroprevalence of anti-HAV IgG was reported in 90% of the Iranian general population [6], 94.3% of homeless individuals [7], and 96.3% of HIV-positive people [8]. Due to the lack of updated information about the history of HAV infection in HIV-positive people in recent years, we aimed to conduct this study to estimate the current seroprevalence of anti-HAV IgG in this group to assess the need for vaccination against HAV.

Material and methods

A cross-sectional study was conducted with 72 HIV-positive people, who referred to the voluntary counseling and testing (VCT) center in Imam Khomeini Hospital Complex, the largest referral hospital in Iran, during 2019-2020. Participants were selected through convenient sampling. Oral and written consents were obtained from each patient. In order to preserve their privacy, each individual was defined by a case number. Participants were informed about the HAV antibody test results as soon as the results were reported. We prepared educational materials explaining the transmission routes and symptoms of hepatitis A, and sent them by email to those participants who had negative test results. Also, we provided participants with verbal information about hepatitis A on their routine visits. We used a questionnaire to collect demographic data (gender, age, educational level, and marital status), addiction history, and HIV risk behaviors. Ten milliliters of blood sample was collected from each participant. Samples were analyzed by enzyme-linked immuno-sorbent assay (ELISA) to measure quantitative level of anti-HAV IgG. More clinical data were obtained from participants' medical records, including hepatitis B and C panel (HBs Ag, HBs Ab, HBc Ab, and HCV Ab), CD4+ lymphocyte count, and HIV viral load. Data were analyzed by SPSS software, version 26.0. A logistic regression test was conducted to determine the associated factors of immunity to hepatitis A (positive result for anti-HAV IgG). Independent variables were tested using univariate logistic regression at p-value ≤ 0.20, and multivariate logistic regression investigated independent association at p-value ≤ 0.05.

The project was evaluated by the Biomedical Research Ethics Committee of Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, and was in accordance with the ethical principles as well as national norms and standards for conducting medical research in Iran. The approval ID number was IR.TUMS.IKHC.REC.1397.183.

Results

The data of 72 participants, including 23 (31.9%) women, and 49 (68.1%) men, with a mean age of 42.9 years were collected. The minimum and maximum ages were 5 and 68 years, respectively. Of the total, 34 individuals (47.9%) were married. Most of the participants had at least a high school degree (34 individuals, 60.7%). Twenty-six (36.6%) of the participants had a history of drug addiction, and 18 (69.2%) of them reported injecting drug use. Unprotected heterosexual intercourse (44 individuals, 62%) and injecting drug use (18 cases, 25.4%) were reported as two main HIV risk behaviors. Sixty-nine of 72 blood samples had adequate quality for antibody analysis. Fifty-seven samples were positive for anti-HAV IgG. The HAV antibody seroprevalence was 82.6%.

The variables significantly associated with anti-HAV IgG seropositivity on bivariate test at $p \leq 0.20$ were analyzed using multivariate test at $p \leq 0.05$. Age (adjusted odds ratio of 27.8 for ≥ 45 years; 95% CI: 0.936-825.387%) and marital status (adjusted odds ratio of 26 for the married group; 95% CI: 1.545-438.523%) were significantly associated with anti-HAV IgG seropositivity.

The frequency and seroprevalence of anti-HAV IgG included in categories of HIV risk behaviors, demographic, and laboratory data are shown in tables below (Tables 1 and 2).

Discussion

In the current study, the seroprevalence of anti-HAV IgG, which indicated the history of hepatitis A and subsequent immunity against HAV, was reported at 82.6%. Age and marital status were independently associated with anti-HAV IgG seropositivity. As we observed an increase of anti-HAV IgG seropositivity with age, the highest seroprevalence was seen in the age group over 45 years. The odds of anti-HAV IgG seropositivity were 27 times higher in the group of above 45 years in comparison with the individuals below 35 years. This finding could be explained by potentially increased risk

Table 1. Frequency and seroprevalence of anti-HAV IgG in HIV-positive individuals categorized according to demographic data and HIV risk behaviors

