



# Seroprevalence and Risk Factors of Hepatitis E in Eastern Iran

Zohreh Azarkar<sup>1</sup>, Azadeh Ebrahimzadeh<sup>1,\*</sup>, Gholamreza Sharifzadeh<sup>1</sup>, Masood Ziaee<sup>1</sup> and Mohammad Fereidouni<sup>2</sup>

<sup>1</sup>Infectious Diseases Research Center, Birjand University of Medical Sciences, Birjand, Iran

<sup>2</sup>Asthma, Allergy and Immunology Research Center, Birjand University of Medical Sciences, Birjand, Iran

\*Corresponding author: Infectious Diseases Research Center, Birjand University of Medical Sciences, Ghafari Avenue, Birjand, Iran. Tel: +98-9153613525, E-mail: mri44556677@gmail.com

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## Abstract

**Background:** Hepatitis E infection is one of the most common causes of acute hepatitis. It is caused by the RNA virus of the heptamegaly viridae family, which is transferred through stool in contaminated water. Cases of infection are most prevalent in developing countries.

**Objectives:** This study was conducted to investigate the seroprevalence of hepatitis E among urban adults. The reason was the current lack of information on the hepatitis E prevalence among the general population in the city of Birjand in eastern Iran. This information is necessary because Southern Khorasan is in close proximity to Afghanistan.

**Methods:** In this cross sectional study, 522 participants aged over 17 years were selected from the city of Birjand, eastern Iran, using the random cluster sampling. The participants completed a researcher-made questionnaire that included demographic characteristics, risk factors for infectious diseases such as records of blood transfusions, specific exposures, intravenous drug abuse, recent diagnosis or a history of liver disease, and other medical information. After selection, a blood sample was taken from each participant to a volume of 5 cc. Each blood sample was then measured for the title of IgG antiviral of hepatitis E by the enzyme-linked immunosorbent assay (ELISA) method using the third generation ELISA kit made by Delavara Company.

**Results:** This study included 554 participants. The mean age of the participants was  $41.4 \pm 14.3$  years (age range, 17 - 72 years). From a total of 554 participants, 295 (53.2%) were females and the remainder were males. Results showed that the hepatitis E antibody title was positive in 139 (25.1%) participants and negative in the others. Comparison of the prevalence rates of positive HEV between men and women showed no statistically significant difference although it was significantly higher in married participants than in single ones ( $P < 0.001$ ). Results also showed that the prevalence was less in participants with a tertiary education compared to those with a lower level education. Along with age, the prevalence of the positive antibody title increased significantly. The prevalence of HEV in participants who were smokers was significantly ( $P < 0.001$ ) lower than in those who were nonsmokers.

**Conclusions:** In this study, the seroprevalence of contact with HEV in urban adults in the city of Birjand was 25%. The results of this study showed that the prevalence of hepatitis E in the city of Birjand, eastern Iran, was higher than in other places compared with previous studies on communities in Iran. Also, the prevalence of HEV in single and educated people was significantly less than that in married and literate individuals.

**Keywords:** Prevalence, Risk Factors, Hepatitis E, Eastern Iran

## 1. Background

As one of the most common causes of acute hepatitis, hepatitis E infection is caused by the RNA virus of the heptamegaly viridae family. The virus remains in sewage and is transferred through the stool through fecal-urals and dirty water, especially in developing countries (1,2).

Most of deaths occurs in developing countries examples Asian countries (3).

One third of the world's population is infected with this virus. Therefore, HEV is a public health issue in all parts of the world. Yet, it is of particular importance in develop-

ing countries because of poor hygiene conditions and lack of standard wastewater treatment systems (4).

The prevalence of hepatitis E is reported 10% - 35% based on enquiries into seroepidemiology in developing countries (5).

While HEV infection is endemic in Asia, Africa, and the Middle East according to the relevant data, research indicates that the infection is increasing in developing countries (1).

Iran is an endemic area for hepatitis E, but HEV seroprevalence is not investigated among the general popu-

lation in all parts of the country. Many studies on Iran have targeted specific groups and only limited research has been conducted on the general population. Reports on Iran show that the HEV seroprevalence is reportedly in the range of 3.8% in Isfahan to 46.1% in Ahwaz (1, 6).

