«Original Article»

Study on the seroprevalence of hepatitis E virus infection in pregnant women referring to Imam Khomeini general hospital in Ahvaz

Mojtaba Rasti[1], Alireza Samarbafzadeh[2], Niloofar Neisi[3*], Manoochehr Makvandi[4], Saeed Najafifard[5], Moosa Sharifat[6], Mahvash Zargar[7]

1-M.Sc. of Virology, Health Research Institute, Infectious and Tropical Diseases Research Center, Department of Virology, Faculty of Medicine, Jundishapur University of Medical Sciences, Ahvaz, Iran.
2-Associated Professor of Virology, Health Research Institute, Infectious and Tropical Diseases Research Center, Department of Virology, Faculty of Medicine, Jundishapur University of Medical Sciences, Ahvaz, Iran.
3-Ph.D. Student of Virology, Health Research Institute, Infectious and Tropical Diseases Research Center and Research Institute for Infectious Diseases of Digestive System, Deptartment of Virology, Faculty of Medicine, Jundishapur University of Medical Sciences, Ahvaz, Iran.
4-Professor of Virology, Health Research Institute, Infectious and Tropical Diseases Research Center and Research Institute for Infectious Diseases of Digestive System, Deptartment of Virology, Faculty of Medicine, Jundishapur University of Medical Sciences, Ahvaz, Iran.
5-M.Sc. of Virology, Health Research Institute, Infectious and Tropical Diseases Research Center, Department of Virology, Faculty of Medicine, Jundishapur University of Medical Sciences, Ahvaz, Iran.
6-B.Sc. of Laboratory Sciences, Department of Pharmacology, Faculty of Medicine, Jundishapur University of Medical Sciences, Ahvaz, Iran.
7-Assistant Professor of Obstetrics and gynaecology, Department of Obstetrics and Gynaecology, Imam Khomeini Hospital, Faculty of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.
*Corresponding author:
Niloofar Neisi; Ph.D. Student of Virology, Health Research Institute, Infectious and Tropical Diseases Research Center and Research Institute for infectious Diseases of Digestive System, Department of Virology, Faculty of Medicine, Jundishapur University of Medical Sciences, Ahvaz, Iran.
Tel:+986113738313
Email: niloofarneisi@yahoo.com

Abstract

Background: Regarding to fecal- oral transmission of hepatitis E virus and risk of fulminant hepatitis in the third trimester of pregnancy, the aim of the present study was to determine seroprevalence of HEV in pregnant women with regard to age, level of education, trimester of pregnancy and residency.

Material and methods: A total of 418 serum samples were collected from January 2010 to January 2011. All pregnant women filled out the questionnaire form. Serum samples were examined for anti-HEV IgG and anti- HEV IgM using ELISA method.

Results: From 418 women, 22 cases were positive for anti-HEV IgG (5.26%) and in one woman (0.23%) anti- HEV IgM was positive. In the age groups of 30-40 and 20-30 years, the seropositivity for anti-HEV IgG was 8.6% and 2.5%, respectively. In group with higher age the positive cases of anti-HEV IgG was higher than in the other group. The rate of positivity of anti-HEV IgG in pregnant women with low level of education was 11.4% whereas 3% in university educated women. There was a significant difference between seropositivity of anti-HEV IgG and the trimester of pregnancy. The most of anti-HEV IgG positive were occurred in the third trimester of pregnancy (8.6%).Out of this 22 anti-HEV IgG positive cases 4.4% were living in urban and 6.3% were in rural areas.

Conclusion: The present results showed that there is a direct relation between age, lower levels of education and trimester of pregnancy with the seroprevalence of HEV.

