ORIGINAL ARTICLE

Seroprevalence of hepatitis E virus among different age groups in Tehran, Iran

S. Sharifipour and K. Davoodi Rad

Department of Pharmacology, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran

Abstract

Hepatitis E virus (HEV) is considered to be a public health problem on a global scale, especially in developing countries. This study aims to investigate the seroprevalence of HEV in the Tehrani population. This descriptive–analytical study was carried out between the years 2017 and 2018 in Tehran, Iran. A total of 493 individuals whose blood samples and demographic data were collected via questionnaires through random cluster sampling were selected. To determine the presence of specific IgG antibody against HEV, commercial kits were used through ELISA. Chi-squared tests, logistic regression and t test were also required to conduct the statistical analysis. Of the 493 participants, with a mean age of 40.98 ± 17.10 years, included in this study, 180 were men and 313 were women. Of these, 48 (9.7%) had IgG antibodies against HEV. No significant difference was observed between the sexes (or different age groups) and positive antibody. It has been reported that the prevalence rate of this infection is high in Tehran, which is indicative of the endemic nature of this infection in society. The results of this study are similar to those obtained from the east of Golestan province, Iran but different from those obtained from Isfahan province, Iran. As a high percentage of people are susceptible to the infection in society, it is likely to have the prevalence of an epidemic.

Keywords: Antibody, epidemiology, hepatitis E virus, prevalence, Tehran
Original Submission: 5 October 2019; **Revised Submission:** 30 November 2019; **Accepted:** 10 December 2019
Article published online: 20 December 2019

Corresponding author: S. Sharifipour, Department of Toxicology and Pharmacology, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran
E-mail: Sharareh_sh50@yahoo.com

Introduction

Hepatitis E virus (HEV) is a small, non-enveloped virus and is approximately 30 nm in diameter. The virus has a single-stranded RNA genome, approximately 7.2 kb in length with positive polarity. It belongs to the *Orthohepevirus* A species and is a member of the genus *Orthohepevirus* and is placed in the family *Hepeviridae* and in realm *Riboviria* [1–3]. HEV is the second most common cause of acute hepatitis in adults and is transmitted through the orofaecal route [4]. Although HEV is the most significant factor in acute hepatitis infection in adult residents of Central Asia, the Indian subcontinent and South East Asia, it is the second leading cause of acute hepatitis infection (after hepatitis B) in the Middle East and North Africa [5–7]. The prevalence rate of HEV infection in developing countries with relatively low levels of health varies from 7.2% to 35%. However, the prevalence rate in developed countries is almost 3% [8–10]. Infection with this virus is usually self-limiting, and its mortality rate is relatively low at around 1%–4%; however, in the case of pregnant women, it increases by approximately 20% [11–13]. HEV has been recognized as a cause of chronic hepatitis, especially in immunocompromised individuals [14–16]. Although the infection may be asymptomatic in a group of people, it may cause clinical disease in another group. Of note, 15–60 days after infection with HEV, symptoms of clinical diseases appear (on average, at 40 days); they appear initially with mild symptoms including restlessness, anorexia, nausea and abdominal pain; subsequently, acute hepatitis appears with symptoms such as jaundice, dark

https://doi.org/10.1016/j.nmni.2019.100638

urination, pale stools and hepatomegaly [10,17]. The IgM antibody against HEV is produced in the infected individuals' sera at the onset of clinical symptoms and is detectable over a period of 2 weeks to 3 months. In the case of infected individuals, IgG antibodies appear later and persist for many years after the virus has disappeared, demonstrating an infection with HEV in the past [18,19]. In regions where the disease is endemic, the infection appears epidemically and endemically. Numerous cases of existing hepatitis E have been reported from Pakistan, Iraq and India [20–22]. Several cases of this disease have also been reported in Iran [23,24]; however, few studies have been conducted on the prevalence of HEV in Iran. Despite the fact that the majority of studies in Iran have been carried out on blood donor groups, there have been few research studies on the seroepidemiology of HEV in the general population in Tehran. Tehran, the capital of Iran, is a large city in the north of the country that has a continental-influenced Hot-summer Mediterranean climate. It is the most populous city in Iran and western Asia and has the second largest metropolitan area in the Middle East with population of about 10 million in the city and 15 million over the larger metropolitan area of Greater Tehran [25–27]. Tehran consists of several various ethnic groups including Iranian Azeris, Baloch, Assyrians, Arabs, Armenians, Georgians, Bakhtyaris, Talysh, Jews, Kurds and Circassians. However, the majority of people in Tehran identify themselves as Persians [28]. Studies concerning the prevalence of the virus in the general population help to predict the incidence of gastrointestinal hepatitis epidemics. The aim of this study is to determine the prevalence rate of HEV among different age groups of Tehrani residents over the years 2017–2018.

