

Seropositivity of Antibodies Against Hepatitis A Virus in Mashhad, Northeast of Iran, 2009: A Cross-Sectional Community-Based Study

Rahele Miri¹; Sanaz Ahmadi Ghezeldasht¹; Mohamad Reza Hedayati-Moghadam^{1,*}; Farhad Fathimoghadam¹; Hamidreza Bidkhorri¹; Seyed Aliakbar Shamsian¹; Seyed Abdolrahim Rezaee¹

¹Research Center for HIV/AIDS, HTLV and Viral Hepatitis, Iranian Academic Center for Education, Culture and Research (ACECR), Mashhad, IR Iran

*Corresponding author: Mohamad Reza Hedayati-Moghadam, Research Center for HIV/AIDS, HTLV and Viral Hepatitis, ACECR-Mashhad Branch, P. O. Box: 91775-1376, Mashhad, IR Iran. Tel: +98-5138821533, Fax: +98-5138810177, E-mail: drhedayati@acecr.ac.ir; drhedayati@yahoo.com

Received: January 17, 2015; Revised: February 5, 2015; Accepted: March 1, 2015

Background: Hepatitis A Virus (HAV) is the most common cause of acute viral hepatitis worldwide, mostly in developing countries.

Objectives: This population-based survey was performed to investigate HAV seroprevalence in Mashhad, northeast of Iran.

Patients and Methods: A cross-sectional study was performed on 1563 randomly selected individuals from general population of Mashhad, Iran, between May and September 2009. Serum samples were tested for total anti-HAV antibodies using the Enzyme-Linked Immunosorbent Assay (ELISA) kit. Data was analyzed using SPSS ver. 18.0 by Chi-square and Student's t-Tests.

Results: Seroprevalence of HAV infection was 69.6% (95% CI: 67.3-71.9%) with no difference between males and females. Anti-HAV seropositivity increased with rising age from 9.4% in subjects younger than 5 years to 100.0% in individuals older than 65 years old ($P < 0.001$).

Conclusions: As it was previously reported by the World Health Organization (WHO) on HAV infection in the country, this study revealed a high prevalence of HAV infection in Mashhad.

Keywords: Hepatitis A Virus; Seroepidemiologic Studies; Cross-Sectional Studies; Iran

1. Background

Hepatitis A virus (HAV) infection is the most common form of acute viral hepatitis worldwide, mostly in developing countries (1). The infection is principally transmitted through fecal-oral route (2, 3) and high prevalence of infection is associated with poor socioeconomic conditions, hygiene status and diverse epidemiological patterns (1). Outbreaks of hepatitis A have been reported for centuries, affecting both military and civilian populations (4). Clinically, mild HAV infections are mostly observed in children (5) and usually followed by a life-long immunity (6). On the other hand, more serious conditions such as liver failure may occur in elderly people following an acute infection (7). During the recent decades, due to an improvement in sanitation, the age of infection by the virus has been shifted from early childhood to adolescence or even later (8-10).

Based on the World Health Organization report (WHO), Iran with a high prevalence of HAV infection is an endemic region for this virus (11). In the systematic review by Farajzadegan et al. (12), HAV seroprevalence in general populations from Golestan, Hormozgan, Tehran and Fars provinces were between 88% and 99%. However, lower

seroprevalence was reported in general populations of some other parts of the country. In a cross-sectional study conducted in 2005, frequency of HAV in rural and urban population of Isfahan was 8.1% (13). Moreover, 24% of general population in Malekan, a city in northwest of Iran, had IgG antibodies against HAV (14).

Mashhad, the main city in northeastern Iran with nearly 2.5 million population (Census, 2006), is located near the geographical border of Afghanistan and Turkmenistan. As a holy city for Muslims, it attracts more than 25 million tourists and pilgrims each year.

2. Objectives

To our knowledge, no epidemiologic research exists exploring the prevalence of HAV infection in this region. Therefore, this study aimed to evaluate the seroprevalence of anti-HAV antibody in general population of Mashhad.

3. Patients and Methods

This cross-sectional study was conducted on general population of Mashhad between May and September

2009. The study was approved by the Research and Technology Deputy of Iranian Academic Center for Education, Culture and Research (ACECR), Mashhad branch regarding methodological and ethical issues. One-thousand five hundred sixty three individuals aged 1-90 years were selected randomly by multistage sampling methods from all of 12 municipality areas and 40 districts of the city. In each household, one person was selected so that we tried to include equal ratios of both genders as well as 10 percentiles for the age according to the 2006 census in each district. Tourists and pilgrims were not included in the study. The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki. A questionnaire including demographic data such as age and gender was completed. Whole blood samples were collected after obtaining an informed consent and sera were stored at -20°C until test performance. Sera were assessed for total anti-HAV antibody using the commercial specific Enzyme-Linked Immunosorbent Assay (ELISA) kit (Diapro, Italy) according to the manufacturer's instruction. Data was analyzed using PASW Statistics for Windows, Version 18.0. (SPSS Inc., Chicago) by Chi-square and Student's t-Tests. P values < 0.05 were considered statistically significant.