Variable	*n* (%)	Anti-HAV IgG (n+)	Anti-HAV IgG seroprevalence (%)[1]	*p*-value
Sex				
Male	49 (68.1)	38	77.6	0.58
Female	23 (31.9)	19	82.6	
Age (year)				
20-35	18 (25.4)	10	55.6	0.01
36-44	24 (33.8)	21	87.5	
≥ 45	29 (40.8)	26	89.7	
Marital status				
Single	26 (36.6)	15	57.7	0.02
Married	34 (47.9)	21	61.8	
Separated	8 (11.3)	7	87.5	
Spousal death	3 (4.2)	3	100.0	
Education level				
Uneducated	1 (1.8)	0	0.0	0.25
Elementary school	11 (19.6)	10	90.9	
Middle school	10 (17.9)	9	90.0	
High school	19 (33.9)	14	73.7	
Higher education	15 (26.8)	11	73.3	
History of drug use	26 (36.6)	21	80.8	0.54
Duration of HIV infection (years)				
≤ 5	24 (34.3)	17	70.8	0.20
5-10	29 (41.4)	23	79.3	
> 10	17 (24.3)	16	94.1	
HIV risk behavior				
Unprotected heterosexual intercourse	44 (62)	37	84.1	0.52
Unprotected homosexual intercourse	6 (8.5)	4	66.7	0.28
Injection drug use	18 (25.4)	14	77.8	0.64
Transfusion of blood or blood products	1 (1.4)	1	100.0	0.55
Vertically infected	1 (1.4)	0	0.0	> 0.9
Non-specified	10 (14.1)	8	80.0	0.73

[1]*Seroprevalence of anti-HAV antibody calculated in proportion to case numbers in each sub-group.*

of fecal-oral exposures to HAV over time. Furthermore, we observed that the anti-HAV IgG seropositivity was highest among married participants in comparison with the other groups. The odds of anti-HAV IgG seropositivity in married participants were 26 times of single group. This observation could be explained by higher mean age of married (45.4 years) compared to non-married group (36.9 years).

A similar cross-sectional study on 247 HIV-positive people who referred to VCT center in the Imam Khomeini Hospital Complex during 2005-2006 reported 96.3% anti-HAV IgG seropositivity in studied population [8]. Compared to our study, the immunity against HAV decreased in HIV-positive people in Iran over the last decade. This could be considered as an improvement in personal and environmental hygiene in recent years, as it seems compatible with the route of HAV transmission. Another study on 596 Iranian homeless people in 2012 found anti-HAV IgG seropositivity in 94.34% of the study group, which was higher than that of the general population [7]. This finding clarifies the role of poor personal hygiene in increasing the chance for HAV transmission. Also, a cross-sectional study on 551 individuals selected from the Iranian general population in 2006-2007, showed that 90% of participants were positive for anti-HAV IgG [6]. They observed that anti-HAV IgG

Table 2. Frequency and seroprevalence of anti-HAV IgG in HIV-positive individuals categorized according to CD4+ cell count, HIV viral load, and hepatitis panel

Variable	*n* (%)	Anti-HAV IgG (n+)	Anti-HAV IgG seroprevalence (%)[1]	*p*-value
CD4+ cell count				
≤ 200	10 (14.3)	7	70.0	0.98
201-350	11 (15.7)	9	81.8	
351-500	12 (17.1)	10	83.3	
≥ 501	37 (52.9)	30	81.1	
HIV viral load				
≤ 200	58 (92.1)	48	82.8	0.52
201-1,000	3 (4.8)	2	66.7	
≥ 1,001	2 (3.2)	2	100.0	
Hepatitis B and C panel				
HBs Ag	1 (1.5)	0	0.0	> 0.9
Anti-HBs Ab	51 (75.0)	42	76.4	0.39
Anti-HBc Ab	16 (24.2)	15	27.8	0.20
Anti-HCV Ab	18 (26.5)	16	29.1	0.13

[1]*Seroprevalence of anti-HAV antibody calculated in proportion to case numbers in each sub-group.*

seroprevalence increased with age, and was higher in male participants, although the authors did not find any correlation between these variables and anti-HAV IgG seropositivity [6]. These findings were in agreement with our study on age as a predictive factor for immunity against HAV. According to the results of the above-mentioned studies, Iran is an endemic country for HAV infection. Thus, routine vaccination against HAV does not currently seem necessary in this country. However, it is important to plan further studies to pursue the future seroprevalence of HAV antibody, particularly in high-risk groups, including HIV-positive patients, especially those who suffer from chronic liver diseases, MSMs and IDUs, who are at risk for hepatitis A outbreaks, and patients who frequently receive blood products [5].