Materials and methods

This descriptive–analytical study was conducted over the years 2017 and 2018 in the eastern cities of Tehran province including Firoozkooh, Damavand, Pakdasht, Varamin, and the northern and eastern districts of Tehran (Fig. 1). The target population was selected by cluster sampling method from families living in these areas. Questionnaires containing demographic information were simultaneously filled in by health workers. Here, 493 out of the total 5176 interviewees, who participated in the study, were randomly selected. These individuals were informed of the project's objectives and, then, gave 5 mL of their blood with their written letter of consent. Samples from younger individuals were taken with the parents' consent. This project was approved by the Professional Ethics Committee of the Liver and Gastroenterology Research Centre of Shahid Beheshti University of Medical Sciences.

After serum separation, the samples were kept at −20 °C until serological tests were performed. The REF EVAB.CE ELISA kit (Dia.pro, Sesto San Giovanni, Italy) was used to measure the presence of IgG antibody against HEV. All steps and cut-off determinations were performed according to the kit instructions. The results of these experiments, along with the information obtained from the questionnaires, were inputted into SPSS software version 23, and demographic analysis was performed. Chi-square test, t test and logistic regression were used to examine the significant relationships among the variables, to compare the differences between the means, and to calculate odds ratios, respectively.

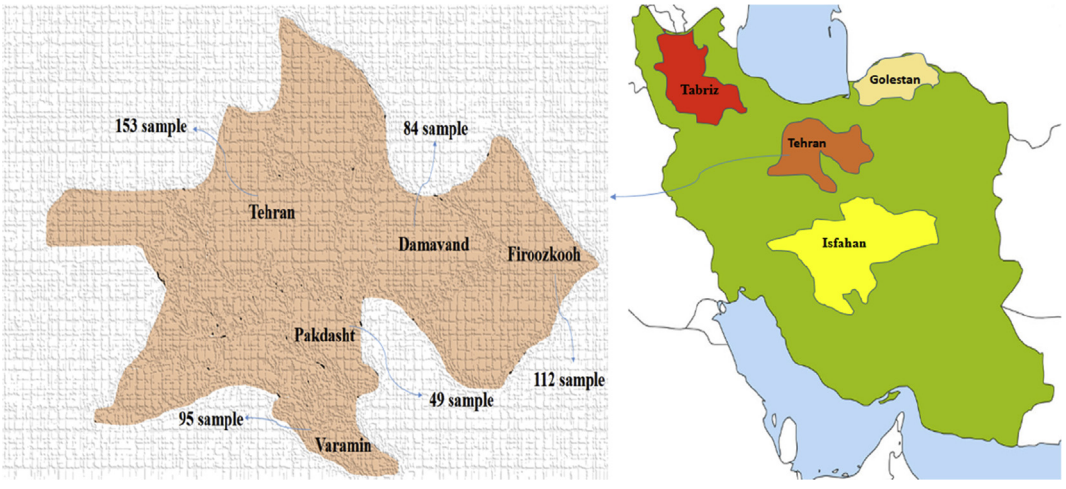

FIG. 1. A schematic map of Tehran with the districts (Firoozkooh, Damavand, Pakdasht and Varamin) and the number of individuals studied in each area.

Results

In all, 493 out of 5176 interviewees were included in this study. The mean age of the population was 40.98 ± 17.10 years (range 11–83 years). Of all the target population, 180 were men and 313 were women (63.5%). The mean age of women was 40.76 ± 15.40 years (range 1–81 years). The mean age of the men was 41.36 ± 19.75 years (range 3–83 years). ELISA results showed that 48 patients (9.7%) had IgG antibody against HEV. Of all the participants with positive antibody, 21 (43.8%) were men and 27 were women (56.2%) and the percentages of infection of men and women were 11.7% and 8.6%, respectively. Although the rate of infection in men was higher than that in women, no significant relationship was found between sex and the positive presence of IgG antibody (OR 0.715, 95% CI 0.391–1.305, p 0.273) (Table 1).

