

Prevalence of antibodies to hepatitis E virus among male blood donors in Tabriz, Islamic Republic of Iran

M. Taremi,¹ L. Gachkar,² S. MahmoudArabi,¹ M. Kheradpezhoh¹ and M. Khoshbaten³

انتشار أضداد فيروس التهاب الكبد من النمط E بين المتبرعين بالدم من الذكور في تبريز، جمهورية إيران الإسلامية

مهناز طارمي، لطيف كجكار، سيد مهدي محمود عربي، مريم خردبزه، منوچهر خوش باطن

الخلاصة: أجريت في مركز لنقل الدم بمدينة تبريز، فحوصات على عينات مصلية من 399 متطوعاً من الذكور المتبرعين بالدم للكشف عن الغلوبين المناعي G المضاد لالتهاب الكبد «E» خلال الشهرين السابع والثامن من عام 2004. وكانت نسبة انتشار هذا الغلوبين المناعي G 7.8% (95% CI: 5.2-10.4). وتضمنت عوامل الاختطار للعدوى كلاً من العمر والمستوى المنخفض من التعليم. فقد تبين أن الانتشار المصلي يزداد ازدياداً كبيراً مع التقدم في العمر، كانت النسبة فيمن هم دون الثلاثين من العمر 3.3% في حين ارتفعت إلى 37.5% في من بلغ منهم خمسين عاماً أو أكثر. وكان الأميون منهم أكثر تعرضاً لمخاطر العدوى من المتعلمين منهم. وهذه المعدلات العالية الإيجابية المصل بين المتبرعين بالدم من الذكور في جمهورية إيران الإسلامية، تتوافق مع معدلات توطئية التهاب الكبد «E».

ABSTRACT Serum samples from 399 voluntary male blood donors were tested for anti-hepatitis E virus (HEV) IgG during July and August 2004 at a blood transfusion centre in Tabriz city. The prevalence of anti-HEV IgG was 7.8% (95% CI: 5.2–10.4). Risk factors for infection included age and a low educational level. Seroprevalence increased significantly with age, from 3.3% in subjects under 30 years of age to 37.5% in individuals 50 years and over. Illiterate individuals were at significantly higher risk for infection than educated persons. The high seropositive rate among our male blood donors is compatible with endemicity of HEV in the Islamic Republic of Iran.

Prévalence des anticorps anti-hépatite E chez des donneurs de sang de sexe masculin à Tabriz (République islamique d'Iran)

RÉSUMÉ Des échantillons sériques prélevés en juillet et août 2004 dans un centre de transfusion sanguine de Tabriz auprès de 399 donneurs de sang volontaires de sexe masculin ont été soumis à un dépistage des IgG anti-hépatite E (anti-VHE). La prévalence des IgG anti-VHE était de 7,8 % (IC 95 % : 5,2-10,4). L'âge et un faible niveau d'instruction sont apparus comme des facteurs de risque d'infection. La séroprévalence a accusé une augmentation significative avec l'âge, passant de 3,3 % chez les moins de 30 ans à 37,5 % chez les sujets de 50 ans et plus. Les analphabètes se trouvent exposés à un risque d'infection significativement plus élevé que les individus ayant reçu une instruction. Le fort taux de séropositivité parmi nos donneurs de sang de sexe masculin est compatible avec l'endémicité du VEH en République islamique d'Iran.

¹Research Centre for Gastroenterology and Liver Diseases; ²Department of Infectious Diseases and Tropical Medicine Research, Shaheed Beheshti University of Medical Sciences, Tehran, Islamic Republic of Iran (Correspondence to: M. Taremi: mmtaremi@yahoo.com).

³Drug Applied Research Centre, Tabriz University of Medical Sciences, Tabriz, Islamic Republic of Iran.

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Introduction

Hepatitis E is an important public health concern in many developing countries of Asia and Africa where environmental sanitation facilities are poor [1]. In addition, a high incidence of sporadic hepatitis E has been observed in several countries in which outbreaks have not been reported [2,3]. In non-endemic areas, travellers to endemic regions are at major risk of HEV infection, but sporadic cases of acute hepatitis E without an implicated travel history have also been reported in Europe and the United States [4,5].

Hepatitis E virus (HEV) is an unclassified non-enveloped virus which is transmitted by the faecal-oral route. HEV infection generally causes self-limited acute hepatitis associated with high mortality in pregnant woman where the mortality rate can be as high as 20% [6].

