Short Communication

Seroprevalence of IgG antibodies to hepatitis E in urban and rural southern India

Rosario Viveka, George M. Chandy, David W. Brown, Gagandeep Kang

Department of Gastrointestinal Sciences, Christian Medical College, Vellore, Tamil Nadu 632004, India

Virus Reference Department, Centre for Infections, Health Protection Agency, 61, Colindale Avenue, London NW9 5HT, UK

Article history:
Received 3 May 2009
Received in revised form 10 July 2009
Accepted 10 July 2009
Available online 2 September 2009

Keywords:
Hepatitis E virus
IgG antibodies
Seroprevalence
Rural populations
Urban populations
India

Abstract

Hepatitis E virus (HEV) is an important cause of sporadic and epidemic hepatitis E infection in northern India. Sera, collected from different age groups in rural (n = 1144) and urban (n = 1135) areas using a probability proportional to size survey, were tested using an ELISA for IgG antibodies. Antibodies increased with age in both populations, but the urban population had higher exposure in all age groups (Mann-Whitney U test, P < 0.001 for all age groups except children <5 years). These results indicate that urban populations with higher density and common water supplies may be at greater risk of hepatitis E.

© 2009 Royal Society of Tropical Medicine and Hygiene. Published by Elsevier Ltd. All rights reserved.

1. Introduction

Hepatitis E virus (HEV) is an important cause of large epidemics of acute hepatitis in South Asia. In northern India, where there are many epidemics and sporadic HEV cases, the IgG antibody levels are as high as 60% in the 0–10-year age group, but no other studies have found similar rates. Our study compared HEV exposure in rural and urban populations for the first time in southern India.

2. Materials and methods

2.1. Population surveys and collection of sera

A population proportional to size survey was carried in 1999 and 2000, in order to collect representative serum samples from healthy rural and urban populations aged between 1 and 40 years in and around Vellore town for a study on congenital rubella.

2.1.1. Rural community survey

Based on the 1999 census, villages were divided into two strata: ≤2000 people and >2000 people. Thirty households in 20 clusters were selected in each stratum using probability proportional to size (PPS). Compliance with sample collection was 94.8%.

The four age groups of pre-school, school age, young adult and reproductive-age adults comprised ages 1–5, 6–15, 16–25 and 26–40, respectively.

2.1.2. Urban community survey

The 1999 census of Vellore municipality was used to select 12 households in 80 clusters (streets) by PPS, with 40 clusters each from streets with a population size of ≤556 or >556. Compliance with sample collection was 87.7%. The serum samples were as described for the rural population.
Table 1
Percent positivity for anti-hepatitis E virus IgG antibodies, determined by ELISA in different age groups from urban and rural populations in Vellore

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Urban population</th>
<th>Rural population</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. positive/no.</td>
<td>No. positive/no.</td>
</tr>
<tr>
<td></td>
<td>tested (%)</td>
<td>tested (%)</td>
</tr>
<tr>
<td>1–5</td>
<td>4/138 (2.9)</td>
<td>1/174 (0.6)</td>
</tr>
<tr>
<td>6–15</td>
<td>31/350 (8.9)</td>
<td>12/358 (3.4)</td>
</tr>
<tr>
<td>16–25</td>
<td>77/326 (23.6)</td>
<td>28/304 (9.2)</td>
</tr>
<tr>
<td>26–40</td>
<td>114/321 (35.5)</td>
<td>63/308 (20.5)</td>
</tr>
</tbody>
</table>

Cut-off = average optical density value of negative control – average optical density value of blank wells + 0.500.

2.2. ELISA

Serum specimens were tested using HEV-antigen-coated plates purchased from Genelabs Diagnostics, Singapore (presently MP Bio), which has four short recombinant proteins derived from the 3’ termini of open reading frame (ORF) 2 (42 amino acids) and ORF3 (33 amino acids) from Burmese and Mexican prototype sequences. Although the IgM kit was commercially available, no IgG assay was being marketed, and the manufacturer agreed to provide coated plates for the IgG assay. The manufacturer’s instructions for washing, detection and calculation of cut-off value were followed. The in-house IgG positive control, included on each plate, was serum from a patient who was icteric and positive for anti-HEV IgM 6 months earlier. The in-house negative control was serum from a child previously tested and found to be negative for anti-HEV IgM and IgG. Internal quality control was performed using a Shewhart chart.

2.3. Statistical analysis

Sample sizes for the four age groups assumed a prevalence of 5, 8, 25 and 25% with a precision of ± 3%. Data analysis used SPSS version 11 (SPSS Inc., Chicago, IL, USA).

3. Results and Discussion

In total, 1144 serum samples from rural areas and 1135 samples from urban areas were tested. Using the ELISA cut-off, the proportion of individuals that could be considered positive for antibodies are shown in Table 1. The proportion of individuals positive for anti-HEV IgG was significantly higher in the urban population than in the rural population ($P < 0.001$).

The results of our study clearly show a higher prevalence of antibodies to HEV in the urban population, starting early and persisting through all age groups. These findings indicate that exposure to, and therefore the circulation of, HEV is likely to be higher in urban dwellers than in the rural population in southern India. As with other enterically transmitted pathogens, asymptomatic infections occur and can be a mechanism for persistence in the general population.

An age-specific rise in prevalence has been reported from India and other developing countries. Although both hepatitis A virus and HEV are enterically transmitted, antibody prevalence appears to be very different, either because antibodies to HEV do not persist or because assays are inadequate. The low prevalence in young children in this study compared with 64% in a report from northern India, using an Abbott anti-HEV ELISA, may be due to varying epidemiological conditions and/or due to differences in the diagnostic techniques or kits.

In an earlier study from Vellore, in which serum samples from blood donors, antenatal women and pre-operative patients from southern Indian states were tested for exposure to HEV, an age-related increase in HEV exposure was observed, but the prevalence was lower in all age groups. This may be due to a difference in hospital- versus community-based sampling. In this study, the higher rates of exposure in urban areas were evident even in young children, thus indicating that exposure to HEV is likely to be influenced by the urban environment. It has been suggested that HEV may also have a zoonotic mode of transmission, although this does not appear to be the case in India, where HEV strains in swine and other animals have been shown to be different from those seen in humans.

The data presented here show that rural areas, where contact with animals would be expected to be greater, had lower seroprevalence than urban areas.

Authors’ contributions: All the authors were involved in designing the study protocol and data analysis and interpretation; MRV collected the data and wrote the first draft; GK revised the manuscript. All authors contributed to and read and accepted the final manuscript. GK and MRV are guarantors of the paper.

Funding: Funding for the study was received from the ICMR Advanced Centre for Liver Diseases, New Delhi, India.

Conflicts of interest: None declared.

Ethical approval: The study protocol was approved by the Institutional Research Board, Christian Medical College, Vellore, India and all participants gave written informed consent.

References