According to medical literature, the anti-HAV IgG seroprevalence considerably differs among countries. In a study on 2,860 HIV-positive people in Taiwan during 2012-2016, anti-HAV IgG seropositivity was reported in 21.2% of studied population. They observed a correlation between age and concurrent HBV infection with anti-HAV IgG seropositivity [9]. Therefore, the immunity against HAV was increased with age in this study, which is compatible with our findings, although we found no correlation between HBV-HIV coinfection and anti-HAV IgG seropositivity. In this study, the seroprevalence of anti-HAV IgG was lower in the MSM group compared to IDUs and heterosexual participants, while the mean age of the MSM group was also lower than the other two groups. So, they recommended vaccination against HAV in the MSM group [9, 10]. Another study in France in 2017 observed that MSMs were at risk for hepatitis A outbreaks even with a competent immune system, regardless of being positive for HIV infection. They strongly suggested that vaccination against HAV is necessary for this group [11]. Also, a review article concluded that HAV outbreaks seem to be occurring in MSMs and IDUs in non-endemic countries [3].

The correlation between age and anti-HAV IgG seropositivity was reported in other studies [9, 12]. In Ireland, a retrospective cohort study with 1,287 HIV-positive people found HAV-IgG antibodies in 75% of participants. They observed that younger age and HBV seronegativity (HBs Ag and anti-HBc Ab negative) were significantly associated with anti-HAV IgG seronegativity [13]. In 1986, 29% of 56 individuals who reported a history of drug addiction were positive for anti-HAV IgG, which was associated with old age [14]. A study in 2001 on 936 people of general population in Hong Kong found that 71% of participants were positive for HAV-IgG antibody [15], and the seroprevalence in participants above 30 years was significantly higher than in younger individuals. Also, manual workers had a higher anti-HAV IgG seroprevalence compared to other occupations [15].

The effectiveness of HAV vaccine is also considered in HIV-positive people, who may lack potent humoral immunity due to loss of CD4+ lymphocytes. In a meta-analysis of eight studies including 458 HIV-positive people, who had received inactivated HAV vaccine, the total vaccine response was reported 64% (ranging from 50% to 95%), which was lower compared to HIV-negative individuals [16]. Receiving a booster dose of HAV vaccine in the fourth month, between routine zero- and sixth-month injections, could develop a vaccine response in this population [3]. It seems important to consider vaccination against HAV in HIV-positive people before developing acquired immunodeficiency syndrome (AIDS) to result in more appropriate vaccine response.

As reviewed, there are significant differences in prevalence of hepatitis A between countries. The necessity of immunization against HAV depends on the prevalence of hepatitis A, and health-related burden that could be caused by this infection in the target population [17-20].

Limitations

A limitation of our study included a potential possibility of under-reporting of addiction history and sexual behaviors due to probable cultural stigma around these subjects. Another limitation of our study was that we collected data from one counseling center. The results could have been more widely applicable by studying more cases from different counseling centers of the country.

Conclusions

According to the results of this study, routine vaccination against HAV does not presently seem necessary among the Iranian HIV-positive population. However, due to the observed 13.7% decrease in HAV antibody seropositivity in the HIV-positive individuals during the last decade, it seems important to commence further studies in the future in order to re-evaluate the immunity against HAV in this group of patients, as they are vulnerable to experience the afore-mentioned effects of HIV-HAV co-infection. Additionally, we recommend vaccination against HAV for travelers from non-endemic countries to Iran.

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Conflict of interest

The authors declare no conflict of interest.

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