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An Evaluation of Hepatitis A Seroprevalence and Vaccination Status in Patients with HIV/AIDS: Data from A 20-year Period

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ABSTRACT

Introduction: Hepatitis A infection, caused by the hepatitis A virus (HAV), is a non-chronic disease that can be prevented with vaccination. It is a significant cause of morbidity in adults. Homosexually active males, drug users, the homeless, and prisoners are at a greater risk of HAV infection. This study aimed to determine the hepatitis A seroprevalence and vaccination rates of people living with human immunodeficiency virus (HIV) followed up in our clinic.

Methods: A retrospective examination was made of the polyclinic files and laboratory test results in the hospital information system of 1,326 patients aged >18 years, who were diagnosed with HIV/AIDS and followed up in the Infectious Diseases Polyclinic of University of Health Sciences Turkey, Haseki Training and Research Hospital between September 30, 2002 and September 30, 2022.

Results: Anti-HAV immunoglobulin G (IgG) positivity was present in 1090 (82.2%) patients. As age increased, anti-HAV IgG positivity also increased, females were significantly more affected, no difference was determined between nationalities, and there was seen to be a significant decrease in the positivity rate over the time period of the study. The positivity rate was determined to be significantly high in heterosexual patients. The hepatitis A vaccination rate was determined to be 16.9%, and serology was examined in 60% of the patients after vaccination. The response to vaccination was determined to be 91.6% in the patients with serology examination.

Conclusion: Although improvements in sanitation and vaccination in childhood have provided a decrease in HAV seropositivity, the key populations must be informed about vaccination and vaccination adherence is ensured to prevent small outbreaks.

Keywords: Hepatitis A infection, HIV/AIDS, vaccination

Introduction

Hepatitis A infection, caused by the hepatitis A virus (HAV), is a non-chronic disease that can be prevented with vaccination (1-3). Although the main route of infection is fecal-oral, it can also be spread through the consumption of contaminated food, direct contact with an infected person, and occasionally through blood transfusion (2). The disease has been closely associated with unsafe drinking water and food, inadequate sanitation, poor personal hygiene, and oral-anal sex (1). Homosexually active males, drug users, the homeless, and prisoners are at greater risk of HAV infection (2,4).

Although HAV infection does not lead to chronic hepatitis, it is a significant cause of morbidity in adults, who experience a more severe disease course than children (3). HAV infection shows the same clinical course in patients with or without human immunodeficiency virus (HIV) infection, but higher levels of viral load and a longer period of viremia can be seen in those with HIV infection (4).

Although Turkey is accepted as an endemic region with respect to HAV infection, the frequency is decreasing. The age at which the virus is encountered has shifted from childhood to adolescence and in young adults (2,5). In 2012, the hepatitis A vaccination was included in the vaccination program in Turkey, and the vaccine started to be administered to children and individuals in high-risk groups (2).

According to the Ministry of Health data for November 2022, there are 36,630 patients with HIV/AIDS in Turkey. Despite the increase in reported cases over the years, Turkey is still among the countries with low prevalence. The cases in 2022 were reported to be 81.4% males, 16.2% of foreign nationality, and 13.8% homosexually active males (6).

This study aimed to determine the hepatitis A seroprevalence and vaccination rates of people living with HIV (PLWH) followed up in our clinic.

Methods

A retrospective examination was made of the polyclinic files and laboratory test results in the hospital information system of 1,585 patients aged >18 years, who were diagnosed with HIV/AIDS and followed up in the Infectious Diseases Polyclinic of University of Health Sciences Turkey,

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Haseki Training and Research Hospital between September 30, 2002 and September 30, 2022. The study included 1,326 patients with complete HAV serology.

The patients were evaluated with respect to demographic data, and HAV, hepatitis B virus, and hepatitis C virus (HCV) serology. Hepatitis B surface antigen (HbsAg) and anti-hepatitis B core antigen immunoglobulin G (IgG) positivity were accepted as chronic hepatitis B infection.

Approval for the study was granted by the Clinical Research Ethics Committee of University of Health Sciences Turkey, Haseki Training and Research Hospital (approval number: 145-2022, date: 27.07.2022).