## 2. Objectives

Information on a regional prevalence of the hepatitis E seroprevalence is important for epidemiologic studies to determine geographical distribution of HEV in Iran. Epidemiologic information is also important for assessing health and hygiene status and for identifying transmission paths of the disease. It is important to determine the prevalence of hepatitis E among the general population in the city of Birjand, eastern Iran, given the lack of information in this regard. The South Khorasan region is in close proximity to Afghanistan; so, each year a large number of Afghan refugees pass through this province to enter Iran, while the neighboring country of Afghanistan has an endemic hepatitis E status (7). Accordingly, this study was performed to investigate the seroprevalence of hepatitis E among urban adults.

## 3. Methods

### 3.1. Design, Sampling and Sample Size

This cross sectional study was approved by the ethics committee of Birjand University of Medical Sciences with a research project number IR.bums.REC.1395.141.

The study was conducted to determine the prevalence of the hepatitis E in the city of Birjand in 2015. The sampling method was of the multistage (clustering and accidental) kind. A total of 55 cluster heads were accidentally chosen from the Birjand city postal department, and 10 samples were chosen from each head. Ten people in 3 age groups, from 17 to 69 years, were selected per group with 5 women and 5 men in each age group.

This study included 544 participants. The sample size was determined by the estimated formula of the prevalence of hepatitis E aiming to address the lack of information on the study area, which reports 14.7% prevalence of hepatitis E (8) with  $P = 0.15$ , and  $d = 0.03$ , and 544 cases.

The selected samples were visited at their homes and invited to participate in sampling for serological diagnosis of hepatitis E after the objectives and plans were explained to them and a written informed consent forms were provided by the participants. After referral, the participants were given a researcher-made questionnaire that included demographic specifications and risk factors of infectious

diseases such as previous records of blood injections, special exposures, intravenous drug abuse, smoking, previous or new records of liver disease, etc. Questionnaires were completed through an interview with each participant conducted by a trained public health expert.

Inclusion criteria for the study were age 17 years and older and willingness to participate in the survey. Exclusion criterion was disagreement as for blood sampling.

### 3.2. Laboratory Test

A blood sample was taken from each individual to a volume of 5 cc without adding an anticoagulant substance in the nonfasting state. The received blood samples were then transferred to the university research laboratory for testing in the shortest possible time. Serum samples were kept in a freezer ( $-70^{\circ}\text{C}$ ) until trials were performed on them. After sampling, the title of IgG antiviral of hepatitis E was measured by the ELISA method on the blood sample taken from each participant using the third generation of the ELISA kit made by Delwera company.

### 3.3. Statistical Analysis

The data were analyzed by the SPSS software version 15 using descriptive statistic methods (percentage, frequency, mean and standard deviation) and chi-square or Fisher's exact test at the level of  $\alpha = 0.05$ . The odd ratio (OR) and 95% confidence intervals (CI) were calculated by multivariate analysis using the backward stepwise logistic regression analysis. P values less than 0.05 were considered statistically significant.

## 4. Results

This study included 554 participants with the mean age of  $14.3 \pm 41.4$  years, a minimum age of 17 years, and a maximum age of 72 years. Among the total number of participants, 295 (53.2%) were females and the remainder were males. In terms of the level of education, 50 cases (9%) were illiterate, 99 (17.9%) had primary education, 58 (10.5%) had junior education, 187 (33.8%) had high school degrees, and 160 (28.9%) had college education. A total of 84 subjects (15.2%) were single, and the remainder were married.

An antibody title of hepatitis E in 139 (25.1%) individuals was positive. The prevalence of positive HEV showed a nonsignificant difference between men and women, but it was significantly ( $P < 0.001$ ) more in married than single people. The prevalence was less in individuals with tertiary education compared to those with other levels of education. Along with increased age, the prevalence of the positive antibody title showed a significant increase such that in participants with illiterate education (level 2.11) was

higher than participants with academic education and in individuals with the primary education it was 3.78 higher than people with academic education and in those with the age range of 30 - 49 years was 8.47 higher than people with 50 years and above. Also, it was 19.8 higher than people with age below 30 years (Table 1).

