

Seroepidemiology of Hepatitis E Virus in Iranian Soldiers

Gholam Ali Ghorbani ^{1*}, Seyed-Moayed Alavian ^{1,2}, Ali Akbar Esfahani ¹, Shervin Assari ³

¹ Military Health Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran

² Baqiyatallah Research Center for Gastroenterology and Liver Diseases (BRCGL), Baqiyatallah University of Medical Sciences & Tehran Hepatitis Center, Tehran, Iran

³ Medicine and Health Promotion Institute, Tehran, Iran

Background and Aims: Hepatitis E virus (HEV) is recognized as a common cause of epidemic and sporadic viral hepatitis. HEV outbreaks have been documented in some military forces in the world. The aim of this study was to evaluate anti-HEV antibody in Iranian soldiers.

Methods: In a cross-sectional study, 800 soldiers were selected by simple random sampling in Tehran, Iran in 2006. A questionnaire of demographic data was completed and blood samples were obtained for anti-HEV IgG & IgM antibody. Data were analyzed using student t-test and chi-square using SPSS 12.

Results: All soldiers were male and their mean age was 19 ± 1.2 . Education level in 553 (69.1%) of them was high school diploma or higher. Anti-HEV IgG antibody was positive in only 9 (1.1%) of them and IgM was negative in all soldiers.

Conclusions: Approximately 98% of soldiers were at risk for HEV infection and before discovering an effective vaccine, preparation of healthy drinking water and personal hygiene education should be considered for prevention of hepatitis E infection.

Keywords: Hepatitis E, Antibody, Soldiers, Iran

Introduction

Hepatitis E virus (HEV), a small non-enveloped RNA virus, is a causative agent of acute hepatitis that is transmitted principally via the fecal-oral route. The virus can cause epidemic hepatitis in developing countries and sporadic outbreaks in non-endemic areas (1, 2). In endemic areas, hepatitis E occurs predominantly in young adults (3). Hepatitis E is an important public health concern in many developing countries of Southeast and Central Asia, the Middle East, Northern and Western parts of Africa, and Mexico; where outbreaks have been reported. Although the overall mortality rate associated with HEV infection is low, it is reportedly as high as 20% in infected pregnant women (4, 5).

Transmission of HEV occurs through contaminated water supplies in developing countries. Recent studies have indicated that zoonosis is involved in the transmission of HEV,

especially in industrialized countries where hepatitis E is believed to be non-endemic (6). Further, vertical transmission of HEV from infected mothers to their children has been observed. Also dental treatments were suspected as risk factors for HEV contamination (7). Epidemic hepatitis E has been reported in Pakistan in a military unit in Sargodha and in the capital city of Islam Abad and in this

* Correspondence:

Gholam Ali Ghorbani MD, Assistant Professor of Infectious Diseases, Military Health Research Center, Baqiyatallah University of Medical Sciences, Mollasadra Avenue, Vanak Square, Tehran, Iran.

Tel: +98 912 2977463

Fax: +98 21 88600062

E-mail: gholamalighorbani@yahoo.com

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epidemic 95% of patients with acute hepatitis had serologic evidence of acute hepatitis E whose source was fecal contamination of a water system but the prevalence of anti-HEV in this population before the outbreak was estimated to be 30%. On the other hand, military persons may drunk unhealthy water in departure area, therefore they had risk for hepatitis E infection (8). HEV has worldwide distribution, but predominating factors include tropical climates, inadequate sanitation, and poor personal hygiene. Outbreaks are associated with rainy seasons, floods, and overcrowding (9). Hepatitis E virus accounts for more than 50% of acute viral hepatitis in young adults in developing countries (10). In unexplained acute hepatitis with or without history of foreign travel to endemic and non-endemic country, the diagnosis of hepatitis E should be considered (11, 12).

HEV is similar to hepatitis A disease with respect to transmission, clinical course, and absence of chronic disease. Hepatitis E attack rates are highest in young adults rather than in children as is the case with hepatitis A virus (13). Use of immune serum globulin as prophylaxis does not provide protection and vaccines aren't currently available for HEV infection (14). Iran was accounted as an endemic country for hepatitis E and its seroprevalence increased significantly with age, from 3.3% in subjects less than 30 years of age to 37.5% in individuals 50 years (5, 15) but prevalence of HEV infection was not determined in military persons, which is why this study was implemented.

