Hepatitis E Virus Seroprevalence Among Blood Donors in Bushehr, South of Iran

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Abstract
Background: Although so far several studies have determined the hepatitis E virus (HEV) prevalence in some parts of Iran, no data exists regarding the HEV seroprevalence in Bushehr province as the southernmost point in Iran yet.
Objectives: The aim of this study was to evaluate the seroprevalence of anti-HEV IgG among the blood donors in Bushehr.
Patients and Methods: A total of 628 blood donor samples were collected from September to October 2013, after obtaining informed written consents, and analyzed for the presence of anti-HEV IgG using commercial HEV enzyme-linked immunosorbent assay (ELISA) kit. All the samples were tested by two ELISA kits and evaluated for liver function test.
Results: Overall, 105 (16.7%) blood samples were positive for HEV-specific-IgG antibodies, while 523 (83.8%) were negative. The presence of anti-HEV IgG was not associated with gender; however, it was correlated with age. It was indicated that the anti-HEV prevalence increases by age and there was a significant difference between the age groups regarding HEV seropositivity.
Conclusions: High HEV seroprevalence (16.7%) was observed among the blood donors in Bushehr province. It appears that exposure to HEV increases with age; although, more people should be examined.

Keywords: Hepatitis E Virus, Seroepidemiological Studies, Enzyme-Linked Immunosorbent Assay, Blood Donors, Iran

1. Background
Hepatitis E virus (HEV) infection is commonly an acute hepatitis infection caused by a non-enveloped, single-stranded RNA virus belonging to genus Hepeviridae (1). This virus remains infectious in sewage; therefore, it can be transmitted by fecal-oral route, especially faeces-contaminated water in developing countries (1, 2).
Blood transfusion and zoonotic HEV infection have a role in the spread of the virus in developed countries where sporadic cases of HEV infection have been reported (3). There is some evidence suggesting that persons who receive blood from HEV infected blood donors experience acute hepatitis after blood transfusion (4). This virus has infected one-third of the world population (5). The clinical symptoms of HEV infection are acute, self-limited hepatitis in healthy individuals (6). Pregnant women and patients with underlying liver disease are at high risk of fulminant and fatal HEV infection (1, 7-9).

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3. Patients and Methods

This study was approved by the Ethics Committee of Bushehr University of Medical Sciences and Bushehr Blood Transfusion Organization to estimate the presence of HEV in voluntary healthy blood donors. Based on previous studies and the reported prevalence (11.5%) in other areas in southwest of Iran (2) as well as the confidence level of 95% and an estimated error of 2.5%, the required sample size was 626. In the present study, 628 anonymized blood samples during a cross-sectional study were collected from Iranian Blood Transfusion Organization from September to October 2013. Blood samples were collected after completing the standard questionnaires (11) and obtaining the formal written consent of Bushehr University of Medical Sciences. All the samples were analyzed for IgG antibody against HEV. The presence of anti-HEV antibody in human sera was tested by a commercial enzyme-linked immunosorbent assay (ELISA) kit (HEV IgG, Pasto, Iran) according to the manufacturer's instructions. All of the reactive samples were analyzed by liver functional tests including albumin, bilirubin, serum glutamic oxaloacetic transaminase (SGOT), and serum glutamic pyruvic transaminase (SGPT) to determine acute HEV infection and were rechecked by Second ELISA kit (HEV IgG/IgM; DIA.PRO Srl, Milan, Italy). All the samples were negative for HIV-antibody (Ab), hepatitis B surface antigen (HBs-Ag), and hepatitis C virus antibody (HCV-Ab).

3.1. Statistical Analysis

All the statistical analyses were carried out by SPSS 16 program (SPSS Inc., Chicago, IL, USA). Descriptive indices, chi-squared and t-test were also used to analyze the data. P value < 0.05 was considered as the significance level.

