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Hepatitis E Virus and Serum Level Aminotransferases in Blood Donors

Abdolreza Sotoodeh Jahromi[1,2], Morteza Pourahmad [*1,3]

Abstract

Background: Hepatitis E virus (HEV) infection is a self-limiting viral infection that can lead to severe complications and death. In different regions the epidemiology of this infection varies. In this study we evaluated the seroepidemiology of hepatitis E infection in Jahrom, a city in southern Iran.

Methods: This was a cross-sectional descriptive study of serum samples from 477 subjects, including 30 females and 447 males. HEV immunoglobulin G (IgG) and immunoglobulin M (IgM) were measured by enzyme-linked immunosorbent assays (ELISA). Alanine transaminase (ALT) and aspartate transaminase (AST) levels were also determined. Four hundred forty-seven subjects were male and 30 were female. Subjects were classified by age and sex.

Results: One woman (3.3%) and 25 men (5.5%) were positive for HEV antibodies (IgG and/or IgM). There was found an association between serum level of aminotransferases and seropositivity for HEV.

Conclusion: The result of this study indicates that HEV is an etiological factor for hepatitis in this area of IRAN. The cost benefit of active immunization in endemic regions should be evaluated because an outbreak could have tragic consequences.

Keywords: Aminotransferase, Hepatitis E, Iran, Seroepidemiology

Introduction

Hepatitis E virus is a non-enveloped single-stranded RNA virus that causes hepatitis E (1, 2). Infection with HEV is a health problem worldwide, especially in developing countries such as Iran. This disease is endemic in Japan and some European countries (3, 4).

Hepatitis E is also a zoonotic disease of some domestic animals such as cattle, sheep, goats, chickens, and pigs, and transmission of the virus to humans may occur via these animals (5-7).

Transmission of the virus occurs mostly via the fecal-oral route and contaminated water plays a major role in the process (4, 8-11); however, the virus may be transmitted by other routes, such as hemodialysis (12, 13, 18, 19). Vertical transmission of HEV from infected mothers to their children has also been described (14). In addition, dental treatments and blood transfusions may be associated with HEV transmission (15-17). Hepatitis E is endemic in Iran and seroprevalence of this infection increases significantly with age (20) and HEV infection should be considered in all hepatitis cases in this country (21).

HEV prevalence varies between countries; for example it's prevalence in Egypt and Taiwan was reported as 26% and 11%, respectively (22, 23). In different cities of Iran this variability is also present; HEV prevalence was reported as 3.8%, 11.5%, 7.8%, and 9.3% in Esfahan, Khozestan, Tabriz, and Nahavand, respectively (20, 24-26).

Hepatitis E infection is usually a self-limiting disease in normal persons, but can develop to a severe and fatal disease in some patients. For example,

1: Zoonoses Research Center, Jahrom University of Medical Sciences, Jahrom, Iran
2: Department of Immunology, Jahrom University of Medical Sciences, Jahrom, Iran
3: Department of Internal Medicine, Jahrom University of Medical Sciences, Jahrom, Iran
***Corresponding author: Morteza Pourahmad; Tel: +98 791 3340405; E-mail: Mortezapourahmad@yahoo.com**
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mortality occurs in 20-25% of pregnant women with hepatitis E, and in patients with liver disorders this ratio may increase to 75% (1, 2, 9, 27, 28). In addition, liver failure and cirrhosis can also result from hepatitis E infections (29).

Mindful of the importance of the epidemiology of HEV infection in various locales, we conducted this study in Jahrom, a city in southern Iran, to evaluate the prevalence of HEV infection in this region.

Materials and Methods

This cross-sectional descriptive study was performed on blood from 484 subjects who had donated at a blood bank center in Jahrom in April through July of 2009. Five ml of venous blood were drawn from each donor and centrifuged. Serum samples were stored at -20 °C and anti-HEV IgG antibodies were measured by ELISA (DIA-PRO, Italy). Serum levels of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were also measured by spectrophotometry. The age and sex of each subject were recorded.

The entrance criteria were that subjects were negative for negative hepatitis B virus surface antigen (HBsAg), hepatitis C virus antibodies (HCVAb), and human immunodeficiency virus antibodies (HIVAb).

SPSS software (v. 11.5) was used for statistical analysis of the data and descriptive statistics were reported. Quantitative variables were expressed as the mean ± the standard deviation (SD), and comparisons performed using the two-sample t test. Statistical significance was set when $p < 0.05$.

