

Seroprevalence of hepatitis E virus among blood donors in tertiary care center of north Gujarat

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Abstract

Introduction: Hepatitis E virus (HEV) is a RNA virus having single strand and spread mainly through contaminated water and food as well as through parenteral route. Very few study has been carried out in India in general public as well as voluntary blood donor to determine HEV prevalence. The prevalence of anti-HEV in India is limited and the results differ depending on the type of population, location and serological test used in the studies.

Materials and Methods: Samples from 1345 voluntary blood donations were tested in the period between November 2014 to December 2017. Samples were tested for the presence of antibody against HEV.

Results: The study population which composed of 1280 male & 65 Female voluntary blood donors. Age of study group ranged from 18 to 60 years with a mean age of 32.48 years. Overall, the harmony among the three ELISA was 92.6% corresponding to a prevalence rate of 2.75% (37/1345). The lowest anti-HEV antibody prevalence values were seen in the younger age groups while the highest prevalence rates were found in the higher age group. No significant variation in anti-HEV antibody prevalence was noticed between genders.

Conclusion: Although hepatitis E is transmitted by fecoral route, seroprevalence of anti-HEV antibody among blood donors need to be addressed using available ELISA test or Polymerase chain reaction. Blood banks in India and other developing country should consider screening for HEV, especially when blood transfusion is given to patients with low immunity or women having pregnancy.

Keywords: Hepatitis E, Blood donor, Seroprevalence.

Introduction

Hepatitis E virus infection is caused by a spherical non enveloped virus, with a single stranded RNA genome. The surface of the virus shows indentations and spikes. The virus is labile in external environment. Physically and morphologically it resembles the Norwalk virus. Carrier state has not been observed. In vitro cultivation of HEV has not been successful. The viral genome has been cloned.

The incubation period ranges from 2 to 9 weeks with an average of six weeks. Most cases occur in the young to middle aged adults (15-40 years old). The disease is generally mild and self limited, with a low case fatality of about one percent. A unique feature is the clinical severity and high case fatality rate of 20-40 percent in pregnant women, especially in the last trimester of pregnancy.

HEV strains are categorized into five major genotypes, with same serotype. Genotypes differ with respect to host species and epidemiological distribution. Genotypes 1 and 2 infect only humans and are endemic in many parts of Asia, Africa and South America. Genotypes 3 and 4 infect humans, pigs and other animal species. Genotype 3 causes sporadic cases of an acute hepatitis in North and South America, Europe and Asia whereas genotype 4 is essentially restricted to Asia. Genotype 5 infects avian species.^{5,6} Comparison of

virus strains from different areas indicates that only on serotype of the virus exist.

Viral hepatitis E was found to be prevalent only in socioeconomically underdeveloped countries. Sporadic cases as well as large epidemic due to the food and water contamination have been reported. In winter season of year 1955-56 largest epidemic occurred in New Delhi affecting over 30,000 persons within 6 weeks. Unless investigated by proper serological test HEV infection can easily be misdiagnosed as Hepatitis A. Recently, increasing numbers of HEV-infected patients with no history of travelling have been found in industrialized countries. Hepatitis E virus cases may be caused by consumption of contaminated meat or through exposure to animals infected with HEV.¹ The recent data of HEV viraemic blood donors in various country should raise concern about safe blood transfusion.²⁻⁴

Hepatitis E virus is not a cause for chronic hepatitis in developed as well as developing countries. Chronic hepatitis E in immunodeficient hosts and some cases of transfusion-transmitted HEV infections have been described.² Due to lower level of symptomatic cases and higher cost of diagnosis variation in the prevalence of HEV antibodies in different set of region has been reported. Developed countries have high seroprevalence rates than expected and show variation not only from nation to nation, but also in the same country. The

variable sensitivities and specificities of the serological test may be the cause for this variability.⁵

Very few study has been carried out in India in general public as well as voluntary blood donor to determine HEV prevalence.⁶⁻⁸ The studies conducted on HEV in recent times in India have focused on epidemiological data. For blood safety of donor HEV seroprevalence study was conducted in blood donors at our center. HEV infection in India is sporadic and the results differ among different population, location and serological test used in the studies.⁹⁻¹² Objective of present study was to assess the prevalence of hepatitis E among healthy voluntary blood donors.