4. Results

A total of 628 blood donors participated in this study; 598 (95.2%) were male and 30 (4.8%) were female with a mean age of 36.3 years (ranging from 19 to 65 years). Of the 628 blood donors, 76 (12.1%) were first-time donors, 450 (71.7%) were regular donors, and others (16.2%) had a record of donation; 401 (63.9%) donors were younger than 40, while 220 (35%) were between 40 - 60 years old and 7 (1.1%) were older than 60 years. General characteristics of all the donors are summarized in Table 1. All the donors were normal for liver function tests which indicated the absence of acute hepatic infection. With regard to age, anti-HEV IgG antibodies were positive in 14 (3.5%) in the group younger than 40, 86 (39.1%) in the group 40 - 60 years, and 5 (71.4%) in the group older than 60 years. Therefore, it indicated that the anti-HEV prevalence increased by increase of age and there was a significant difference between the age groups regarding HEV seropositivity ($P = 0.001$). Regarding the analysis of the subjects according to gender, 100 (16.7%) in the male group and 5 (16.7%) in the female group were positive for anti-HEV IgG antibodies. However, the difference between males and females was not significant ($P = 0.614$). Overall, 105 blood samples (16.7%) showed positive HEV-specific-IgG antibodies while 523 (83.8%) donors were negative (Table 1).

5. Discussion

Anti-HEV IgG antibody is a demonstrator of past infection and can be used for studying the HEV epidemiology. HEV prevalence has been determined in different parts of Iran which is considered as an endemic country for HEV infection (4, 6). However, there are no documented data regarding the HEV prevalence in Bushehr province. Therefore, we measured the anti-HEV seroprevalence among healthy blood donors in Bushehr and noticed a prevalence of 16.7%, which was higher than what was reported among Iranian blood donors (Table 2).

### Table 1. Results of Anti-Hepatitis E Virus Reactivity in Blood Volunteers in South of Iran$^{a,b}$

| Variables | All Donors | HEV-Negative | HEV-Positive |
|-----------|------------|--------------|--------------|
| Overall seropositivity | 628 | 523 (83.3) | 105 (16.7) |
| Gender | | | |
| Male | 598 (95.2) | 498 (83.3) | 100 (16.7) |
| Female | 30 (4.8) | 25 (83.3) | 5 (16.7) |
| Age, y | | | |
| < 40 | 401 (63.9) | 387 (95.5) | 14 (3.5) |
| 40 - 60 | 220 (35) | 134 (60.9) | 86 (39.1) |
| > 60 | 7 (1.1) | 2 (28.6) | 5 (71.4) |

$^a$Abbreviation: HEV, hepatitis E virus.
$^b$Values are presented as No. (%).
The HEV seroprevalence among the general populations of developed countries is low (0.4% - 3.9%) (6). According to our results, a high HEV seroprevalence rate of 16.7% was observed among volunteer blood donors in Bushehr province, which was higher than those obtained among the blood donors in Switzerland (4.9%) (9), Brazil (2.3%) (16), and France (3.2%) (17). However, it was less than the reported values of blood donors in China (27.42% and 32.60%) (18, 19), Saudi Arabia (18.7%) (20), and The Netherlands (27%) (21).

We noticed that the HEV seroprevalence increased with age and there was a significant association between age and higher HEV prevalence. This finding agrees with a similar study in Isfahan, Iran, which showed that HEV seropositivity increased with age from 0.9% in children to about 8% in subjects aged over 50 years (22). Seropositivity was 3.5% in people aged below 40 years and 71.4% in people over 60 years old. In the present study, no association between gender and HEV seroprevalence was detected and none of the studied samples were positive for HIV, HBV, and HCV infectious markers. Similar results were reported by most other studies (4, 6, 9, 21).

In conclusion, the high HEV seroprevalence of 16.7% was observed among the blood donors in Bushehr province, Iran. According to our results, we came to this conclusion that Bushehr province is an endemic area for HEV infection. It appears that exposure to HEV increases with the increase of age; although, more people should be examined. Epidemiological information regarding HEV prevalence is important in evaluating the safety of blood products. However, further studies are needed to assess this matter with studying more populations and considering similarity of numbers of each studied group according to gender and age.

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Footnotes
Authors’ Contribution: Gholamreza Khamisipour: design and managing the project, editing, and preparing the initial draft; Behrouz Naeimi: implementation of study and editing; Farnaz Mazloom Karimian and Alireza Mankhian: performing the tests; Faramraz Kooshesh and Masoud Azimzadeh: collecting the samples and preparing the questionnaire; Ali Akbar Pourfartolah and Samad Akbarzadeh: editing the paper; Gholamreza Hajiani: financial and technical support in blood transfusion center.

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