4. Results

A total of 1563 individuals including 709 (45.4%) males and 854 (54.6%) females with a mean age of 29.3 ± 18.4 years were assayed for HAV antibodies. One-thousand eighty eight individuals (69.6%, 95% CI: 67.3-71.9%) showed reactivity for HAV antibodies. The seroprevalence of HAV infection in males and females were 67.1% (476/709) and 71.7% (612/854) respectively ($p = 0.053$). As Figure 1 shows, the seroprevalence of HAV increased significantly with rising age, from 9.4% in subjects younger than five years to 100% in those aged 65 years and older ($P < 0.001$). Moreover, 84.9% of individuals aged 15 years or older had positive results for HAV antibodies. Furthermore, HAV prevalence in 11 districts of Mashhad ranged from 63.2% to 75.7% and one area had a prevalence of 91.7% ($P = 0.08$).

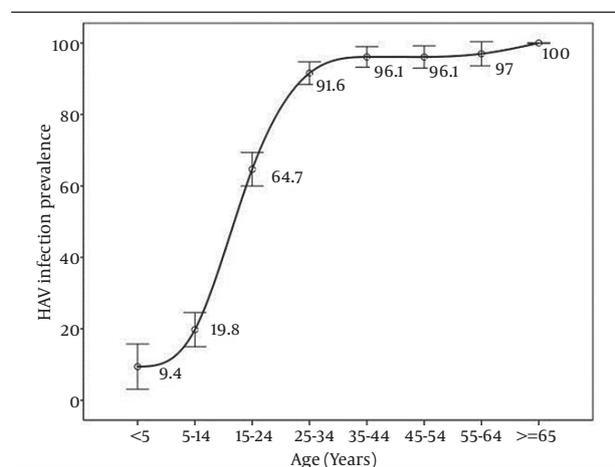


Figure 1. Prevalence of Hepatitis A Virus (HAV) According to Subject's Age in Mashhad, Northeast of Iran

5. Discussion

This study showed that most of our population had been infected by HAV. High prevalence rates have been also reported from different geographical areas of Iran. HAV seroprevalence in populations older than 15 years from Golestan, Hormozgan, Tehran, Fars, Qom and Qazvin provinces were between 78% and 99% (15-18). Similar to our results, HAV seroprevalence from different regions of China was reported to be 72.9%, which increased with age (19). Moreover, despite a dramatic decrease in HAV prevalence in developed countries during the last decades, some European countries still have a high prevalence of the infection, especially among younger population. As an example, in the community-based study on multi-ethnic neighborhood in the Netherlands, Markers for hepatitis A infection were present in 68% of individuals (20). Additionally, the prevalence of HAV among Kosovarian population was 88.6%, which displays a decreasing pattern compared to previous data (21). On the other hand, extremely lower seroprevalence of HAV has been reported from some provinces of the country. The study by Ataei et al. (22) stated the prevalence in Isfahan province, central Iran, as low as 8.3%, probably due to improved sanitary conditions. Heterogeneity in seroprevalence of HAV within a country has been demonstrated in several studies. This divergence could be partly related to differences in socioeconomic and health states of populations; however, using different selection methods could contribute this dissimilarity (12).

In our study, seroprevalence of HAV among females was quietly higher than males; however, this difference was not statistically significant. A meta-analysis included 11 studies from Iran showed that HAV prevalence among females was slightly higher than males, which was not statistically significant. Furthermore, the seroprevalence of hepatitis A in the general population of Tehran, Golestan and Hormozgan provinces did not differ between males and females (15). Moreover, same anti-HAV seropositivity among males and females has been observed in other countries such as Croatia (23). These could reflect similar risk factors for infection between both genders.

In our study, children and adolescents were more susceptible to acquire HAV infection since only 17.3% of individuals younger than 15 years had anti-HAV antibodies. In consistent with our findings, in 6 months to 15 years old children visited in pediatric hospitals of Tehran, HAV seroprevalence was reported to be 22.3% (24). Moreover, the age-specific seroprevalence rate of HAV antibodies was determined in the study in Sari (25). Seroprevalence rates increased significantly from 5.2% in age group of 1-5 years in urban areas to 82.0% in 15 - 25 years age group of rural areas. Moreover, a significant increase of anti-HAV seropositivity with age has been observed in European countries such as Italy and Croatia (25, 26).