The largest number of referrals (297 people; 60.2%) belonged to the 30–60-year age group, whereas the lowest number of referrals (71; 14.4%) comprised those over 60 years. The highest rate of infection was seen in the age group >60 years (15.5%) and the lowest rate in the age group <29 years (9.6%). There was no significant relationship found between the positive IgG antibody against HEV and different age groups (OR 1.726; 95% CI 0.719–4.164, p 0.195) (Table 1).

The mean age of individuals with positive IgG antibody was 42.15 ± 19.98, whereas the mean age of those with negative IgG antibody was 40.85 ± 16.79. The results showed that the mean ages of the individuals with IgG antibody and those without IgG antibody were not significantly different (p 0.620) (Table 2). No significant difference was observed between different age groups of women (p 0.051) and of men (p 0.977) in terms of gender comparison. In the male and female groups, the ORs were 0.875 (95% CI 0.222–3.362) and 2.958 (95% CI 0.914–9.978), respectively (Table 3). Women's mean ages in groups with positive and negative IgG antibody were 44.22 ± 19.30 and 40.43 ± 14.99 years, respectively. In addition, men's mean ages in groups with positive and negative IgG antibody were 39.48 ± 20.98 and 41.61 ± 19.64, respectively. There was no significant difference between the mean age and positive IgG antibody against HEV in both sexes p = 0.222 and p = 0.643 in women and men, respectively.

TABLE 2. Variations between genders in Tehran, Iran

	Results of ELISA	Mean ± SD	p-value
Gender			
Female	No. of anti-HEV IgG-positive participants	44.22 ± 19.30	0.222
	No. of anti-HEV IgG-negative participants	40.43 ± 44.99	
Male	No. of anti-HEV IgG-positive participants	39.48 ± 20.98	0.643
	No. of anti-HEV IgG-negative participants	41.61 ± 19.64	
Antibody			
Positive		42.15 ± 19.98	0.620
Negative		40.85 ± 16.79	

Discussion

The results of the present study show that the presence of IgG antibody in Tehran's general population is 9.7%. There are various reports of the prevalence of hepatitis E antibodies in different regions of Iran, the Middle East and other countries around the world [29–31]. According to the CDC report, Iran is among the countries with the highest prevalence of this infection [32]. The rate of IgG antibody present in blood donors in industrialized countries has been reported to range from 2% to 6% [31]. This figure reaches 24% in countries with high infection prevalence, including Egypt [33]. In the neighbouring countries of Iran, the prevalence of antibodies varies from 17.5% in Pakistan [20] to 2.6% in some regions of Turkey [29].

In a limited number of studies conducted in Iran, researchers have reported that the IgG antibody levels range from 3.8% in the general population of Isfahan province [34] to 11.8% in the eastern regions of Golestan province [35]. In the blood donor population, this level varies from 12.9% in Hamadan [36] to 7.8% in Tabriz [37]. The prevalence of IgG antibody among the blood donor population in Tehran has also been reported to be 7.6% [38]. Moreover, the results of this study demonstrate that the infection rate in Tehran, Iran is quite similar to that in Golestan province, Iran. In total, the comparison of the results in Iran and its neighbouring

TABLE 1. Hepatitis E virus seroprevalence among different age groups and genders in Tehran, Iran

	No. of all participants (%): *n* = 493 (100%)	No. of anti-HEV IgG-positive participants (%): *n* = 48 (9.7%)	No. of anti-HEV IgG-negative participants (%): *n* = 445 (90.3%)	OR (95% CI)	p-value
Gender					
Female	180 (36.5%)	27 (11.7%)	153 (88.3%)	ref	0.273
Male	313 (63.5%)	21 (8.6%)	292 (91.4%)	0.715 (0.391–1.305)	
Age groups (years)					
<30	125 (25.4%)	12 (9.6%)	113 (90.4%)	ref	0.204
30–60	297 (60.2%)	25 (8.4%)	272 (91.6%)	0.866 (0.42–1.782)	0.695
>60	71 (14.4%)	11 (15.5%)	60 (84.5%)	1.726 (0.719–4.146)	0.222

TABLE 3. Seroprevalence of hepatitis E virus among different age groups based on male and female genders in Tehran, Iran