Keywords: Seroprevalence, Hepatitis E virus, Pregnant women, Ahvaz

Introduction

Hepatitis E virus (HEV) recently classified in *hepeviridae* family and *hepevirus* genus (1). The genome of the virus is single stranded positive sense RNA (7.5 kb) (1). Hepatitis E virus is associated with fecal contamination of drinking water (2). The virus leads to acute viral hepatitis in the adults, fulminant hepatitis in men and in pregnant and non-pregnant women (3). The high rates of mortality (20%-30%) are observed in third trimester of pregnant women as a result of fulminant liver disease (4). Malnutrition and suppression of immune system in pregnancy have been postulated to be the contributing factors (5). Diagnosis of HEV infection can be occur by either detection of viral particles in stool by electron microscopy, detection of anti-HEV Ab in serum by ELISA or detection of viral genome by PCR. Viral shedding of HEV in stool continues two weeks after the unset of jaundice, but Ab against HEV is detectable in all patients after presentation of the illness (6). IgM anti-HEV is found during the early acute phase of disease and may be detected for 4 days after the onset of jaundice and lasts for up to five months. The following of IgM anti-HEV,the level of IgG anti-HEV rises, so that both seem to appear almost simultaneously in the acute phase of infection. IgG anti-HEV persists for a longer time and may be detectable for 1–14 years (7).

The prevalence of HEV in under developed countries is different (varies from 7.2% to 24.55%). In Iran, surveys on various populations showed that the prevalence of HEV is 7.8% to 30.8 (9 and 11). Similar studies in Iran indicated that the rate of anti- HEV IgG was 12.2% in blood donors (10), 30.8% in renal transplant recipients (11) and 8.5% in children (12). The seroprevalence of HEV in pregnant women is not similar in different countries: India: 3.63% (13), Turkey: 12.6% (14) and United Arab Emirates: 20% (15). In Gorgan city (north of Iran), the seroprevalence of HEV in pregnant women has been 7.4% (16,17). In endemic regions, the age range of the HEV patients is 15-40 years old (17,18,19). Due to contamination of drinking water in Ahvaz and fecal-oral route of transmission of the virus and importance of hepatitis E virus in pregnancy, this study was aimed to investigate the seroprevalence of virus in Ahvaz, southwest of Iran, in pregnant women.

Material and methods

A total of 418 serum samples were collected from january 2010 to january 2011. In this cross sectional study the mean age of pregnant women was 30 ± 10. Pregnant women were questioned about their age, trimester of pregnancy, level of education, residency and history of hepatitis to fill out the questionnaire forms. Women with HBsAg+, HCVAb+, HDVAg+, acute fatty liver of pregnancy, drug induced jaundice, were excluded from the study. Inclusion criteria were pregnant women in whom pregnancy was confirmed by gynecologist(14).

Serology

For the seroprevalence study, blood samples were taken from women volunteers and sera were separated and kept at $-20^\circ C$ until analysis. All samples were examined for qualitative HEV total Ab using an Elisa kit according to the manufacturer's instructions (Diapro, Italy). The sensivity and specifity of kit was 95% and 99% respectively. Serum samples showing a cut off value greater than one were positive and lower than 1 were determined to be negative.

Statistical analysis

Data are shown as mean±S.E.M. Statistical analysis was performed by Chi-square and fisher exact tests. Significance was set at a $P<0.05$ level.

Results

Serum samples of 418 pregnant women were evaluated for serological test. From these women, 22 cases were positive for

anti-HEV IgG (5.26%) and one woman (0.23%) for anti- HEV IgM. Of these 22 samples, the age of 16 women were 30-40 and 6 cases were 15-30 years old. The results showed a direct relation between age and anti-HEV IgG; so that the number of positive cases of IgG in group 30-40 years old was significantly higher than in 20-30 years old group (P<0.005). Also one case with anti-IgM positive was in the 20-30 years old group. There was a direct relation between the number of positive cases and level of education. The results showed that the anti-HEV IgG positive pregnant women with lower education levels was higher than in higher educated women (P<0.001, Table 1).The another analysis was done to determine the relation between the number of positive cases with trimester of pregnancy. The number of positive cases varied in different periods of pregnancy; So that most of the antibody-positive cases were observed in the third trimester (8.6%) (Table1). There was no association between residency of pregnant women (urban and rural areas) and the positive number of anti-HEV IgG (Table 1).

Table1. Seroprevalence of the anti-HEV IgG on the basis of age, level of education, trimester of pregnancy and residency (n=418)

	IgG(+)	IgG(-)	%
Age			
20-30	6	231	2.5
30-40	16[*]	195	8.6
Trimester			
First	*5*	*80*	*5.9*
Second	*1*	*146*	*0.7*
Third	16	170	8.6
Residency			
Urban	10	219	4.4
Rural	12	177	6.3
Level of education			
Under educated	13	101	11.4
Higher educated	9	295	3

[*]P<0.005 V.S. 20-30 years old; P<0.01 V.S. other trimesters and   P<0.001 V.S. higher educated pregnant women.