The anti-HAV seroprevalence rate is presently decreasing in many parts of the world probably due to socio-

economic improvement, increased hygienic drinking water accessibility and hepatitis A vaccine availability (27-29). In many countries of the Middle East such as Saudi Arabia and Turkey, HAV prevalence has been declined in children (8). Similarly, Iran has experienced major improvement in socioeconomic and health status including sanitation of drinking water during the past decades (22, 30). These changes would reduce the rates of HAV infection in our population, which has been reflected as a relative low prevalence of infection among our children and adolescents.

This epidemiologic study on general population would help policy makers to know more about HAV prevalence, routes of transmission and strategies to control the infection. The strength of this study was that we undertook a population-based study on all age groups and both genders, selected randomly in proportion to the distribution of population in the city from all 12 municipality areas and 40 districts of the city. On the other hand, since the serum samples were assayed for the presence of anti-HAV total antibodies not anti-HAV IgM and anti-HAV IgG separately, we were unable to distinguish acute from chronic infection which should also be highlighted as a limitation of our study.

In conclusion, our area is an endemic region for HAV infection as previously reported by WHO. Therefore, an efficient surveillance system is seriously needed to prevent spreading of the virus. Moreover, it seems that seroprevalence of HAV infection has been decreased in the young population and therefore more children would be susceptible to the infection.

Acknowledgements

We appreciate the personnel of the Central Laboratory of the ACECR, Mashhad Branch for their great cooperation in conduction of the current investigation. The authors declared to have no competing interests.

Funding/Support

This study was financially supported by the Research and Technology Deputy of Iranian Academic Center for Education, Culture and Research (ACECR), Mashhad Branch, Mashhad, IR Iran.