Materials and Methods

This is a cross-sectional study conducted in 800 on-duty soldiers in Tehran, Iran between April and May 2006. Five mL of venous blood sample was taken from each soldier and then centrifuged immediately. Sera were stored at -20°C, coded and further tested at the laboratory of Baqiyatallah Hospital for anti-HEV IgG and IgM antibodies by Enzyme Immunometric Assay (HEV-EIA, Diapro, Italy). Cut-off was defined with positive and negative control sera that were included in each assay, according to manufacturer's instruction. Samples were considered positive if the optical density (OD) value was above the cut-off value and all positive samples were retested in duplicate with the same EIA to confirm the initial results. An interview questionnaire of demographic data such as age, educational level and occupation before conscription and past history of hepatitis was taken

from each soldier. Data were analyzed using SPSS 12 by means of student t-test and chi-square tests. $P < 0.05$ was considered significant.

Results

All soldiers were male with mean age of 19 ± 1.2 (rang: 17-23 years). Almost all soldiers were single (99.3%, $n=795$). The length of service was 3.3 ± 2.3 (range: 2-24 months). Educational level was high school diploma and higher in 553 (69.1%) and 247 (30.9%) had lower educational level. Regarding occupation before conscription, most of them were students (88%, $n=702$). All soldiers had negative HEV IgM antibody and 791 (98.9%) of them had negative HEV IgG antibody while only 9 (1.1%) had positive IgG. Past history of hepatitis was negative in all soldiers. None of the variables had significant relationship with anti-HEV antibody.

Discussion

This study defined that anti-HEV IgG antibody was positive in only 1.1 % of soldiers and IgM was negative in all cases and showed that up to 98.9% of soldiers had no immunity to HEV. This finding agrees with that of other studies which showed low prevalence of anti-HEV antibodies in general population in non-endemic countries (16). Although Iran was accounted as an endemic country for HEV infection, in our study, the prevalence of HEV infection was insignificant opposite to another study in an endemic country which showed the seroprevalence of 10-30% in general population (8). This difference may be due to different levels of sanitation in these countries. Seroprevalence of HEV was different in each province of Iran and Tehran may have a good sanitation condition and this subject may cause deduction of anti-HEV antibody prevalence opposite in here (5, 15).

In here HEV infection probably occurred as sporadic in ancient years but military persons in remote areas with poor sanitation may drink unhealthy water and contract infection from contaminated water, which causes outbreak in them (17).

Military people are at risk for hepatitis E infection because it is transmitted via oral-fecal route. HEV is responsible for a high morbidity and mortality (13) and an outbreak arises in them especially in countries suffering from poor hygiene and massive water pollution (18).

Past history of symptomatic hepatitis was

negative in our study, like the study of Tanaka *et al.*; they may have been infected many years ago asymptotically⁽¹⁹⁾. Occupation is an important risk factor for HEV infection and working in poor sanitary areas can predispose people to HEV infection. In our study occupation of soldiers before conscription was traditional student and they did not have any risk for infection⁽²⁰⁾.

Anti-HEV IgM antibody may be positive in acute hepatitis E infection and is not detected for long time. Anti-HEV IgM antibody was not detected here; may be due to primitive HEV infection and in time of study⁽²¹⁾. Long-time anti-HEV IgG can persist for years⁽²²⁾ and it should be used for diagnosis of hepatitis E seroepidemiology study in mass population as shown in Bryan *et al.* study [8]. When soldiers used unhealthy water, there was an outbreak of HEV infection, but in our study HEV infection probably occurred sporadically that may be due to consumption of healthy drinking water⁽¹⁴⁾.

The length of service in this study was not more than two years, but long-time in service such as formal military persons was important because they compelled to departure in low sanitation area and risk of HEV infection should be considered for them⁽¹⁷⁾. In this study all soldiers were male and association between sex and HEV infection was not seen, but the distribution of HEV infection through sex has pointed to higher values in males than in females, this is probably the result of more involvement of males in low sanitation situation⁽²³⁾. In endemic areas such as Iran, seroepidemiological survey has shown that anti-HEV antibodies in normal populations appears to be unexpectedly low, which may be due to disappearance of anti-HEV antibody and did not persistent for long-time⁽¹²⁾.