Statistical Analysis

Data obtained in the study were analyzed statistically using SPSS vn. 15.0 for Windows. Descriptive statistics were stated as median, minimum, and maximum values for continuous variables, and as number (n) and percentage (%) for categorical variables. Rates between the groups were compared with the chi-square test. As the numerical variables did not conform to the normal distribution, comparisons between two independent groups were made with the Mann-Whitney U test. The level of statistical alpha significane was accepted as $p<0.05$.

Results

The evaluation was made of 1,326 patients followed up in our polyclinic, comprising 1187 (89.5%) males with a mean age of 37.8 years (range: 18-84 years). Of the 1,326 patients, 44 (3.3%) were foreign nationals, 285 (21.4%) were sexually active homosexual males, and the sexual orientation was unknown in 631 (47.5%).

Anti-HAV IgG positivity was present in 1090 (82.2%) patients. As age increased, anti-HAV IgG positivity also increased, females were significantly more affected, no difference was determined between nationalities, and there was seen to be a significant decrease in the positivity rate over the time period of the study.

Sexual orientation was determined to create a significant difference with a significantly higher anti-HAV IgG positivity rate determined in heterosexual patients.

In anti-HAV IgG-negative patients, lower CD4 (+) T-lymphocyte counts were determined, and no difference was observed in respect to HIV-RNA values, hepatitis B infection, and anti-HCV positivity. The results are shown in Table 1.

Of the 236 patients determined with anti-HAV IgG negativity, 40 (16.9%) were seen to have been vaccinated. Serology was not examined after vaccination in 16 (40%) of the vaccinated patients, and of the 24 patients with serology examined, anti-HAV IgG positivity was determined in 22. Of the 2 patients who remained anti-HAV IgG negative after vaccination, one was 23 years old and the other was 26 years old, both were male, of Turkish nationality, and both were diagnosed after 2013. One of these two patients was a sexually active homosexual, and the sexual orientation of the other was not known. CD4 (+) T-lymphocyte counts were 422 and 424, respectively, and there was no hepatitis B co-infection or anti-HCV positivity in either case.

Table 1. Prevalence of HAV immunity by baseline characteristics

	Anti-HAV IgG (+), (n=1090)	Anti-HAV IgG (-), (n=236)	p-value
Age at diagnosis			
<30 years	243 (22.3)	161 (68.5)	<0.001
30-50 years	665 (61.1)	72 (30.6)	
>50 years	181 (16.6)	2 (0.9)	
Gender			
Male	964 (88.4)	223 (94.5)	0.006
Female	126 (11.6)	13 (5.5)	
Nationality			
Turkish	1053 (96.6)	229 (97.0)	0.739
Not Turkish	37 (3.4)	7 (3.0)	
Year of diagnosis			
2003-2012	212 (19.5)	16 (6.8)	<0.001
2013-2022	877 (80.5)	220 (93.2)	
Sexual orientation			
Homosexual	209 (19.2)	76(32.2)	<0.001
Heterosexual	372 (34.1)	38 (16.1)	
Unknown	509 (46.7)	122 (51.7)	
HIV-RNA* (IU/mL)	297420 (38-1028842249)	253789 (152-46189016)	0.196
CD4 (+) T-lymphocyte count* cells/mm³	416 (1-9494)	351 (1-1714)	0.002
HBV infection	63/1088 (5.79)	11/235 (4.68)	0.502
Anti-HCV positivity	10/1077 (0.93)	3/234 (1.28)	0.713

*mean (minimum-maximum). HAV: Hepatitis A virus, HIV: Human immunodeficiency virus, HBV: Hepatitis B virus, HCV: Hepatitis C virus, IgG: Immunoglobulin G

No acute hepatitis A infection developed during the follow-up of any patient in the study who were anti-HAV IgG negative, and not vaccinated or who did respond to the vaccination.

Discussion

Although the main route of spread of HAV infection is the fecal-oral route, it can also be spread through blood transfusion or oral-anal sex. In regions where inadequate sanitation, a high prevalence is reached during childhood (1). The frequency is reduced with improvements in hygiene conditions and socioeconomic status. Vaccination is important for protection against disease (2). The USA Centre for Disease Control (CDC) has reported that since vaccination started in 1995, there has been a 95% decrease in the incidence of hepatitis A (3). In Turkey, the HAV vaccination was included in the national immunity program in 2012, but the effect on seroprevalence is not known as yet (2).

