

Epidemiology of Hepatitis E Virus Infection in Western India

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Background and Aims: Hepatitis A virus infection (HAV) has a world-wide distribution and affects infants and young children in developing countries but epidemics are rare; whereas hepatitis E virus infection (HEV) is restricted to tropical countries and affects older children and young adults and epidemics are common. Exposure rates for HEV are different in various regions of India and different in various socioeconomic groups of the country. In previous series from Western India, age-specific HEV exposure rates were as follows: a. In 1993 (Mumbai) - 5% at age < 20 years and 17.5% at age > 20 years; b. In 1998 (Pune) - 5.6% at age < 25 years and 35.3% at age > 25 years.

Methods: In December 2003, an epidemiological survey (total number= 1163 persons, mean age= 28.9 ± 9.2 years, male: female ratio= 0.9: 1, middle and high socio-economic class) was carried out in two western railway residential colonies of Mumbai. To detect the exposure rate for HEV and HAV, serological tests for IgG antiHEV and IgG antiHAV were carried out in all individuals. An epidemic of HEV mainly affecting middle or high socio-economic class was noted after 10 months of this survey (from October 2004 to February 2005) in Mumbai, India. During the HEV epidemic, a total of 140 patients were visited at Bombay Hospital (mean age= 35 ± 12 years, male: female ratio= 1.2: 1). For comparison, 140 patients (mean age=32.44 ± 9 years, male: female=0.9: 1, middle and high socio-economic class) with sporadic HEV, visited from February 1999 to October 2004, were analyzed. These data were analysed using chi square test.

Results: Overall exposure rates for HEV and HAV were 35.76% and 87.18% respectively. Age-specific exposure rates for HEV and HAV were as follows, respectively: age groups- 0-10 years: 17.75% and 59.17%; 11-20 years: 25.08% and 86.76%; 21-30 years: 41.71% and 94.65%; 31-40 years: 43.28% and 94.02%, 41-50 years: 42.02% and 93.08%; 51-60 years: 57.42% and 94.05%; and > 60 years: 40% and 96.6%. Age-specific exposure rates (HEV and HAV) for the age group ≤ 20 years (456 persons) were 22.36% and 76.53%, and for the age group > 20 years (707 persons) were 44.41% and 94.05%, respectively. Age distribution of epidemic and sporadic HEV, respectively, was as follows: age group ≤ 20 years-12.14% and 17.85%; 21-40 years: 58.57% and 53.57%; and > 40 years: 28.57% and 27.85%.

Conclusions: HEV age-specific exposure rates suggest the presence of high endemicity and age-infection curve parallel to HAV, but at a lower level of seroprevalence. Exposure rates of HEV have increased significantly in all age groups as compared to previous data, especially in the age group < 20 years. Age distribution of cases in epidemic and sporadic HEV is similar.

Keywords: Seroepidemiology, Age-Specific Seroprevalence, Hepatitis A, Hepatitis

Introduction

Hepatitis A virus infection (HAV) and hepatitis E virus infection (HEV) are enterically transmitted viral diseases of great public health importance in the developing countries like India. HAV has a world-wide distribution and affects infants and young children in developing countries but its epidemics are rare; whereas HEV is restricted to tropical countries and affects older children and young adults and its epidemics are

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common (1-3). In developing countries like India, HAV and HEV both are endemic. Exposure rates over a period of time are different in different parts of the country and in different socioeconomic groups (1). Comparing the epidemiology of HEV in the countries with similar environmental conditions contributing to feco-oral transmission shows that HAV is universally acquired by the age of 5 in both India and Egypt, whereas HEV most commonly infects young adults. Seroprevalence of HEV is only 30 to 40% in the adult population in India, whereas it exceeds 60% by the age of 10 in Egypt (2). It is unknown why age-specific seroprevalence rates of HAV and HEV are dissimilar in the same country and why antibody acquisition rates are different in different countries with similar environmental conditions.

