

# Hepatitis E Virus and Serum Level Aminotransferases in Blood Donors

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## 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,

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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  $\pm$  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  $35.42 \pm 9.38$ . 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 26.9%	113 25%	120 25%
26 to 35	7 26.9%	101 22.3%	108 22.6%
36 to 45	11 42.3%	183 40.5%	194 40.6%
46 to highest	1 3.8%	55 12.2%	56 11.7%
<b>Total</b>	<b>26</b> <b>100%</b>	<b>452</b> <b>100%</b>	<b>477</b> <b>100%</b>

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

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

## 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)

Liver enzymes	IgG			IgM		
	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

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