Results

In this study serum samples from 477 subjects between 17 and 59 years of age were evaluated. The mean age of the subjects was 35.42 ± 9.38. We divided the subjects into 4 age groups. Twenty six samples (5.4%) were positive for HEV antibodies (IgG or IgM). The highest proportion of HEV-positive samples came from subjects who were 36 to 45 years old (11 of 26, or 42.3%) (Table 1). A significant positive correlation was observed between the ages of the subjects and the positivity of HEV serology (*cor* = +1 and *P* = 0.48).

Thirty subjects were female (6.3%) and 447 (93.7%) were male. One woman (3.3%) and 25 men (5.5%) were HEV sero-positive (Table 2). All 26 HEV-positive samples (100%) were positive for IgG and 11 (42%) were positive for IgM antibodies. The levels of ALT and AST in the HEV-positive samples were significantly higher than those in the HEV-negative samples (P = 0.001, Table 3).

Table 1. Age groups and serology of subjects.

Age group	HEV Positive	HEV Negative	Total
Lowest to 25	7	113	120
	26.9%	25%	25%
26 to 35	7	101	108
	26.9%	22.3%	22.6%
36 to 45	11	183	194
	42.3%	40.5%	40.6%
46 to highest	1	55	56
	3.8%	12.2%	11.7%
Total	**26**	**452**	**477**
	100%	**100%**	**100%**

Table 2. Sex and HEV serology of the studied blood donors.

Sex	HEV Positive	HEV Negative	Total
Female	1	29	30
	3.3%	96.7%	100%
Male	25	422	447
	5.5%	95.4%	100%
Total	**26**	**451**	**477**
	5.6%	**94.4%**	**100%**

Discussion

In this study 5.4% of the subjects were HEV-positive. This result is similar to studies conducted in Brazil (2-7.5%) (16, 30, 31) and Japan (7.1%) (32).

The extent of HEV infection is relatively high in some developing countries; for example, HEV seropositivity in India has been reported to be 18.6% (33); however the infection rates in most developing countries have been reported to be much lower than that (0.4 to 3.9%) (17, 34, 35).

Serosurveys in developed countries in which HEV infection is not thought to be endemic have consistently indicated seropositivity rates of 1-5% (36). Reports from Europe and the United States suggest HEV may be endemic in some developed countries (36). Based on these reports, HEV infection is not unique to underdeveloped countries, which may be due to the mechanism of transmission. Although HEV is mainly transmitted via the fecal-oral route, the infection is a commonly transmitted between humans and animals, especially domestic animals such as pig, sheep, and goats, and human-to-human transmission may occur via blood transfusion

and hemodialysis (37). Therefore, HEV is not area- or person-specific and everyone worldwide is at risk for infection.

Infection rates were higher in men than women (5.5% vs. 3.3%). This finding may be due to contact factors. HEV is a zoonotic virus that infects some domestic animals; therefore, in areas where men have more occupational contact with animals than women, the chance for infection is greater in men than women.

Outbreaks of HEV infection have also been reported in Iran and failure to immunize women of child-bearing age could result in high mortality rates (20). ALT and AST levels were significantly higher in seropositive HEV subjects than HEV seronegative subjects .Similar results were reported in other studies (30, 32). In a study in the Nile Delta conducted on 47 subjects with ALT levels at least two times normal, 40 of those subjects (89%) were positive for anti HEV IgG (38). To date the degree and duration of HEV viremia have not been directly correlated with ALT or HEV antibody levels (39); however our results and previous studies indicate that elevated ALT may be due to sub-clinical HEV infections (40). Therefore in patients with unexplained elevated ALT and AST, hepatitis E as a differential diagnosis is logical.

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Table 3. Liver enzymes and serology of the samples, levels of anti- HEV (IgG and IgM)

	IgG			IgM		
Liver enzymes	Positive	Negative	P	Positive	Negative	P
ALT (units/L)	62.69 ±50.21	20.81 ±23.43	0.001	93.90 ±55.97	21.41 ±23.88	0.001
AST (units/L)	53.15 ±42.31	20.83 ±19.42	0.001	81.81 ±46.11	21.20 ±19.64	0.001