Although transmission of HEV is generally via the faecal-oral route, person-to-person transmission, and transmission via the parenteral route or blood transfusion, have been suggested [7,8]. Anti-HEV seroprevalence of 1%–5% in blood donors has been reported from several countries where HEV is not endemic using commercially available recombinant protein-based tests [9,10]. It has been reported that a substantial proportion of blood donors (1.5%) were positive for HEV RNA and viraemic blood donors are potentially able to cause transfusion-associated hepatitis E in areas of high endemicity [11,12]. Thus the importance of HEV in endemic areas cannot easily be estimated, and must be measured specifically.

There have been few reports of suspected outbreaks of HEV in Islamic Republic of Iran [13], but no data has been reported on the prevalence of hepatitis E antibodies in the community. One study in the city of Nahavand in the western part of the country,

using a complex sampling design, detected anti-HEV IgG in 170 of 1824 (9.3%) individuals among the population aged 6 years and over [14].

To our knowledge, no epidemiological reports on the prevalence of hepatitis E antibodies in Iranian blood donors have been published. Therefore, in the present study, we investigated whether Iranian blood donors in an urban area are likely to have HEV infection, in an attempt to gain insight into the possible blood-borne transmission of HEV in the Islamic Republic of Iran.

Methods

In August 2004, 399 serum samples were collected from consecutive, voluntary, apparently healthy, male blood donors attending the blood transfusion centre in the city of Tabriz, northwestern Islamic Republic of Iran. Demographic data were collected using a questionnaire.

After routine blood screening for HBV, hepatitis C virus (HCV) and human immunodeficiency virus (HIV) markers, sera were stored at -70°C until tested for IgG anti-HEV using a commercial enzyme immunoassay (EIA) (Dia Pro, Italy HEV EIA) according to the manufacturer's instructions. The cut-off was defined with positive and negative control sera that were included in each assay, according to the manufacturer's instruction. Samples were considered positive if the optical density (OD) 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

Statistical analyses were performed by the chi-square test. Differences were considered to be statistically significant at $P <$

0.05. The study was endorsed by the ethics committee of the Research Centre for Gastroenterology and Liver Diseases, Shaheed Beheshti University of Medical Sciences.

Results

A total of 399 serum samples were obtained. The mean age was 31.4 (standard deviation = 9.8) years. The overall seroprevalence of hepatitis E was 7.8% (95% CI: 5.2%–10.4%). Seropositive subjects had a mean age of 40.7 (SD = 12.4) years.

Table 1 shows the age-specific prevalence of anti-HEV. Seroprevalence increased significantly with age, from 3.3% in subjects under 30 years of age to 37.5% in individuals 50 years and over ($P < 0.0001$).

Illiterate individuals (3/11) were at higher risk for infection than educated persons (27/388) ($P < 0.042$). All 399 donors were negative for hepatitis B surface antigen, and antibodies to HCV, HCV and HIV types 1.

All of the study population had access to chlorinated water with indoor plumbing.

Discussion

The overall prevalence of anti-HEV antibodies among our blood donors was 7.8%,

which is generally higher than figures reported from developed countries (0.4% to 3.9%) [15,16], although lower than those from other countries of the Eastern Mediterranean Region where reports of up to 52% seroprevalence for anti-HEV have been observed [17].

In the current study, seroprevalence increased significantly with age, from 3.3% in subjects under 30 years of age to 37.5% in those 50 years of age and over. A marked trend of seroactivity associated with increasing age was also observed in other studies among persons living in HEV endemic and non-endemic regions [18,19]. Illiterate individuals were at higher risk for infection than educated people. This result, similar to other countries, indicates that age and educational level are associated with risk for HEV infection [20,21].

In outbreak settings, HEV transmission is most often associated with faecally contaminated drinking water. However, risk factors for infection among sporadic cases of hepatitis E in both HEV-endemic and non-endemic regions have not been determined.

Healthy blood donors in the preicteric phase of the diseases and presumably infectious, could theoretically transmit HEV to recipients of their blood [22]. The importance of HEV in relation to blood transfusion practices stems from the possibility that there is evidence that the virus could be transmitted parenterally [23]. The blood products that theoretically carry the risk of transmission of HEV are packed red cells, whole blood or platelet concentrate collected from an asymptomatic donor during the viraemic phase [24]. However, the presence of anti-HEV is not a measure of infectivity, and no tests are available that would be appropriate for hepatitis E. Even the use of IgM anti-HEV EIA kits has its limitations. It has been reported that antibody responses

Table 1 Age-specific prevalence of anti-hepatitis E virus (HEV) among male blood donor in Tabriz, Islamic Republic of Iran

Age group (years)	No. positive/ tested	% positive
< 30	7/211	3.3
30–49	15/164	9.1
≥ 50	9/24	37.5
Total	31/399	7.8

$P < 0.0001$.

are detected in 21% of 67 patients in whom viraemia or faecal shedding (or both) were detected [25]. This suggests that some persons do not produce an IgM antibody response to infection with HEV. Although the HEV-specific polymerase chain reaction test is sensitive and specific, screening of the blood supply for HEV infection would not be cost-effective.