Statistics for the history of jaundice showed a significant difference in the HEV state according to the hepatitis history in person, and family and the prevalence of HEV in smokers was lower than in nonsmokers (Table 2).

## 5. Discussion

In this study, the seroprevalence of contact with HEV in urban adults of Birjand City was 25%. The results of this study showed that compared with previous studies on the Iranian population, the prevalence of hepatitis E in Birjand City in eastern Iran was higher than that in other places. Most studies on Iran were conducted before 2014, during the period 2005 - 2009, and the reported prevalence of hepatitis E was 31% in some countries for example the Netherlands and between 3.8% and 11.5% across the various regions of Iran (3, 6, 9).

Sepanlo et al. reported that the prevalence of HEV in Iran was higher than figures for other developed countries (3.9% - 14%) and from Turkey (3.8%) specifically, but lower than other neighboring countries such as Iraq (14.8%), Saudi Arabia (18.8%), and Pakistan (17.51%) (10).

Seroepidemiologic studies present varying results from around the world. It seems that the seroprevalence rate of hepatitis E is higher in underdeveloped or less developed countries. The high prevalence is often reported in south Asian countries; Far East except for Japan, and Egypt in the Middle East, while a lower prevalence is reported in Europe and America (1).

Iran can be considered endemic for hepatitis E among the general population due to the seroprevalence of above 5% of HEV (10).

Based on the literature, among general populations of other countries, overall prevalence of HEV in Bangladesh was 22.5%, in Eastern china 13%, in India 1.9%, and in United States 6.27% (11-14).

In recent investigations, the seroprevalence of HEV was 25.1% in the general population of adults of Birjand City. This result is higher than the results for other parts of Iran, such as Nahavand (9.3%), Isfahan (8.1%), Sari (7.3%), and Tehran (7.9% - 15%) (9, 15). Also, in Iran the sero-HEV prevalence range in different regions of Iran was 10.2% - 22.8% among general population, 4.5% - 14.3% among blood donors, 6.1% - 22.8% in IV addicts, 6.3% - 28.3% in hemodialysis patients, 1.6% - 11.3% in people infected with other viral hepatitis, and 27.5% in Patients with chronic liver diseases.

The results of this study showed a lower prevalence than that of some other studies in Iran. It was reported, for example, that 46.1% of the general population had a positive serology in Ahwaz in 2014 (1).

In other countries such as the Yantai City 22.2% in seafood processing, 16.9% in east China and 13.1% in Mainland China, in India, 16% - 77% of the adults had a positive serology for HEV and in Malaysia, 50% - 67% of the general population recorded positive serology for HEV. Also, in Portugal, a case control study and different studies have shown the anti-HEV IgG prevalence of 2.1% - 29% that was due to the different specificities and sensitivities of the assay (16-18).

Difference in results of these reports represents regional differences in terms of contact with the virus. Other considerations that may affect results are type of kit used for testing, time of testing, the population under the study, and sample size (1, 2).

These results seem to show that the eastern part of Iran had a higher level of contamination than most other parts of Iran, which can be due to living conditions in the area that can increase the likelihood of transmission of HEV fecal-oral. The high prevalence may also be attributed to the close proximity of Birjand and the border with Afghanistan and transmission from Afghan refugees. As it is endemic, hepatitis E can be the reason for high incidence of the disease in the eastern region of the country (8).

In this study, the prevalence of HEV showed increased significance as age grew such that positive serology in  $\geq$  50-year-old age group was 8.84 times than that of the 30 - 49 year olds and 19.8 times that of people under 20 years old. This result conforms to the results determined by most other studies. Similarly, a study in China found the high seroprevalence among people above 60 years (70% - 80%). Also, a study conducted in Bangladesh reported the seroprevalence rate of 67% in people over the age of 80 years and the results also reported a rate of 52% - 62% in the population over 80 years of Honk Kong (1, 15, 19-21). These results showed that age can be a risk factor for the prevalence of hepatitis E. However, an improved state of health and hygiene conditions in society reduces exposure to the virus over time.

