

# Seroprevalence of hepatitis E in Nahavand, Islamic Republic of Iran: a population-based study

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الانتشار المصلي لالتهاب الكبد E في نهاوند، جمهورية إيران الإسلامية: دراسة سكانية  
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**الخلاصة:** أُجري مسح مجتمعي لمدة شهرين في شباط/فبراير وآذار/مارس 2003، لدراسة الانتشار المصلي للعدوى بفيروس التهاب الكبد E في نهاوند، جمهورية إيران الإسلامية. وتم أخذ عينة عشوائية بطريقة منهجية، قوامها 304 من السكان ممن هم في عمر 6 أعوام أو أكثر من كل منطقة حضرية من المناطق التي في نهاوند (العدد الإجمالي 1824 فرداً). وتم اختبار المشاركين لتحري الغلوبولين المناعي G المضاد لفيروس التهاب الكبد E، باستخدام مقاييس الممتز المناعي المرتبط بالإنزيم (إليزا). وقد بلغ الانتشار المصلي الإجمالي لهذا الفيروس 9.3% (عند فاصلة ثقة 95% مُتراوحاً بين 8.2% و10.9%). وعندما أُجريَ التصحيح المتعدد المتغيرات، تبين أن الجنس [الاحتمال 1.61 (عند فاصلة ثقة 95% مُتراوحاً بين 1.13 و2.28)] والعمر [الاحتمال 1.03 (عند فاصلة ثقة 95% مُتراوحاً بين 1.01 و1.04)] هما عاملاً الاختطار الوحيدان اللذان يُعتدُّ بهما إحصائياً. وهذا الانتشار المتوسط يدعو إلى مزيد من البحث في العدوى بفيروس التهاب الكبد E.

ABSTRACT A 2-month community-based survey in February/March of 2003 was carried out to study the seroprevalence of hepatitis E virus (HEV) infection in Nahavand, Islamic Republic of Iran. From each of 6 urban regions of Nahavand, 304 inhabitants  $\geq$  6 years were recruited through systematic random sampling (total 1824). Participants were tested for anti-HEV IgG using ELISA. The overall seroprevalence of HEV was 9.3% (95% CI: 8.2%–10.9%). Based on multivariate adjustment, only sex (OR = 1.61, 95% CI: 1.13–2.28) and age (OR = 1.03, 95% CI: 1.01–1.04) emerged as significant risk factors. This intermediate prevalence urges further investigations on HEV infection in the Islamic Republic of Iran.

## Séroprévalence de l'hépatite E à Navahand (République islamique d'Iran) : étude en population générale

RÉSUMÉ Une enquête communautaire d'une durée de 2 mois a été conduite en février et mars 2003 afin de déterminer la séroprévalence de l'infection par le virus de l'hépatite E (VHE) à Navahand en République islamique d'Iran. Dans chacune des 6 zones urbaines que compte Navahand, 304 habitants âgés de 6 ans et plus ont été recrutés par échantillonnage aléatoire systématique, soit un total de 1824 participants. Le test ELISA a été utilisé pour la détection des anticorps anti-VHE de type IgG. La séroprévalence globale du VHE était de 9,3 % (IC<sub>95%</sub> : 8,2-10,9 %). Après ajustement multivarié, seuls le sexe (OR = 1,61 ; IC<sub>95%</sub> : 1,13-2,28) et l'âge (OR = 1,03 ; IC<sub>95%</sub> : 1,01-1,04) se sont signalés comme facteurs de risque significatifs. Cette prévalence intermédiaire appelle une enquête plus poussée sur l'hépatite E en République islamique d'Iran.

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## Introduction

Hepatitis E virus (HEV) is a small, non-enveloped, single-stranded positive sense RNA virus. HEV infection, which often spreads through faeces-contaminated drinking water, causes a self-limiting acute hepatitis [1]. The overall mortality rate associated with HEV infection is low, but it can be as high as 20% in pregnant women. No chronic infection with HEV has been described [2,3].