Previously in India, Age-specific prevalence of HAV and HEV in Pune was checked in 1982, 1992 and 1998 (1, 4). Similar studies were carried out in Andaman-Nicobar islands in 1989 and 1999 (5). We have reported age-specific HEV prevalence in Mumbai in the population < 40 years of age in 1993 (3). To document changes in the pattern of age-specific prevalence rates of HAV and HEV, this epidemiological study was planned.

Materials and Methods

Over a period of two months i.e. in December 2003 and January 2004, an epidemiological survey was carried out in two western railway residential colonies of Mumbai (Matunga and Bandra), India. In residents of these colonies, detailed clinical history and examination, anthropometry, laboratory tests (aminotransferase levels and fasting blood sugar), ultrasonography of abdomen and viral markers including HBsAg, total antiHBc, antiHBs, anti HCV, IgG antiHAV and IgG antiHEV were carried out. A total of 1163 persons (Mean age= 28.9 ± 9.2 years, Age range= 9 months to 93 years, Male: female ratio= 0.9:1, Socio-economic class= middle and high, Ethnicity= Asian Indian) were screened during the survey. Age-specific exposure rates for HAV and HEV in the study population were defined based on IgG antiHAV and IgG antiHEV.

An epidemic of acute HEV mainly affecting middle or high socio-economic class was noted after 10 months of this survey (from October 2004 to February 2005) in Mumbai, India. During the HEV epidemic, a total 140 patients (Mean age= 35 ± 12 years, Male: female ratio= 1.2: 1, Socio-economic class= middle and high, Ethnicity= Asian Indian)

were visited at Bombay Hospital, Mumbai. For comparison, 140 consecutive patients (Mean age=32.44 ± 9 years, Male: female=0.9: 1, socio-economic class= middle and high, Ethnicity= Asian Indians) with sporadic acute HEV, visited from February 1999 to October 2004, were analyzed.

Statistical analysis was carried out using chi square test.

Results

Age distribution and age-stratified seroprevalence of HEV and HAV are demonstrated in table 1 and in figures 1 and 2. Overall exposure rates for HEV and HAV were 35.76% and 87.18% respectively. Age-specific exposure rates for HEV and HAV were as follows, respectively: age groups- 0-10 years: 17.75% and 59.17%; 11-20 years: 25.08% and 86.76%; 21-30 years: 41.71% and 94.65%; 31-40 years: 43.28% and 94.02%, 41-50 years: 42.02% and 93.08%; 51-60 years: 57.42% and 94.05%; and > 60 years: 40% and 96.6%. Age-specific exposure rates (HEV and HAV) for the age group ≤ 20 years (456 persons) were 22.36% and 76.53%, and for the age group > 20 years (707 persons) were 44.41% and 94.05%, respectively. There was an increase in

Table 1. Comparative Exposure Rate of HEV and HAV according to Age: present series.

Age, years	Number (%)	IgG antiHEV +ve (%)	IgG antiHAV +ve (%)
0-10	169 (14.53)	30 (17.75)	100 (59.17)
11-20	287 (24.67)	72 (25.08)	249 (86.76)
21-30	187 (16.07)	78 (41.71)	177 (94.65)
31-40	201 (17.28)	87 (43.28)	189 (94.02)
41-50	188 (16.16)	79 (42.02)	175 (93.08)
51-60	101 (8.68)	58 (57.42)	95 (94.05)
>60	30 (2.56)	12 (40)	29 (96.66)

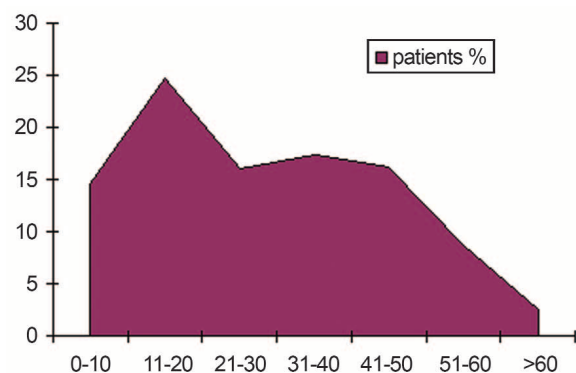


Figure 1. Age distribution in the study population of epidemiological survey.