In the majority of the studies, no relation was established between age and prevalence of the disease, which is similar to the current study (3, 6, 8, 10). Results of this study showed that a positive serology of HEV was lower in educated people, which conforms to the results of the previous studies in Iran (6, 8, 10). Positive serology in people with primary education was 3.87 compared to people with an academic education. The presence of HEV antibody in people with lower education can be attributed to the

**Table 1.** Comparison of the Hepatitis E Virus Seroprevalence According to Demographic Variables in Subject Samples

Anti-HEV Variable	Positive Frequency (%)	Negative Frequency (%)	P Value Chi-Squared Test	OR (CI 95 % OR) P Value
<b>Sex</b>				
Male	72 (27.8)	187 (72.2)	$\chi^2 = 1.89$ , df = 1, P = 0.17	1.31 (0.89 - 1.93)
Female	67 (22.7)	228 (78.3)		1
<b>Marital</b>				
Single	4 (4.8)	80 (95.2)	$\chi^2 = 21.9$ , df = 1, P < 0.001	1
Married	133 (28.9)	328 (71.1)		8.13 (2.91 - 22.7)
<b>Education</b>				
Illiterate	15 (30)	35 (70)	$\chi^2 = 25.5$ , df = 4, P < 0.001	2.11 (1.02 - 4.31) 0.046
Primary	43 (43.4)	56 (56.6)		3.78 (2.13 - 6.7) < 0.001
Secondary	14 (24.1)	44 (75.9)		1.57 (0.76 - 3.25)
High	40 (21.4)	147 (78.6)		1.34 (0.78 - 2.3)
Academic	27 (16.9)	133 (83.1)		1
<b>Age, y</b>				
< 30	5 (3.5)	134 (96.5)	$\chi^2 = 65$ , df = 2, P < 0.001	1
30 - 49	55 (24)	174 (76)		7.47 (3.3 - 21.7) < 0.001
> 50	79 (42.5)	107 (57.5)		1.98 (7.74 - 5.06) < 0.001

**Table 2.** Comparison of the Hepatitis E Virus Seroprevalence Rates According to Risk Factors in the Samples

Anti-HEV Characteristics	Positive Frequency (%)	Negative Frequency (%)	P Value Chi-Squared/Fisher's exact test	OR (CI 95 %OR) P Value
<b>Hepatitis history in person</b>				
Yes	3 (75)	1 (25)	Fisher = 0.051	9.13 (0.94 - 88.5)
No	136 (24.7)	414 (75.3)		1
<b>Icter</b>				
Yes	8 (34.8)	15 (65.2)	$\chi^2 = 1.19$ , df = 1, P = 0.27	1.63 (0.67 - 3.9)
No	131 (24.7)	400 (75.3)		1
<b>Hepatitis history in family</b>				
Yes	5 (33.3)	10 (66.7)	Fisher = 0.54	1.51 (0.51 - 4.5)
No	134 (24.9)	405 (75.1)		1
<b>Smoking</b>				
Yes	9 (23.7)	29 (76.3)	$\chi^2 = 0.04$ , df = 1, P = 0.84	1
No	130 (25.2)	386 (74.8)		1.1 (0.5 - 2.4)

role of knowledge and observation of personal hygiene as a means of disease prevention.

Also, interestingly, hepatitis E was found to be of greater prevalence among married than single individuals. The association between the hepatitis E prevalence and marital status was found significant, a finding that has not been reported in any previous study.

The main strength of the study is the large population under coverage, while its main weakness can be the fact that focus was on the urban population that are of higher socioeconomic and education levels than the rural population.

### 5.1. Conclusions

Based on this study, the positive serology of HEV was 25% in Birjand city in the east of Iran. Furthermore, the prevalence of hepatitis E was significantly lower in married and educated people. Also, the prevalence of hepatitis E was lower in people that were smokers.

### 5.2. Suggestions

Even though the findings of this study show that hepatitis E infection was endemic in the area, a large proportion of the general population was sensitive to this virus. Given that the main route of transmission of hepatitis E was the fecal-oral route, the promotion of hygiene status in the society is very important. Proper hygiene and waste disposal methods in cities and villages are a priority. Also, enquiry into other factors such as smoking and marriage, both of which showed a positive relation with serology of HEV, needs to be followed.

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### Footnotes

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