Higher educational level caused better attention to hygiene and therefore diminished the risk for HEV infection but in our study association between educational level and antibodies against HEV infection was not determined because samples were not enough.

The groups between 15 and 40 years of age⁽¹⁹⁾, adolescence and young adults show the highest attack rate for HEV infection in world⁽²⁴⁾. The reason for this unusual age distribution for an enterically transmitted infection is still unclear but sources may be caused with drugs abuse⁽²⁵⁾, blood⁽²⁶⁾ and contact with animal⁽²⁾. Source of HEV infection was not determined in this study and these subjects yet need further evaluation. Prevalence of HEV infection is very low in this study and one of the reasons may be ascribed to differences in assays for anti-HEV antibody and future studies using

standard assay is recommended⁽²⁷⁾. Hepatitis E, like hepatitis A is a great public health problem in many developing countries⁽²¹⁾ and poor socio-economic or hygiene conditions and the high population density contribute to maintain these infections⁽⁷⁾. Hepatitis A infection occurs at an early age and causes immunity in adults while hepatitis E probably infects adults and is a life threatening in career of age and prevention of this infection should be considered⁽²⁸⁾.

In conclusion, because soldiers have no immunity against HEV infection; prevention of HEV infection is important for them and before making an effective vaccine, when they travel to low sanitation areas, they should be trained to avoid drinking water of unknown purity.

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References

1. Dalton HR, Thurairajah PH, Fellows HJ, Hussaini HS, Mitchell J, Bendall R, *et al.* Autochthonous hepatitis E in southwest England. *J Viral Hepat* 2007; **14**: 304-9.
2. Peron JM, Bureau C, Poirson H, Mansuy JM, Alric L, Selves J, *et al.* Fulminant liver failure from acute autochthonous hepatitis E in France: description of seven patients with acute hepatitis E and encephalopathy. *J Viral Hepat* 2007; **14**: 298-303.
3. Ducancelle A, Payan C, Nicand E, Le Guillou H, Cales P, Lunel-Fabiani F. Intrafamilial hepatitis E in France. *J Clin Virol* 2007; **39**: 51-3.
4. Buti M, Clemente-Casares P, Jardi R, Formiga-Cruz M, Schaper M, Valdes A, *et al.* Sporadic cases of acute autochthonous hepatitis E in Spain. *J Hepatol* 2004; **41**: 126-31.
5. Taremi M, Khoshbaten M, Gachkar L, EhsaniArdakani M, Zali M. Hepatitis E virus infection in hemodialysis patients: a seroepidemiological survey in Iran. *BMC Infect Dis* 2005; **5**: 36.
6. Shukla P, Chauhan UK, Naik S, Anderson D, Aggarwal R. Hepatitis E virus infection among animals in northern India: an unlikely source of human disease. *J Viral Hepat* 2007; **14**: 310-7.
7. Arankalle VA, Tsarev SA, Chadha MS, Alling DW, Emerson SU, Banerjee K, *et al.* Age-specific prevalence of antibodies to hepatitis A and E viruses in Pune, India, 1982 and 1992. *J Infect Dis* 1995; **171**: 447-50.
8. Bryan JP, Iqbal M, Tsarev S, Malik IA, Duncan JF, Ahmed A, *et al.* Epidemic of hepatitis E in a military unit in Abbotabad, Pakistan. *Am J Trop Med Hyg* 2002; **67**: 662-8.
9. Lin CC, Wu JC, Chang TT, Chang WY, Yu ML, Tam AW, *et al.* Diagnostic value of immunoglobulin G (IgG) and IgM anti-hepatitis E virus (HEV) tests based on HEV