References

1. Balayan MS. Epidemiology of hepatitis E virus infection. J Viral Hepat. 1997 May; 4(3):155-65.
2. Miller MJ. Viral taxonomy. Clin Infect Dis. 1993 May;16(5):612-13.
3. Emerson SU, Purcell RH. Hepatitis E Virus. In: Knipe DM, Howley P. Fields Virology. 6th ed, Philadelphia: Lippincott Williams and Wilkins; 2013 Jun.
4. Okamoto H, Takahashi M, Nishzawa T, Fukai K, Muramatsu U, Yoshikawa A. Analysis of the complete genome of indigenous swine hepatitis E virus isolated in Japan. Biochem Biophys Res Commun. 2001 Dec;289(5):929-36.
5. Choi IS, Kwon HJ, Shin NR, Yoo HS. Identification of swine hepatitis E virus (HEV) and prevalence of anti-HEV antibodies in swine and human populations in Korea. J Clin Microbiol. 2003 Aug;41(8):3602-8.
6. Takahashi M, Nishzawa T, Yoshikawa A, Sato S, Isoda N, Ido K, et al. Identification of two distinct genotypes of hepatitis E virus in a Japanese patient with acute hepatitis who had not travelled abroad. J Gen Virol. 2002 Aug;83(Pt 8):1931-40.
7. Tokita H, Harada H, Gotanda Y, Takahashi M, Nishzawa T, Okamoto H. Molecular and serological characterization of sporadic acute hepatitis E in a Japanese patient infected with a genotype III hepatitis E virus in 1993. J Gen Virol. 2003 Feb;84(Pt 2):421-7.
8. Worm HC, Schlauder GG, Wurzer H, Mushahwar IK. Identification of a novel variant of hepatitis E virus in Austria: sequence, phylogenetic and serological analysis. J Gen Virol. 2000 Dec; 81(Pt 12):2885-90.
9. Hussaini SH, Skidmore SJ, Richardson P, Sherratt LM, Cooper BT, O'Grady JG. Severe hepatitis E infection during pregnancy. J Viral Hepat. 1997 Jan;4(1):51-4.
10. Meng XJ. Novel stains of hepatitis E virus identified from humans and other animal species: is hepatitis E a zoonosis? J Hepatol. 2000 Nov; 33(5):842-5.
11. Halbur PG, Kasorndorkbua C, Gilbert C, Guenette D, Potters MB, Purcell RH, et al. Comparative pathogenesis of infection of pigs with hepatitis E viruses recovered from a pig and a human. J Clin Microbiol. 2001 Mar; 39(3):918-23.
12. Psichogio M, Vaindirli E, Tzala E, Voudiclari S, Boletis J, Vosnidis G, et al. Hepatitis E virus (HEV) infection in hemodialysis patients. The Multicenter Hemodialysis cohort study on viral hepatitis. Nephrol Dial Transplant. 1996;11(6):1093-5.
13. Fabrizi F, Lunghi G, Bacchini G, Corti M, Pagano A, Locatelli F. Hepatitis E virus infection in haemodialysis patients: a seroepidemiological survey. Nephrol Dial Transplant. 1997 Jan; 12(1):133-6.
14. Khuroo MS, Kamili S, Jameel S. Vertical transmission of hepatitis E virus. Lancet. 1995 Apr;345(8956):1025-26.