Discussion

Hepatitis E virus, an infectious agent, cause to acute hepatitis in endemic regions and poor hygienic countries. High rate of morbidity and mortality of HEV in pregnant women (especially in the third trimester of pregnancy) resulted from fulminant hepatitis (18,20,21). Measurement of anti-HEV IgG against hepatitis E virus indicates past exposure to the virus (13). Our study showed that the rate of anti-IgG against hepatitis E virus was 5.26%. The seroprevalence of HEV in similar studies was 33.67% in India (13), 12.6% in Turkey (14) and 20% in United Arab Emirates (15). In one study in Gorgan, north of Iran, the seroprevalence of hepatitis E virus in pregnant women was 7.36%. These results are close to the results of the present study (16).

These results conducted that the seroprevalence of anti-IgG is variable in different country depending on the endemicity of virus, economic income, age, level of hygiene and other risk factors (9). Our findings showed the seroprevalence of hepatitis E virus in the age range of 30- 40 years was higher than in 20- 30 years old. Therefore, it seems that the higher age of pregnancy is as a risk factor for hepatitis E virus infection.

Gorgans study was also showed there is a direct relation between age and HEV prevalence (16). In similar study in Turkey anti-HEV IgG in pregnant women under the age of twenty years was 3.7% and in group with higher age was 33% (14). These findings are in agreement with the results of this study and suggest that there is a relationship between gestational age and the seroprevalence of HEV.

Our results demonstrated higher educated women had lower antibody levels than in under educated women. It seems to be higher educated women have enough knowledge in preventing of fecal- oral disease such as HEV infection and other enteric disease. Other researchers have been reported that higher education reduces the risk of enteric diseases. So that in Gorgan's study the difference in higher educated and under educated women was significant (17). In Turkey 13.8% of higher educated pregnant women had positive anti-HEV IgG but in under educated pregnant women this number was 24% (14). Consistent with these results, our findings showed that the most positive cases was seen in the third trimester (8.6%). Since, women in the third trimester of pregnancy are at higher risk of mortality and morbidity and the results of the present study showed the highest rate of seropositive cases are seen in the third trimester of pregnancy; so that considering to this point that these women have higher exposure to the virus is important (4).

According to table1, the seroprevalence of hepatitis E in rural pregnant women was lower than in urban women. It was anticipated that hepatitis E virus is more prevalent in the rural population as a result of water pollution but the results of this study was in contrast. The possible cause is more pollution of monucipal water with hepatitis E virus due to the overflow of sewage in drinking water. As respects to

Ahvaz city is in tropical region and transmission of hepatitis E infection through polluted drinking water in these regions is high; unfortunately overflow of sewage from homes, factories, hospitals … in Karoon river, natural source of drinking water in Ahvaz, leading to increased pollution of city piped water. Thus, exposure of individuals with variety of infectious agents that transmitted via oral – fecal route (for example: hepatitis E) has been very high (10).

In conclusion, we showed that seroprevalence of HEV increases with age, low level of education, third trimester of pregnancy. According to oral – fecal route transmission of hepatitis E infection, it seems that overflow of sewages in source of drinking water "Karoon river" can be considered as a major cause of infection with enteric viruses such as hepatitis E virus. Also noting that in our study high rate of anti-HEV IgG was seen in third trimester of pregnancy and these women are at higher risk than in other periods of pregnancy; so that attention to hygiene, individual health education and decontamination of drinking water is very important. Finally, according to information obtained from this study and with regard to researchers findings of neighboring countries (13-15) that some of which are endemic for the virus (13). Assessment and screening of pregnant women for hepatitis E infection especially in the third trimester of pregnancy need to be more attention.

References

1-Ahn JM, Kang SG, Lee DY, Shin SJ, Yoo HS. Identification of novel human hepatitis E Virus (HEV) Isolates and determination of the Seroprevalence of HEV in Korea. J Clin Microbiol 2005;43(7):3042-8.