References

1. Struchiner CJ, de Almeida LM, de Azevedo RS, Massad E. Hepatitis A incidence rate estimates from a pilot seroprevalence survey in Rio de Janeiro, Brazil. *Int J Epidemiol*. 1999;**28**(4):776-81.
2. Tosun S, Ertan P, Kasirga E, Atman U. Changes in seroprevalence of hepatitis A in children and adolescents in Manisa, Turkey. *Pediatr Int*. 2004;**46**(6):669-72.
3. Sagnelli E, Stroffolini T, Almasio P, Mele A, Coppola N, Ferrigno L, et al. Exposure to HAV infection in patients with chronic liver disease in Italy, a multicentre study. *J Viral Hepat*. 2006;**13**(1):67-71.
4. Krugman S. The Gordon Wilson Lecture. The ABC's of viral hepatitis. *Trans Am Clin Climatol Assoc*. 1992;**103**:145-56.
5. Koff RS. Clinical manifestations and diagnosis of hepatitis A virus infection. *Vaccine*. 1992;**10 Suppl 1**:S15-7.
6. Acharya SK, Batra Y, Bhatkal B, Ojha B, Kaur K, Hazari S, et al. Seroprevalence of hepatitis A virus infection among school children in Delhi and north Indian patients with chronic liver disease: implications for HAV vaccination. *J Gastroenterol Hepatol*. 2003;**18**(7):822-7.
7. Saab S, Lee C, Shpaner A, Ibrahim AB. Seroprevalence of hepatitis A in patients with chronic liver disease. *J Viral Hepat*. 2005;**12**(1):101-5.
8. Jacobsen KH, Koopman JS. Declining hepatitis A seroprevalence: a global review and analysis. *Epidemiol Infect*. 2004;**132**(6):1005-22.
9. Hendrickx G, Van Herck K, Vorsters A, Wiersma S, Shapiro C, Andrus JK, et al. Has the time come to control hepatitis A globally? Matching prevention to the changing epidemiology. *J Viral Hepat*. 2008;**15 Suppl 2**:i1-15.
10. Melnick JL. History and epidemiology of hepatitis A virus. *J Infect Dis*. 1995;**171 Suppl 1**:S2-8.
11. Saffar MJ, Abedian O, Ajami A, Abedian F, Mirabi AM, Khalilian AR, et al. Age-specific seroprevalence of anti-hepatitis A antibody among 1-30 years old population of savadkuh, mazandaran, iran with literature review. *Hepat Mon*. 2012;**12**(5):326-32.
12. Farajzadegan Z, Hoseini SG, Kelishadi R, Jamshidi F, Nokhodian Z, Noori R, et al. Systematic review and meta-analysis on the age-specific seroprevalence of hepatitis A in Iran. *J Res Med Sci*. 2014;**19**(Suppl 1):S56-63.
13. Ataei B, Nokhodian Z, Javadi AA, Kasaeyan N, Farajzadegan Z, Shoaie P, et al. Seroprevalence of hepatitis A virus infections in Over 6-years population in Isfahan-Iran: A community-based study. *J Isfahan Med Sci*. 2007;**25**(86):46-53.
14. Hu MD, Schenzle D, Deinhardt F, Scheid R. Epidemiology of hepatitis A and B in the Shanghai area: prevalence of serum markers. *Am J Epidemiol*. 1984;**120**(3):404-13.
15. Merat S, Rezvan H, Nouraei M, Abolghasemi H, Jamali R, Amini-Kafiabad S, et al. Seroprevalence and risk factors of hepatitis A virus infection in Iran: a population based study. *Arch Iran Med*. 2010;**13**(2):99-104.
16. Taghavi SA, Hosseini Asl MK, Talebzadeh M, Eshraghian A. Seroprevalence study of hepatitis A virus in Fars province, southern Iran. *Hepat Mon*. 2011;**11**(4):285-8.
17. Noroozi M, Moradi F, Hasanzadeh A. Seroprevalence of hepatitis A and hepatitis E in Qom province, 2011. *Iran J Infect Dis Trop Med*. 2012;**17**(4):19-23.
18. Ramezani H, Bozorgi SH, Nooranipour M, Mostajeri A, Kargar-Fard H, Molaverdikhani S, et al. Prevalence and risk factors of hepatitis A among blood donors in Qazvin, central Iran. *Singapore Med J*. 2011;**52**(2):107-12.
19. Lu J, Zhou Y, Lin X, Jiang Y, Tian R, Zhang Y, et al. General epidemiological parameters of viral hepatitis A, B, C, and E in six regions of China: a cross-sectional study in 2007. *PLoS One*. 2009;**4**(12):e12000.
20. Veldhuijzen IK, van Driel HF, Vos D, de Zwart O, van Doornum GJ, de Man RA, et al. Viral hepatitis in a multi-ethnic neighborhood in the Netherlands: results of a community-based study in a low prevalence country. *Int J Infect Dis*. 2009;**13**(1):e9-e13.
21. Quaglio G, Ramadani N, Pattaro C, Cami A, Dentico P, Volpe A, et al. Prevalence and risk factors for viral hepatitis in the Kosovar population: implications for health policy. *J Med Virol*. 2008;**80**(5):833-40.
22. Ataei B, Javadi AA, Nokhodian Z, Kassaeyan N, Shoaie P, Farajzadegan Z, et al. HAV in Isfahan province: a population-based study. *Trop Gastroenterol*. 2008;**29**(3):160-2.
23. Vilbic-Cavlek T, Kucinar J, Ljubin-Sternak S, Kolaric B. Seroprevalence of hepatitis A in the croatian population. *Hepat Mon*. 2011;**11**(12):997-9.
24. Elikaei A, Sharifi Z, Shooshtari M, Hosseini M, Maroufi Y. Prevalence of HAV among healthy blood donors referring to Tehran transfusion center. *Iran J Pub Health*. 2008;**37**(4):126-30.
25. Alian S, Ajami A, Ghasemian R, Yadegarinia D. Age-specific seroprevalence of hepatitis A in Sari, northern Islamic Republic of Iran. *East Mediterr Health J*. 2011;**17**(10):754-8.
26. Campagna M, Siddu A, Meloni A, Basciu C, Ferrai L, Pettinau A, et al. Changing pattern of hepatitis A virus epidemiology in an area of high endemicity. *Hepat Mon*. 2012;**12**(6):382-5.
27. Jacobsen KH. *The Global Prevalence of Hepatitis A Virus Infection and Susceptibility: A Systematic Review*. Geneva, Switzerland.: World Health Organization; 2004.

- Health Organization; 2009. Available from: http://whqlibdoc.who.int/hq/2010/WHO_IVB_10.01_eng.pdf.
28. Wasley A, Fiore A, Bell BP. Hepatitis A in the era of vaccination. *Epidemiol Rev.* 2006;**28**:101-11.
29. Jacobsen KH, Wiersma ST. Hepatitis A virus seroprevalence by age and world region, 1990 and 2005. *Vaccine.* 2010;**28**(41):6653-7.
30. Cech TV. *Principles of water resources: history, development, management, and policy*. USA: John Wiley & Sons; 2010.