Hepatitis E is a major health concern in many developing countries. The disease is common among young and middle-aged adults, but rare in children and the elderly [4,5]. Hepatitis E is endemic in some parts of Asia, Africa, the Middle East and North America [6,7], where the occurrence of outbreaks have been reported [7,8]. Sporadic cases have also been identified among travellers to these regions [9,10]. The overall seroprevalence of anti-HEV, even in hyperendemic areas, rarely exceeds 25%. Frequent low-dose exposure to HEV has been suggested to have a probable protective role in people of lower socioeconomic or poor hygiene status [11]. In non-endemic regions, the prevalence of anti-HEV antibodies has been reported to be 1%–5% [12,13].

Most studies have looked into the prevalence of HEV infection in patients with hepatitis or in selected settings [14,15]. Community-based surveys are limited and information on HEV infection in populations is scant. There have been reports on suspected outbreaks of HEV in the Islamic Republic of Iran [16], but no data exist on the prevalence in the community. This study aimed to assess anti-HEV prevalence in the city of Nahavand in the western part of the country. The possible contribution of sociodemographic factors on this prevalence was also examined.

## Methods

This cross-sectional study was conducted during a 2-month period (February to March 2003) on individuals aged  $\geq 6$  years in the city of Nahavand, located in the western part of the Islamic Republic of Iran. Nahavand has a population of around 72 000. The 6 urban regions of Nahavand were taken as strata and 304 people in each stratum were recruited through systematic random sampling (1824 in total). Questionnaires to collect sociodemographic variables were completed by face-to-face interview. The study was endorsed by the responsible ethics committee.

Blood samples were taken from each individual. Sera were stored at  $-20^{\circ}\text{C}$  and then tested for anti-HEV IgG by a commercial enzyme immunoassay (EIA) (Dia.Pro, Italy HEV EIA) following the manufacturer's instructions. The cut-off was defined with the positive and negative control sera that were included in each assay, according to the manufacturer's instructions. Samples were considered positive if the optical density value was above the cut-off value and all positive samples were retested in duplicate with the same EIA assay to confirm the initial results.

Statistical analysis was performed using *Stata*, version 8. The 95% confidence interval (CI) of overall seropositivity was estimated. The bivariate and multivariate associations of seropositivity (as the binary dependent variable) with other independent variables were examined by logistic regression model (svylogit command) and the crude and adjusted odds ratio (OR) and corresponding 95% CI were estimated. Age was entered in the models as a continuous variable.

## Results

Of the 1824 subjects, 799 (43.8%) were men and 1025 (56.2%) were women. The mean age was 34.7 years [standard deviation (SD) 19.5] and median age was 32 years. The overall seroprevalence of hepatitis E was 170/1824 [9.3%, 95% CI: 8.2–10.9]. Seropositive participants had a mean (SD) age of 42.6 years (15.6) and median age of 40.5 years. Table 1 shows the age-specific prevalence of anti-HEV. Anti-HEV IgG was not evenly distributed among age groups, as a higher prevalence (52.4% of participants) was seen in the 31–50 year age group ( $\chi^2$  for trend = 22.7,  $df = 1$ ,  $P < 0.001$ ).

Table 2 reports the frequency of HEV seropositivity by the sociodemographic characteristics of the subjects. It also shows the crude and adjusted OR and corresponding 95% CI. Based on multivariate adjustment, only sex and age could be considered as risk factors for HEV, as the adjusted ORs for age and sex were 1.03 (95% CI: 1.01–1.04) and 1.61 (95% CI: 1.13–2.28) respectively. No statistically significant association was observed between HEV seropositivity and family size ( $> 4/\leq 4$ ) (adjusted OR = 0.78, 95% CI: 0.56–1.09). Additionally, the association between HEV

seropositivity and education level was not statistically significant.

## Discussion

Studies on HEV seroepidemiology in many parts of the world have found conflicting results. It is not known why the overall seroprevalence of anti-HEV in normal populations of endemic areas is low or why a low but constant presence of anti-HEV is observed in normal human populations of non-endemic industrialized countries [17].

This study indicated an overall prevalence of anti-HEV of 9.3%, which is similar to studies reported from Turkey (6.3%) and Saudi Arabia (8.6%) [18,19], but markedly lower than in countries such as Egypt (17.2%) and Pakistan (16%–19%) [20,21]. It can be concluded that HEV infection has an intermediate prevalence among Iranians compared with data from other populations [13,22,23].

Environmental and socioeconomic factors are of major importance for anti-HEV IgG prevalence, with HEV infection being influenced by sanitary status. Although most of the study group had access to chlorinated water with indoor plumbing, there was an intermediate prevalence of HEV infection among Nahavand inhabitants. This can be attributed to a less hygienically developed sewage disposal system.