According to the Ministry of Health data for November 2022, cases were reported to be 81.4% males, 16.2% of foreign nationality, 13.8% homosexually active males, and most were in the 25-34 years age group (6). In a study by Şenoğlu and Yeşilbağ (7), 90.2% of the cases were male, 49.9% were homosexually active males, and the mean age was 35.75±11.22 years. Yemisen et al. (8) conducted a study of 829 patients and reported that 84.4% of the cases were male, 30.9% were homosexually active males, and the mean age was 37 years. In a study by Altuntas Aydin et al. (9) of 242 patients, 83% of the cases were male, 30.1% were homosexually active males, and the mean age was 38 years. In the current study, the patients were 89.5% male, 3.3% were of foreign nationality, 21.4% were homosexually active males, and the mean age was 37.8 years (range: 18-84 years). The low rate of foreign patients compared with the Ministry of Health data was thought to be due to the exclusion of cases with incomplete data. As in other studies and the Ministry of Health data, the majority of patients in the current study were male. The difference in the rate of homosexually active males was attributed to the fact that almost 50% of the current study patients did not provide information about sexual orientation.

Previous studies in Turkey have reported seroprevalence varying between 50% and 100% in the adult age group, and have reported that seroprevalence increased with increasing age, a decrease has been seen in seropositivity at younger ages recently, and there are regional differences (5). In the study by Şenoğlu and Yeşilbağ (7), the rate of anti-HAV IgG positivity was found to be 74.8%, and positive patients were determined to be significantly older than negative patients. Altuntas Aydin et al. (9) reported the positivity rate to be 91%. In the current study, the rate of anti-HAV IgG positivity was determined to be 82.2% and the positivity rate was seen to increase together with increasing age. This finding was consistent with previous data in Turkey.

In a study from Brazil, which included 581 PLWH, the anti-HAV IgG positivity rate was found to be 79.8% (10). A study in Korea of 756 PLWH reported an anti-HAV IgG positivity rate of 79.8% (11). This rate was reported to be 60.8% in a cohort of 1580 PLWH between 2004 and 2007 (12), and 21.2% in a cohort of 2860 PLWH in the period 2012-2016 (13). A study of 897 homosexually active males living with HIV reported anti-HAV IgG positivity of 35.7% (14). In the current study, the positivity rate was found to be 82.2%. When evaluated according to the World Bank data of the income levels of countries (15), it can be seen that the anti-HAV IgG positivity rate is high in low-income and low-mid-income countries (e.g., Brazil, Turkey), and the rate is low in high-income and mid-high-income countries (e.g., Taiwan, Korea, Greece). The income level of a country has an effect on sanitation.

According to the CDC data, the infection has been seen at the same rate in males and females in the general population since 2003, and after 2016, a significant increase was seen in males compared to females, which was attributed to the more widespread use of drugs by males (3). In a study of the general population by Alıcı et al. (16), no difference was determined between the sexes with respect to the distribution of HAV seropositivity. In another study that examined HAV seropositivity in PLWH according to age and years, seropositivity was found to be higher in males, which was attributed to 65% of the study population being male (10). Altuntas Aydin et al. (9) determined no difference between the sexes, whereas a study in Korea reported higher seroprevalence in females, but the reason for this was not explained (11). In the current study, HAV seropositivity in females was statistically significantly higher than the rate in males, and there can be considered as a need for a more detailed evaluation to be able to explain the reason for this.

The CDC reported that hepatitis A is seen at the same rate in all race and ethnic groups in the general population (3). In a study by Kourkounti et al. (14), 7.5% of PLWH were reported to be immigrants, the seropositivity rate of immigrants was 67.7%, and ethnicity was found to be statistically significant. In the current study, no statistically significant difference was determined with respect to ethnicity. This absence of difference was thought to be due to the high rates of seropositivity both in Turkey and in the countries from which the immigrants had come.