In conclusion, seroprevalence of HEV-antibody among blood donors in our study in Islamic Republic of Iran is high, but we cannot recommended screening of all blood donors for HEV until more data becomes

available and until more is known about the mode of transmission of HEV.

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References

- Smith JL. A review of hepatitis E virus. *Journal of food protection*, 2001, 64:572–86.
- Pillot J et al. Frequent sporadic hepatitis E in West Africa evidenced by characterization of a virus-associated antigen in the stool. *Journal of hepatology*, 1992, 15:420–1.
- Goldsmith R et al. Enzyme-linked immunosorbent assay for diagnosis of acute sporadic hepatitis E in Egyptian children. *Lancet*, 1992, 339:328–31.
- Dawson GJ et al. Detection of long-lasting antibody to hepatitis E virus in a US traveler to Pakistan. *Lancet*, 1992, 340:426–7.
- Heath TC et al. Locally acquired hepatitis E in the Northern Territory of Australia. *Medical journal of Australia*, 1995, 162:318–9.
- Tsega E et al. Acute sporadic viral hepatitis in Ethiopia: causes, risk factors, and effects on pregnancy. *Clinical infectious diseases*, 1992, 14:961–5.
- Nanda SK et al. Protracted viremia during acute sporadic hepatitis E virus infection. *Gastroenterology*, 1995, 108:225–30.
- Schlauder GG et al. Viraemia in Egyptian children with hepatitis E virus infection. *Lancet*, 1993, 341:378.
- Dawson GJ et al. Solid-phase enzyme-linked immunosorbent assay for hepatitis E virus IgG and IgM antibodies utilizing recombinant antigens and synthetic peptides. *Journal of virological methods*, 1992, 38:175–86.
- Gessoni G et al. Hepatitis E virus infection in north-east Italy: serological study in the open population and groups at risk. *Journal of viral hepatitis*, 1996, 3:197–202.
- Arankalle VA et al. Hepatitis E virus: can it be transmitted parenterally? *Journal of viral hepatitis*, 1999, 6:161–4.
- Arankalle VA et al. Retrospective analysis of blood transfusion recipients: evidence for post-transfusion hepatitis E. *Vox sanguinis*, 2000, 79:72–4.
- Ariyegan M et al. Hepatitis E epidemic in Iran. *Journal of Medical Council of Islamic Republic of Iran*, 1998, 15:139–43.
- Zali MR et al. Seroprevalence of hepatitis E in Nahavand, Iran: a population-based study. *Proceedings of the Digestive Dis-*

- eases week, 15–19 May 2004, New Orleans, USA.
15. Mast EE et al. Prevalence of and risk factors for antibody to hepatitis E virus seroreactivity among blood donors in Northern California. *Journal of infectious diseases*, 1997, 176:34–40.
 16. Mateos ML et al. Hepatitis E virus: relevance in blood donors and risk groups. *Vox sanguinis*, 1999, 76:78–80.
 17. Ritter DA et al. A seroprevalence study of hepatitis E in Europe and the Middle East. *Viral hepatitis and liver diseases*, 1994, 432–4.
 18. Arankalle VA et al. Age-specific prevalence of antibodies to hepatitis A and E viruses in Pune, India, 1982 and 1992. *Journal of infectious diseases*, 1995, 171:447–50.
 19. Bernal W et al. A community prevalence study of antibodies to hepatitis A and E in inner-city London. *Journal of medical virology*, 1996, 49:230–4.
 20. Thomas DL et al. Epidemiology of hepatitis E virus infection in Turkey. *Lancet*, 1993, 341:1561–2.
 21. Hyams KC et al. Hepatitis E virus infection in Peru. *Clinical infectious diseases*, 1996, 22:719–20.
 22. Nanda SK et al. Protracted viremia during acute sporadic hepatitis E virus infection. *Gastroenterology*, 1995, 108:225–30.
 23. Wang J et al. Hepatitis E virus and post transfusion hepatitis. *Journal of infectious diseases*, 1994, 169:229–30.
 24. Mannucci PM et al. Low risk of transmission of hepatitis E virus by large-pool coagulation factor concentrates. *Lancet*, 1994, 343:597–8.
 25. Clayson ET et al. Viremia, fecal shedding, and IgM and IgG responses in patients with hepatitis E. *Journal of infectious diseases*, 1995, 172:927–33.