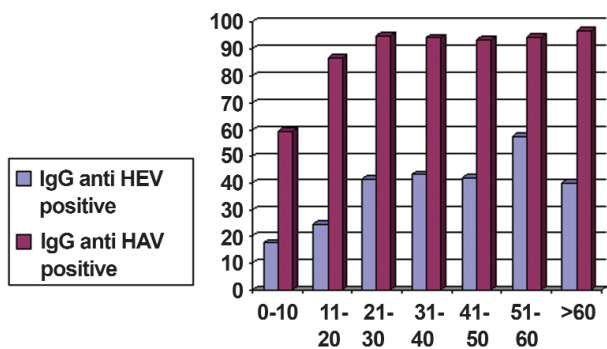


Figure 2. Comparative Exposure Rate of HEV and HAV According To Age: Present Series.

the seroprevalence of both HEV and HAV with the increase in age. In all age groups, seroprevalence of HEV was significantly lower than that of HAV.

Comparison of age distribution for epidemic and sporadic acute HEV cases is shown in table 2 and figure 3. Age distribution of epidemic and sporadic HEV, respectively, was as follows: age group ≤ 10 year: 0.71% and 0.71%; ≤ 20 years: 12.14% and 17.85%; 21-40 years: 58.57% and 53.57%; and > 40 years: 28.57% and 27.85%. Maximum number

Table 2. Comparison of age distribution in epidemic and sporadic HEV cases and comparative exposure rate of HEV in community (epidemiological survey).

Age group	IgG antiHEV + ve (%) - exposure/1163 population	Epidemic HEV no (%) /140 patients	Sporadic HEV no (%) /140 patients
0-10	30 (17.75)/169	1 (0.71)	1 (0.71)
11-20	72 (25.08)/287	16 (11.42)	24 (17.14)
21-30	78 (41.71)/187	51 (36.42)	56 (40)
31-40	87 (43.28)/201	31 (22.14)	19 (13.57)
41-50	79 (42.02)/188	18 (12.85)	23 (16.42)
51-60	58 (57.42)/101	12 (8.57)	11 (7.85)
>60	12 (40)/30	10 (7.13)	5 (3.57)

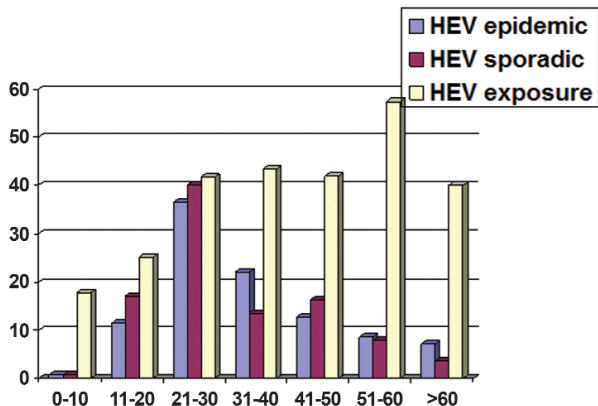


Figure 3. Comparison of age distribution in epidemic and sporadic HEV cases and comparative exposure rate of HEV in community (epidemiological survey).

of cases of both epidemic (36.42%) and sporadic (40%) acute HEV were in the age group of 21-30 years. In the epidemiological survey, there was a significant rise in the seroprevalence of HEV in the age group 21-30 years (41.71%) compared to the age group 11-20 years (25.08%).