- RNA in an area where hepatitis E is not endemic. *J Clin Microbiol* 2000; **38**: 3915-8.
10. Safary A. Perspectives of vaccination against hepatitis E. *Intervirology* 2001; **44**: 162-6.
 11. Ijaz S, Arnold E, Banks M, Bendall RP, Cramp ME, Cunningham R, *et al.* Non-travel-associated hepatitis E in England and Wales: demographic, clinical, and molecular epidemiological characteristics. *J Infect Dis* 2005; **192**: 1166-72.
 12. Waar K, Herremans MM, Vennema H, Koopmans MP, Benne CA. Hepatitis E is a cause of unexplained hepatitis in The Netherlands. *J Clin Virol* 2005; **33**: 145-9.
 13. Coursaget P, Buisson Y, Enogat N, Bercion R, Baudet JM, Delmaire P, *et al.* Outbreak of enterically-transmitted hepatitis due to hepatitis A and hepatitis E viruses. *J Hepatol* 1998; **28**: 745-50.
 14. Wang L, Zhuang H. Hepatitis E: an overview and recent advances in vaccine research. *World J Gastroenterol* 2004; **10**: 2157-62.
 15. Taremi M, Gachkar L, MahmoudArabi S, Kheradpezhoh M, Khoshbaten M. Prevalence of antibodies to hepatitis E virus among male blood donors in Tabriz, Islamic Republic of Iran. *East Mediterr Health J* 2007; **13**: 98-102.
 16. Toole MJ, Claridge F, Anderson DA, Zhuang H, Morgan C, Otto B, *et al.* Hepatitis E virus infection as a marker for contaminated community drinking water sources in Tibetan villages. *Am J Trop Med Hyg* 2006; **74**: 250-4.
 17. Bauduceau O, Berlioz A, Buisson Y. Hepatitis B, C, and E in New Caledonia. Seroepidemiologic study in military recruits. *Med Trop (Mars)* 2000; **60**: 167-70.
 18. Okamoto H, Takahashi M, Nishizawa T. Features of hepatitis E virus infection in Japan. *Intern Med* 2003; **42**: 1065-71.
 19. Tanaka E, Matsumoto A, Takeda N, Li TC, Umemura T, Yoshizawa K, *et al.* Age-specific antibody to hepatitis E virus has remained constant during the past 20 years in Japan. *J Viral Hepat* 2005; **12**: 439-42.
 20. Jeggli S, Steiner D, Joller H, Steffen R, Hotz P. Hepatitis E and exposure to waste water. *Schweiz Rundsch Med Prax* 2003; **92**: 433-5.
 21. Hurtado C, Munoz G, Brahm J. Detection of IgM antibodies against hepatitis E virus. *Rev Med Chil* 2005; **133**: 645-7.
 22. Chau TN, Lai ST, Tse C, Ng TK, Leung VK, Lim W, *et al.* Epidemiology and clinical features of sporadic hepatitis E as compared with hepatitis A. *Am J Gastroenterol* 2006; **101**: 292-6.
 23. Balayan MS, Andjaparidze AG, Savinskaya SS, Ketiladze ES, Braginsky DM, Savinov AP, *et al.* Evidence for a virus in non-A, non-B hepatitis transmitted via the fecal-oral route. *Intervirology* 1983; **20**: 23-31.
 24. Trinta KS, Liberto MI, de Paula VS, Yoshida CF, Gaspar AM. Hepatitis E virus infection in selected Brazilian populations. *Mem Ins Oswaldo Cruz* 2001; **96**: 25-9.
 25. Christensen PB, Engle RE, Jacobsen SE, Krarup HB, Georgsen J, Purcell RH. High prevalence of hepatitis E antibodies among Danish prisoners and drug users. *J Med Virol* 2002; **66**: 49-55.
 26. Vitral CL, Pinto MA, Lewis-Ximenez LL, Khudyakov YE, dos Santos DR, Gaspar AM. Serological evidence of hepatitis E virus infection in different animal species from the Southeast of Brazil. *Mem Ins Oswaldo Cruz* 2005; **100**: 117-22.
 27. Tan CR, Bao ZY, Sun HY, Hu M, Chen Y, Chen M, *et al.* Serological antibodies comparison of a hepatitis E outbreak. *Zhonghua Shi Yan He Lin Chuang Bing Du Xue Za Zhi* 2005; **19**: 35-8.
 28. Alavian SM, Ghorbani G. Hepatitis A in soldiers of Iran. *Hep Mon* 2007; **7**: 34-7.