15. Tassopoulos NC, Krawczynski K, Hatzakis A, Katsoulidou A, Delladetsima I, Koutelou MG, et al. Case report : role of hepatitis E virus in the etiology of community acquired non A, non B hepatitis in Greece. J Med Virol. 1994 Feb;42(2):124-8.
16. Arankalle VA, Chobe LP. Hepatitis E virus: can it be transmitted parenterally? J Viral Hepat. 1999 Mar;6(2):161-4.
17. Arankalle VA, Chobe LP. Retrospective analysis of blood transfusion recipients: evidence for post transfusion hepatitis E. Vox Sang. 2000 Sep;79(2):72-4.
18. Halfon P, Quzan D, Chanas M, et al. High prevalence of hepatitis E virus antibody in hemodialysis patients. Lancet. 1994 Sep;344(8924):746.
19. Dalekos GN, Zervou E, Elisaf M, Germanos N, Galanakis E, Bourantas K, et al. Antibodies to hepatitis E virus among several populations in Greece: increased prevalence in an hemodialysis unit. Transfusion. 1998 Jun;38(6):589-95.
20. Taremi M, Gachkar L, MahmoudArabi S, Kheradpezhouh 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 Jan-Feb;13(1):98-102.
21. Alavian SM. Hepatitis E virus infection: A neglected problem in our region. Hepat Mon. 2007 Sep;7(3):119-21.
22. Aboulata AA, Ahmad MS, Shaban MM, Zayd KM, Abd El-Moktader AM. Prevalence of hepatitis E virus in Egyptian children presented with minor hepatic disorders. Egypt J Immunol. 2005 Nov;12(2):71-6.
23. Lin CC WJ, 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 Nov;38(11):3915-8.
24. Ataei B, Nokhodian Z, Javadi AA, Kassaian N, Shoaei P, Farajzadegan Z, et al. Hepatitis E virus in Isfahan Province: a population-based study. Int J Infect Dis. 2009 Jul;13(1)67-71.
25. Assarehzadegan MA, Shakerinejad G, Amini A, Rezaee SA. Seroprevalence of hepatitis E virus in blood donors in Khuzestan Province, Southwest Iran. Int J Infect Dis. 2008 Jul; 12(4):389-90.
26. Taremi M, Mohammad Alizadeh AH, Ardalan A, Ansari S, Zali MR. Seroprevalence of hepatitis E in Nahavand, Islamic Republic of Iran: a population-based study. East Mediterr Health J. 2008 Jan-Feb; 14(1):157-62.
27. Mushahwar IK. Hepatitis E virus: Molecular virology, clinical features, diagnosis, transmission, epidemiology and prevention. J medical virol. 2008 Apr; 80(4):646-58.
28. Maila HT, Bowyer SM, Swanepoel R. Identification of a new strain of hepatitis E virus from an outbreak in Namibia in 1995. J Gen Virol. 2004 Jan;85(Pt 1):89-95.
29. Buisson Y, Grandadam M, Nicand E, Cheval P, Van cuyck-Gandre H, Innis B, et al. Identification of a novel hepatitis E virus in Nigeria. J Gen Virol. 2000 Apr;81(Pt 4):903-9.
30. Lin JB, Lin DB, Chen SC, Chen PS, Chen WK. Seroepidemiology of hepatitis A, B, C, and E viruses infection among preschool children in Taiwan. J Med Virol. 2006 Jan;78(1):18-23.
31. Psichogiou MA, Tassopoulos NC, Papatheodoridis GV, Tzala E, Klarmann R, Witteler H, et al. Hepatitis E virus infection in a cohort of patients with acute non-A, non-B hepatitis. J Hepatol. 1995 Dec;23(6):668-73.
32. Gotanda Y, Iwata A, Ohnuma H, Yoshikawa A, Mizoguchi H, Endo K, et al. Ongoing subclinical infection of hepatitis E virus among blood donors with an elevated alanine aminotransferase level in Japan. J Med Virol. 2007 Jun;79(6):734-42.
33. Psichogiou M, Tzala E, Boletis J, Zakopoulou N, Loutradi A, Maliori M, et al. Hepatitis E virus infection in individuals at high risk of transmission of non-A, non-B hepatitis and sexually transmitted diseases. Scand J Infect Dis. 1996 Jan;28(5):443-5.
34. Khuroo MS, Kamili S, Yattoo GN. Hepatitis E virus infection may be transmitted through blood transfusions in an endemic area. J Gastroenterol Hepatol. 2004 Jul;19(7):778-84.
35. Irshad M, Peter S. Spectrum of viral hepatitis in thalassemic children receiving multiple blood transfusions. Indian J Gastroenterol. 2002 Sep-Oct;21(5):183-4.
36. Widdowson MA, Jaspers WJM, Van der poel WHM, Verschoor F, Husman AM, Winter HL, et al. Cluster of cases of acute hepatitis associated with hepatitis E virus infection acquired in the Netherlands. Clin Infect Dis. 2003 Jan;36(1):29-33.
37. Pourahmad M, Sotoodeh AR, Nasiri H. Hepatitis E Virus infection in hemodialysis patients: seroepidemiological survey in Jahrom, southern Iran. Hepat Mon. 2009 Sep;9(3):232-235.
38. Meky FA, Stoszek SK, Abdel-Hamid M, Selim S, Abdel-Wahab A, Mikhail N, et al. Active surveillance for acute viral hepatitis in rural villages in the Nile Delta. Clin Infect Dis. 2006 Mar;42(5):628-33.
39. Zhao ZY, Ruan B, Shao H, Chen ZJ, Liu SL. Detection of hepatitis E virus RNA in sera of patients with hepatitis E by polymerase chain reaction. Hepatobiliary Pancreat Dis Int. 2007 Feb;6(1):38-42.
40. Gao DY, Peng G, Zhu JM , Sun L, Zheng YJ , Zhang J . Investigation of sub-clinical infection of hepatitis E virus in blood donors. Zhonghua Gan Zang Bing Za Zhi. 2004 Jan;12(1):11-2.