According to the CDC data, since the start of hepatitis A vaccination in children in 1996, the frequency of HAV infection in the general population has decreased, and small increases have been seen because of contaminated foodstuffs or intravenous drug use (3). Lee et al. (13) determined a decrease in HAV seropositivity over the years and it was reported that improvements in sanitation had contributed to this, and although the vaccination rate was very low, mathematical modeling showed that 70% of potential outbreaks had been prevented. In the current study, the patients were examined in 2 periods of 10 years, and a significant decrease was determined in the positivity rate in the second 10-year period. When it is considered that vaccinations started in 2012 in Turkey, this can be considered to be not an effect of the vaccination but of improvements in sanitation.

In a study by Şenoğlu and Yeşilbağ (7), which evaluated 788 PLWH between 2015 and 2019, HAV seronegativity was found to be statistically significantly high in homosexually active males. Altuntas Aydin et al. (9) evaluated 242 PLWH between 2006 and 2011 and found HAV seronegativity was statistically significantly high in homosexually active males. The results of the current study were similar. In a study that evaluated 581 PLWH between 1988 and 2004, Aloise et al. (10) found no significance of sexual orientation in respect to seropositivity. Similarly, Lee et al. (11) found no significance of sexual orientation in respect to seropositivity in a study of 756 PLWH between 2012 and 2021, but also

reported that there was a significant increase in seroprevalence in the group of young homosexually active males, although the reason for this was not explained. These differences can be considered as due to the years and places where the studies were conducted.

Vaccination is recommended for all PLWH with negative HAV serology, independently of the CD4 (+) T-lymphocyte count (3,4). Since 2012, the vaccine has been provided free of charge to PLWH in Turkey (2). The CDC has reported that seroconversion could sometimes occur at 6 months after HAV vaccination in PLWH, and there could be a poor response to the vaccine in those with low CD4 (+) T-lymphocyte count. If HAV serology examination is necessary after examination, it is recommended that the patient is vaccinated again (3). In a review by Lin et al. (17), it was reported that in countries with low HAV endemicity low adherence to the recommended HAV vaccination for PLWH, sensitivity to HAV infection continued because of high-risk sexual behavior and intravenous drug use, acute HAV infections were seen in children despite hepatitis A vaccinations, and it was emphasized that hepatitis A vaccination is necessary for both populations at risk and healthcare providers.

In a multicentre study by Hoover et al. (18), HAV serology was examined in 47% of 1,329 patients, with seronegativity determined in 526 (84%) of the 627 patients examined in respect to serology, and 150 (29%) were found to have been vaccinated, but no information was provided about the results of the vaccinations. In a retrospective study of 18095 PLWH by DeGroote et al. (19), of 3640 homosexually active males and/or intravenous drug addicts with HAV seronegativity, 360 (9.8%) were found to have been vaccinated, but no information was given about the response to vaccination. Kourkounti et al. (14) reported a vaccination rate of 66.3% and a response to a vaccine of 76%. In the current study, the vaccination rate was 16.9%, and the vaccine response was examined in 60% of these patients. Seropositivity developed at a rate of 91.6% after vaccination. There is a need for further more detailed studies to determine the reasons why the vaccination rates remain low despite the recommendations.

In a study by Aloise et al. (10), it was reported that of the PLWH with HAV seronegativity, acute hepatitis A infection developed in 5 (4.2%). DeGroote et al. (19) reported that anti-HAV IgG positivity developed in 27 (0.7%) unvaccinated PLWH throughout a one-year follow-up period, but no information was provided about the symptoms of the patients. In the current study, no acute HAV infection developed in the 196 PLWH who were not vaccinated and were determined with anti-HAV IgG negativity.

Study Limitations

Due to single-center design with relatively small sample size potential lack of generalizability is an important limitation of the current study.

Conclusion

Although improvements in sanitation and vaccination in childhood have provided a decrease in HAV seropositivity, the key populations must be informed about vaccination, and vaccination adherence is ensured to prevent small outbreaks.

Ethics Committee Approval: Approval for the study was granted by the Clinical Research Ethics Committee of University of Health Sciences Turkey, Haseki Training and Research Hospital (approval number: 145-2022, date: 27.07.2022).

Informed Consent: Retrospective study.

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