Materials and Methods

1345 volunteer blood donors from tertiary care center of North Gujarat were selected for blood sample testing after explaining about the study and proper consent is taken. Details history is taken from blood donor about age, sex, occupation, residence, any relevant history for blood transfusion related disease. All samples from 1345 volunteer blood donor were analysed for presence of HEV antibody with three different, enzyme-linked immunosorbent assays. Retesting is done in positive patient and also correlation with history is done. All donor samples were also tested for elevation of serum enzyme of liver e.g. Serum Alanine transaminase. HEV-specific antigens from all human HEV genotypes is tested in first antibody assay; Genotypes 1, 2 and 3 are analyzed in another method from recombinant HEV antigen. Total HEV antibodies using recombinant HEV-specific virus-like particles are tested in third method. Manufacturers' instructions were followed for all tests.

Appropriate statistical test by available software is applied and based on that results were analysed.

Results

The 1345 blood donors were studied in tertiary care centre of north Gujarat and 1280 male and 65 female. (95% male, 5% female). Their average age at the time of blood donation was 40 years (range, 18–60 years).

Forty five of the 1345 blood donors (3.34%) tested positive for anti-HEV immunoglobulins G (IgG) with assay 1 while 42 (3.12%) tested positive with assay 2 ($p=n.s.$). Anti-HEV antibody prevalence detected by assay 3 was 76 (5.65%), which was apparently higher than the prevalence detected by the remaining two assays ($p<0.05$). Out of 76 plasma samples found to be positive by assay 3, 37 were positive by both the other two tests, 11 were positive either by assay 1 or 2, whereas only 28 were confirmed positive by assay 3 only (Table 1).

Overall, the harmony among the three ELISA was 92.6% (37 positive and 1209 negative results), corresponding to a prevalence rate of 2.75% (37/1345). The agreement between at least two assays was 98.6%.

The concordance was 97.2% (1308/1345) between assays 1 and 2, 93.7% (1260/1345) between assays 1 and 3 and 93.2% (1253/1345) between assays 2 and 3 (Fig. 1).

As shown in Fig. 2, we have found an age-related variation in the prevalence of anti-HEV antibody with all three tests performed. The lowest anti-HEV antibody prevalence values were seen in the younger age groups while the highest prevalence rates were found in the oldest age groups. No significant variation in anti-HEV antibody prevalence was noticed between genders.

The study population which composed of 1280 male voluntary blood donors and their age ranged from 18 to 60 years with a mean age of 32.48 years. The donors were stratified on the basis of age into three groups: 856 (63.6%) from 18 to 30 years, 254 (18.9%) from 31 to 40 years and 235 (17.5%) from 41 to 60 years.

Table 1: Anti-HEV results obtained by three different ELISA used to determine the prevalence among blood donors

Anti-HEV result	Assay 1 n (%)	Assay 2 n (%)	Assay 3 n (%)
Positive	45(3.34%)	42(3.12%)	76(5.65%)
Negative	1300 (96.6%)	1303(96.8%)	1266(94.1%)
Equivocal	0	0	3
Total	1345 (100%)	1345 (100%)	1345 (100%)

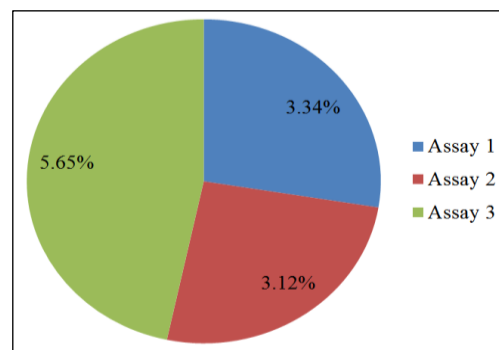
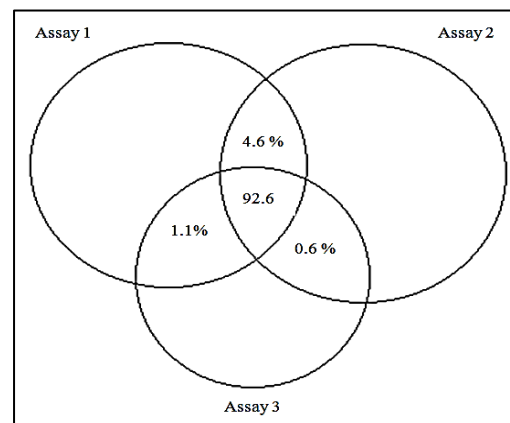


Fig. 1: Concordance among all results obtained by three ELISA for anti HEV



Concordance between at least two test – 98.8 %
Assay 1 & 2= 97.2%; Assay 2 & 3 = 93.2; Assay 1 & 3= 93.7