Discussion

India is considered to be a hyperendemic region for HAV (6). In the present population-based study, the overall seroprevalence of HAV is high (87.18%) and has remained almost unchanged in the age group >10 years as compared to previous series (1, 4, 5, 7). But HAV seroprevalence in the age group < 10 years in the present study (59.17%) has declined to the low endemicity region pattern, which may be important in forming future strategies for HAV vaccination. Similar results were also seen in a population-based study from Andaman-Nicobar (60% in 1999) (5). In the present study, the trend of the decrease in the seroprevalence of young children was in accordance with shifting patterns of seroprevalence over the past 20 years seen in South-east Asia and China reflecting improved living standards and environmental hygiene (8). This was in sharp contrast to previous series, where seroprevalence in the age group < 10 years was reported to be above 80% (1, 4, 7, 9).

In most disease-endemic areas like India, HEV seroprevalence is as low as 5% in the population under the age of 10, but increases to 10-40% among adults > 25 years of age (1, 10). The results of the present epidemiological study showed the presence of an overall high endemicity of HEV infection (35.68%) and a significantly lower seroprevalence in the age groups <10 years and <20 years as compared to any age group > 20 years. Compared to other series, the higher rate of HEV seroprevalence in the population under the age of 10 was seen in the present series (17.75%), in series from Andaman-Nicobar (32.9%) (5) and in one from North India (>60%) (11). This was in sharp contrast to series from Pune, where age >15 years was strongly associated with HEV infection (1). These differences might be due to either varying environmental conditions in different geographical areas or the differences in the diagnostic tests used.

Age distribution of acute HEV cases, both epidemic and sporadic, is almost similar and remains comparable to previous data (12). HEV mainly affects young adults of 15-40 years of age and relatively spares children (10). In India, HEV is responsible for 50-70% of all cases of sporadic acute

viral hepatitis (13, 14), and also is responsible for large outbreaks with source of infection mainly being contaminated water supplies (2, 10). The occurrence of large epidemics of HEV in disease-endemic areas, as it was the case in the present study, suggests the possibility of doubtful protection from the antibody, gradual decline in the protective level of the antibody or infection from divergent strains of the virus (4, 10). However, previous studies have shown that antibodies do protect against the disease (15), HEV virus strains involved in multiple outbreaks in different parts of India are closely related (16), and anti HEV titres persist for a long time (15). The reason for this phenomenon remains unknown.

Age-specific exposure rates for HEV and HAV were almost parallel to each other as seen in figure 2. However, there was a lower level of endemicity for HEV compared to HAV. In table 3 and figure 4 (A and B), results of the epidemiological survey are compared with results of previous Indian series. As compared to previous series from Mumbai, a city in western India, there was a significant rise in exposure rates for HEV in both age groups (<20 and >20 years) (3). This data was similar to data from Andaman-Nicobar (islands of East Indian coast), but was different from Pune (another western Indian city). In series from Andaman-Nicobar, data of 1989 and 1999 suggested a significant rise in the age-stratified seroprevalence of HEV in all age groups: <10 years: 0% and 32.9%; 11-20 years:

15.2% and 42.5%; 21-30 years: 23.5% and 48.9% and >30 years: 31% and 60.4% respectively (5). Similar data for HAV suggested a higher seroprevalence than HEV (Table 4, Fig. 4) (5). In the series from Pune, data of 1982, 1992 and 1998 suggested that there was no significant change in exposure rates for HEV in age groups <15 and >15 years (1, 4). There was a significant drop in the seroprevalence of HEV in the age group 11-15 years in 1998 (6.3%) as compared to 1982 (16%) and in the age group 16-25 years in 1998 (7.8%) as compared to 1992 (40%) (1). There was no change in exposure rates of HAV in the age group <10 years and the age group >16 years, but in the age group 11-15 years there was a significant drop in the seroprevalence of HAV in 1998 (87.9%) as compared to 1982 (99%) and 1992 (99%) (1, 4); this decline in HAV seroprevalence was more significant in high socio-economic status. Age >15 years, lower socio-economic status and use of well water were associated with HEV seroprevalence in Pune (1). Although the major route of transmission of HAV and HEV is feco-oral route and poor sanitation and contaminated food/water supplies are frequently cited as source of infection; changes in exposure rates of HAV and HEV in all age groups suggest either a difference in mode of transmission (poor person-to-person transmission for HEV, but strong water/ food related transmission for HEV; possibility of zoonotic or parenteral transmission for

Table 3. Comparison to Previous Series of Age Specific Exposure of HEV (1-4).