2-Escribà JM, Nakoune E, Reico C, Massamba PM, Matsika-Claquin MD, et al. Hepatitis E, Central African Republic. Emerg Infect Dis 2008; 14(4): 681–3.

3-Banait VS, Sandur V, Parikh F, Murugesh M, Ranka P, Ramesh VS, et al. Outcome of acute liver failure due to acute hepatitis E in pregnant women. Indian J Gastroenterol 2007;26(1):6-10.

4-Kumar S, Ratho RK, Chawla YK, Chakraborti A. Virological investigation of a hepatitis E epidemic in North India. Singapore Med J 2006;47(9):769-73.

5-Beniwal M, Kumar A, Kar P, Jilani N, Sharma JB. Prevalence and severity of acute viral hepatitis and fulminant hepatitis during pregnancy: a prospective study from north india. Indian J Med Microbiol 2003;21(3):184-5.

6-Zaki Mel S, Salama OS, Mansour FA, Hossein S. Hepatitis E virus co infection with hepatotropic viruses in Egyptian children. J Microbiol Immunol Infect 2008;41(3):254-8.

7-Khudyakov Y, Kamili S. Serological diagnostics of hepatitis E virus infection. Virus Res 2011;161(1):84-92.

8-Smith JL. A review of hepatitis E virus. J Food Prot 2001;64(4):572–86.

9-Alavian SM. Fallahian F, Bagheri Lankarani K. Epidemiology of Hepatitis E in Iran and Pakistan. Hepat Mon 2009;9(1):60-5.

10-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;12(4):387-90.

11-Rostamzadeh Khameneh Z, Sepehrvand N, Masudi S. Seroprevalence of Hepatitis E among Iranian Renal Transplant Recipients. Hepat Mon 2011;11(8):646-51.

12-Shamsizadeh A, Nikfar R, Makvandi M, Shamsizadeh N. Seroprevalence of Hepatitis E Virus Infection in Children in the Southwest of Iran. Hepat Mon 2009;9(4):261-4.

13-Begum N, Devi SG, Husain SA, Kumar A, Kar P. Seroprevalence of subclinical HEV infection in pregnant women from north India: A hospital based study. Indian J Med Res 2009;130:709-13.

14-Cevrioglu AS, Altindis M, Tanir HM, Aksoy F. Investigation of the incidence of hepatitis E virus among pregnant women in Turkey. J Obstet Gynaecol Res 2004;30(1):48–52.

15-Kumar MR, Uduman S, Rana S, Kochiyil JK, Usmani A, Thomas L. Sero-prevalence and mother-to-infant transmission of hepatitis E virus among pregnant women in the United Arab Emirates. Eur J Obstet Gynecol Reprod Biol 2001;100(1):9-15.

16-Tabarraei A, Moradi A, Rodgari D, Javid N, Bakhshandeh Nosrat S. Anti-Hepatitis E Virus seroprevalence in pregnant women, in Gorgan, Iran, North East of Caspian Sea. Proceedings of the International Conference on Life Science and Technology; 2011.

17-Al-Azmeh J, Frösner G, Darwish Z, Bashour H, Monem F. Hepatitis E in Damascus. Infection 1999;27(3): 221-3.

18-Mushahwar IK. Hepatitis E virus: molecular virology, clinical features, diagnosis, transmission, epidemiology, and prevention. J Med Virol 2008;80(4):646-58.

19-Davari Dehkordi N, Ahmadi M, Amoozgari Z, Rasekh A. The relationship between the serum zinc levels of pregnant mothers and their infants' birth weight in Imam Khomeini hospital of Ahvaz in 2010 Jentashapir J Health Res 2012; 3(3): 409-15.

20-Habibian A, Makvandi M, Samarbaf-zadeh AR, Neisi N, Ranjbari N. Epstein-Barr Virus DNA frequency in paraffin embedded tissues of Non-Hodgkin lymphoma patients from Ahvaz, Iran. Jentashapir J Health Res 2013;4(4): 315-20.

21-Parhizgari N, farajzadeh Sheikh A, Sadeghi P. Identification of bacteria isolated from mobile phone of three medical and teaching hospital staff in Ahvaz. Jentashapir J Health Res 2013;4(5):397-403.