		No. of all participants (%): n = 493 (100%)	No. of anti-HEV IgG-positive participants (%): n = 48 (9.7%)	No. of anti-HEV IgG-negative participants (%): n = 445 (90.3%)	OR (95% CI)	p-value
Gender	Age groups (years)					
Female	<30	77 (24.6%)	6 (7.8%)	71 (92.2%)	Ref	0.051
	30–60	201 (64.2%)	14 (7%)	187 (93%)	0/886 (0/328 to 2/395)	0.811
	>60	35 (11.2%)	7 (20%)	28 (80%)	2/958 (0/914 to 9/578)	0.070
Male	<30	48 (26.7%)	6 (12.5%)	42 (87.5%)	Ref	0.977
	30–60	96 (53.3%)	11 (11.5%)	85 (88.5%)	0/906 (0/313 to 618/2)	0.855
	>60	36 (20%)	4 (11.1%)	32 (88.9%)	0/875 (0/228 to 3/462)	0.846

countries showed that the seroprevalence of HEV in Tehran province was lower than that in Pakistan and higher than that in Turkey. In this study, residents in the suburbs of Tehran were also sampled; therefore, a simple comparison between the findings of this study and the results of the previous ones indicates that these findings present accurate statistics of the prevalence of these infections in the province. Given the fact that sampling in this study was performed for all age groups, the obtained data provide researchers with a more accurate representation of the IgG antibody status in society.

In this study, no relationship was found between sex and the presence of antibodies, which was similar to the results obtained in other studies in Iran and other countries [31,32,39]. Due to the specific risk factors of some infections, the prevalence rates are different in terms of the sexes [40]. The results of the present study show that there is no significant relationship between different age groups in terms of positive IgG antibody, which is similar to the results obtained in Isfahan, Turkey, and in French homeless people [41,42]. Moreover, the rate of positive IgG antibody gradually increases as the population ages, which is consistent with our prediction that while aging, the risk of exposure to the virus increases. When age groups were disaggregated by gender, it was found that women in the age group <30 years accounted for an infection rate of 7.8%, whereas the infection rate increased to 20% in the age group >60 years (Table 3). This difference was not found in the male group. It can be assumed that older individuals (especially women) have a higher rate of prevalence just because they have lived longer and had more opportunities to encounter the virus. It can be concluded, by and large, that the presence level of IgG antibody in this study (9.7%) is in line with the prediction of the CDC, claiming that HEV infection is endemic in Iran. According to the WHO, most countries with an inappropriate sewage disposal system at greater risk of exposure to the virus. For example in our study, the reason of this high endemicity is most likely Karaj River as the drinking water source of the inhabitants, where the city sewage is also discharged in. Therefore, improvement of sewage disposal system, is critical to drive down HEV prevalence in the society. For example, the WHO recommends using a proper sewage disposal system for areas where drinking water contamination by stool is a major cause of epidemics [43].

Although HEV infection is endemic in Tehran based on our findings, it should be kept in mind that a high percentage of the general population in the region are still susceptible to the virus and that the outbreak of an epidemic in this region originating from water and food is still a possibility. Therefore, commitment to adhering to health concerns and guidelines in food preparation and cooking, and the use of purified water can help prevent epidemics caused by HEV. Further related studies are required to obtain an overview of the presence of IgG antibody in the general population of the country and in different populations of varying age groups.

Overall, the comparison of the results and those of the previous studies concerning Iran and other parts of the world showed that the performance characteristics of tests (ELISA) for the detection of anti-HEV IgG varied considerably. These results revealed that rates of seroprevalence could not be reliably compared on an inter-study basis. It can be concluded that one reason for the existing differences in seroprevalence rates may be differences in the demographics and sizes of the populations studied, differences in the ELISA detection kits used, and the time of sampling [44]. Moreover, the comparison indicates that several factors such as different levels of exposure to infection over time, different living conditions in various regions, and faecal–oral transmission of HEV can affect the geographic distribution of HEV infection within a specific country.

Conflict of interest

All of the authors declare that there are no commercial, personal, political, or any other potentially conflicting interests related to the submitted manuscript.

Funding

This research did not receive any specific grant from funding agencies in public, commercial or not-for-profit sectors.

Acknowledgements

We appreciatively acknowledge the funding and all the support from the Gastroenterology and Liver Diseases Research Centre of Shahid Beheshti University of Medical Sciences, Tehran, Iran. The authors would like to thank the assiduous health workers of Tehran's provincial health centres for their generous cooperation in the process of sampling and filling in the questionnaires.

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