Year of study	1982	1992	1998	Year of study	1989	1999	1993	2004
Study centre	Pune	Pune	Pune	Study centre	Andaman-Nicobar	Andaman-Nicobar	Mumbai	Mumbai
Subjects	485	664	4091	Subjects	240	814	80	1163
<15 years	8.5%	7.7%	5.0%	<20 years	13.42%	40.2%	5%	22.36%
>15 years	25.1%	31.1%	22.4%	>20 years	28.47%	55.67%	17.5%	44.41%

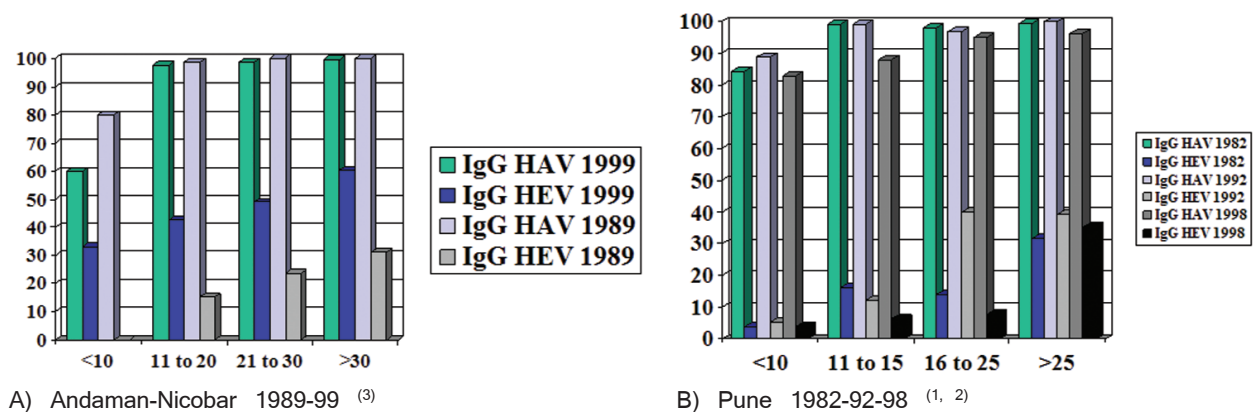


Figure 4. Comparative Exposure Rates of HAV and HEV according to age: Previous Series.

Table 4. Comparative seroprevalence rate of HEV and HAV in previous series.

Seroprevalence %, year of study	Age groups, years			
	<10	11-20	21-30	>30
Andaman-Nicobar				
HEV 1989	0	15.2	23.5	31
HEV 1999	32.9	42.5	48.9	60.4
HAV 1989	80	98.7	100	100
HAV 1999	60	97.6	98.6	99.7
Pune				
HEV 1982	3.7	16	14	31.7
HEV 1992	5.2	12	40	39.2
HEV 1998	3.8	6.3	7.8	35.3
HAV 1982	84.4	99	98	99.3
HAV 1992	88.8	99	97	100
HAV 1998	82.7	87.9	95.2	96.3

HEV) or a difference in reservoirs of infection (swine, pig, deer, lamb, sheep, cattle, rodents etc.) or a difference in the characteristics of virus (virulence-infectivity/ viability/ transmissibility) or a difference in sensitivities and concordance rates of various anti HEV assays (2, 10, 17).

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