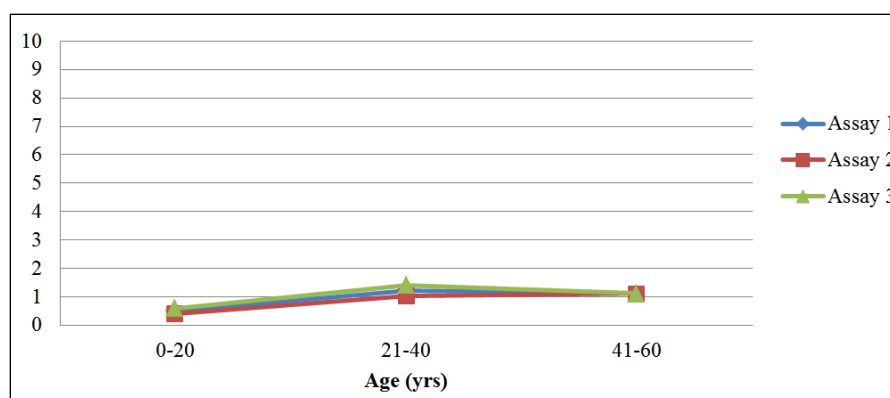


Fig. 2: Prevalence of anti-HEV, detected by three ELISA, among blood donors according to age groups.

Discussion

In this study, we evaluated the anti-HEV antibody prevalence in blood donors in north Gujarat of India using three different ELISA kit and we obtained an overall anti-HEV prevalence of 2.75% when considering aggregate results for all three tests. However, individual percentages of anti-HEV antibody positivity were 3.34, 3.12 and 5.65%, respectively. In our study, we therefore, confirm the variability in anti-HEV seroprevalence depending on the different ELISA kit used, as previously observed in study done in Denmark (10.7% vs 19.8%)¹³ and Spain (10.7% vs 19.96%).¹⁴

The anti-HEV seroprevalence in our study population was slightly lower than in other region blood donors.

The seroprevalence in our study is comparable with that of Switzerland.²³ The study conducted among 200 blood donors in Pune, India has shown HEV RNA prevalence of 1.5%.¹⁶ One study carried out at another center from India shows anti-HEV IgM seroprevalence of 4.78%, which is comparable to our study. Increase seroprevalence observed in our study may be due to the larger sample size (n = 460). Asian subcontinent countries such as Japan, China, Philippines and Korea have higher seroprevalence. Most of the subjects under our study belonged to areas of proper sanitation facilities which may be responsible for lower seroprevalence. HEV infection in other Asian countries like China, Japan, Vietnam and Philippines is mainly animal origin transmitted spread by non vegetarian food product and in developing countries through contaminated water, which may reflect the differences in seroprevalence in different countries. Difference of seroprevalence among various countries may be due to different test methodology selected of HEV. Lower seroprevalence in our study may due to wide variation in of risk factors such as work pattern, hobbies, diet, and social status.

While comparing above results with data collected in the same population from the same country, we noted that several studies conducted in India on blood donors have already shown large differences in anti-HEV

seroprevalence especially according to different area and different immunoenzymatic assay done. In another study on HEV seroprevalence carried out in central Italy, 49% of the tested blood donors were anti-HEV IgG-positive using the HEV IgG Wantai.¹¹ Lower rates have been observed in southern Italy (1.3%)¹⁰ and Sardinia (5%)⁹ using the HEV IgG Dia.Pro.

In harmony with all the mentioned studies, we found no difference in anti-HEV prevalence between genders and an increase of anti-HEV positivity with age. Our finding of 92.6% concordance among the three ELISA used in this study is low. This value, which cannot be compared with those of other similar reports, suggests the importance of standardising serological diagnostic tests for HEV.

Thus, in the absence of standardized commercially available confirmatory assays such as Western blot, differences in seroprevalence rates between different populations must be interpreted with caution.

Conclusions

As compared to Hepatitis A, B & C, Hepatitis E infection is not a major public health problem in India. However, the prevalence of anti-HEV antibody in blood donors in our study is lower than expected, suggesting that the prevalence is less in our country. HEV seroprevalence greatly varies, in same country and also between different country and the population studied and assay used in HEV detection. Standard immunoenzymatic assay (ELISA), avoiding variability in terms of sensitivity and specificity, is required. Currently HEV screening is not required as per our study if proper history is taken before blood collection. Also cost of testing is another hindrance to do HEV screening in all blood donor.

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