The current study indicated an association of age and sex with the risk of HEV infection. The highest prevalence was observed in the group aged 31–50 years, which is similar to data reported from Turkey [24]. Higher prevalence among the females in the current study does not concur with other studies, which have shown the same anti-HEV prevalence for males and females [25], or higher rates in males [17]. The higher prevalence of anti-HEV among

Table 1 Age-specific seroprevalence of anti-hepatitis E virus (HEV) among a population aged 6 years and over in Nahavand, Islamic Republic of Iran

Age (years)	No. HEV positive/ no. tested	%
6–30	35/884	4.0
31–50 <sup>a</sup>	89/529	16.8
51–70	36/300	12.0
> 70	10/111	9.0
Total	170/1824	9.3

<sup>a</sup> $\chi^2$  for trend = 22.7,  $df = 1$ ,  $P < 0.001$ .

**Table 2 Prevalence of anti-hepatitis E virus (HEV) by sociodemographic factors among a population aged 6 years and over in Nahavand, Islamic Republic of Iran**

Variable	No. positive/ no. tested	%	Crude OR (95% CI)	Adjusted OR (95% CI)
<i>Sex</i>				
Male	59/799	7.4	1	1
Female	111/1025	10.8	1.52 (1.09–2.12)	1.55 (1.10–2.19)
<i>Age</i>				
	–		1.02 (1.01–1.03)	1.02 (1.01–1.03)
<i>Family size</i>				
≤ 4	94/931	10.1	1	1
> 4	76/893	8.5	0.79 (0.58–1.09)	0.78 (0.56–1.09)
<i>Education level</i>				
Illiterate	55/400	13.8	1	1
Elementary	46/428	10.7	1.02 (0.64–1.61)	1.05 (0.66–1.66)
Middle	13/249	5.2	0.77 (0.44–1.36)	0.80 (0.45–1.42)
High school	42/581	7.2	0.91 (0.59–1.41)	0.98 (0.63–1.54)
University	14/166	8.4	0.91 (0.48–1.70)	0.98 (0.52–1.85)

OR = odds ratio; CI = confidence interval.

females in the current study might be attributed to their lifestyle. During housework, women have greater exposure to sewage, so may be more prone to acquiring HEV infection. Based on our data, there was no association between educational level and anti-HEV. Other factors such as cultural factors, socioeconomic level and occupational risks for HEV exposure need to be further evaluated.

Similar to the Mexico City study [25], no association existed between family size and seropositivity in the present study. This could be explained by the fact that HEV is rarely transmitted from person-to-person [11].

Epidemiologic data on HEV infection in the Eastern Mediterranean Region is scarce. However, some regions endemic for HEV infection have been reported [19,20]. The existence of pockets of high endemicity for HEV infection may lead to outbreaks in surrounding areas with intermediate endemicity. This is especially problematic in countries such as the Islamic Republic of

Iran where, according to the results of our study, HEV infection seems not to be highly endemic, at least among the inhabitants of Nahavand.

In conclusion, this study demonstrated that HEV infection is of intermediate prevalence in Nahavand city and further investigations are needed to establish the real situation of HEV infection in other regions of the Islamic Republic of Iran. Moreover, it is also imperative to study the relative contribution of HEV infection to the disease burden of acute viral hepatitis.

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### Hepatitis E

Hepatitis E was not recognized as a distinct human disease until 1980. It is caused by infection with the hepatitis E virus (HEV), a non-enveloped, positive-sense, single-stranded RNA virus.

HEV is transmitted via the faecal–oral route. Hepatitis E is a water-borne disease, and contaminated water or food supplies have been implicated in major outbreaks. Consumption of faecally contaminated drinking-water has given rise to epidemics, and the ingestion of raw or uncooked shellfish has been the source of sporadic cases in endemic areas. There is a possibility of zoonotic spread of the virus, since several non-human primates, pigs, cows, sheep, goats and rodents are susceptible to infection. The risk factors for HEV infection are related to poor sanitation in large areas of the world, and HEV shedding in faeces. Person-to-person transmission is uncommon. There is no evidence for sexual transmission or for transmission by transfusion.

Source: WHO Fact sheet, No. 280  
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