

RESEARCH ARTICLE

## Feco-orally transmitted viral hepatitis in a tertiary care hospital in urban India

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### ABSTRACT

**Objective:** To investigate the magnitude and pattern of hepatitis viral markers in feco-orally transmitted acute viral hepatitis with their relation to age and sex.

**Methods:** This prospective study was carried out in two groups of subjects including the study group of 600 patients with clinically suspected infectious hepatitis and control group of 200 patients showing no clinical evidence of acute infectious hepatitis. Serum samples were tested for the presence of anti-hepatitis A virus (HAV) IgM and Anti-hepatitis E virus (HEV) IgM antibodies using commercial ELISA test kits.

**Results:** The seroprevalence rate of feco-orally transmitted acute viral hepatitis was 11.8% in the study group compared to 4.5% in the control group ( $p=0.007$ ). The prevalence of anti-HAV IgM was 8.3% while that of anti-HEV IgM was 3.5% in the same group. Maximum seropositivity of anti-HAV IgM was seen in 0-10 years of age in the study group (16.8%) followed by 11-20 years (7.2%) and 21-30 years (4.6%). In the study group, the maximum seropositivity of anti-HEV IgM was seen in 21-30 years (10.7%) followed by 31-40 years (2.9%), 11-20 years (2.7%) and 0-10 years (0.9%). Male predominance was seen in both types of acute viral hepatitis.

**Conclusion:** While HEV infection was predominantly seen in young adults, HAV infection was predominantly a childhood infection and its prevalence decreased by age. Being enterically transmitted viral diseases it is recommended that immunization programs, public awareness measures for hygiene and safe drinking water should be consolidated. *J Microbiol Infect Dis 2013;3(4): 181-185*

**Key words:** Acute hepatitis, hepatitis A virus, hepatitis E virus, IgM seroprevalence

## Hindistan kentsel kesimde bir üçüncü basamak hastanesinde fekal-oral yolla bulaşan viral hepatit

### ÖZET

**Amaç:** Fekal-oral yolla bulaşan akut viral hepatit belirleyicilerinin sıklığı ve özellikleri ile yaş ve cinsiyet ilişkilerinin belirlenmesi.

**Yöntemler:** Bu ileriye dönük araştırma klinik olarak infeksiyöz hepatitten şüphelenilen ve 600 hastayı içeren çalışma gurubu ve akut infeksiyöz hepatit kliniğine sahip olmayan ve 200 hastayı içeren kontrol gurubunda yapıldı. Hasta ve kontrol gurubuna ait serum örnekleri anti-hepatitis A virus (HAV) IgM ve anti-hepatitis E virus (HEV) IgM antikorlarının varlığı açısından ticari ELISA test kitleri ile tarandı.

**Bulgular:** Çalışma gurubunda akut viral hepatit seroprevalansı % 11,8, kontrol gurubunda ise % 4,5 olarak belirlendi ( $p=0,007$ ). Aynı gurupta anti-HAV IgM prevalansı % 8,3 ve anti-HEV IgM prevalansı %3,5 idi. Çalışma gurubunda en fazla anti-HAV IgM seropozitifliği 0-10 yaş gurubunda (%16,8), daha sonra 11-20 yaş gurubunda (%7,2) ve 21-30 yaş gurubunda (% 4,6) idi. Yine çalışma gurubunda en fazla anti-HEV IgM pozitifliği 21-30 yaş gurubunda (% 10,7) idi ve bu gurubu 31-40 yaş gurubu (% 2,9), 11-20 yaş gurubu (% 2,7) ve 0-10 yaş gurubu (% 0,9) takip ediyordu. Her iki tip akut viral hepatit için erkekler ağırlıktaydı.

**Sonuç:** HEV infeksiyonu ağırlıklı olarak genç erişkin yaş gurubunda görülmekte iken, HAV infeksiyonu ağırlıklı olarak çocuk yaş gurubunda görülmekte ve prevalansı da yaşla birlikte azalmakta idi. Bu viral enfeksiyonların barsak yoluyla bulaşma özelliğinden dolayı aşılama programları ve halkın hijyen ve sağlıklı su tüketimi konusunda bilgilendirilmesinin gerektiğini düşünüyoruz.

**Anahtar kelimeler:** Akut hepatit, hepatit A virus, hepatit E virus, IgM seroprevalans

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Received: 06.04.2013 Accepted: 14.07.2013

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## INTRODUCTION

Hepatitis A and hepatitis E are enterically transmitted viral illnesses of significant public health importance. Hepatitis A virus and Hepatitis E virus are both devoid of a lipid envelope and are stable when they are secreted from infected liver cells into the bile.<sup>1,2</sup> They gain entry to the intestinal tract through this route and are spread by a fecal-oral mode.<sup>3</sup> They continue to be significant public health problem in India despite improving sanitation, health awareness and socio-economic conditions. Hepatitis A causes subacute disease of global prevalence affecting children which occurs sporadically or as outbreaks while Hepatitis E is the commonest cause of feco-orally transmitted viral hepatitis in adults occurring as epidemics and point source outbreaks.<sup>4,5</sup> India is hyper-endemic for Hepatitis A and E.<sup>6</sup>

The prevalence of feco-orally transmitted viral hepatitis still remains debatable in developing and developed countries with only few prevalence studies from urban northern India on exposure and infection. There is paucity of data regarding prevalence of different markers of hepatitis and also their age and sex related prevalence.<sup>7</sup> As most of the cases of enterically transmitted viral hepatitis are preventable, the burden of the disease could be reduced to a considerable extent, if seroprevalence of different viruses are better known in different age groups.<sup>8</sup> For this reason, in this report we investigated the seroprevalence of acute viral hepatitis A and acute viral hepatitis E in an urban area of Northern India.

## METHODS

This prospective study was conducted in the Department of Microbiology at Lady Hardinge Medical College, New Delhi, which is a tertiary care hospital in urban Northern India, over a period of one year from January 2008 to December 2008. Subjects were divided into 2 groups. Group 1 was the study group of 600 patients with clinically suspected infectious hepatitis attending the outpatient department of various specialties in Kalawati Saran and Smt. Sucheta Kriplani Hospital, New Delhi both attached to Lady Hardinge Medical College. Group 2 was the control group of 200 patients showing no clinical evidence of acute infectious hepatitis.

### Inclusion criteria

- Recent onset of jaundice (<6 months) defined by serum bilirubin level >2.5 mg/dl and/or increase in

serum transaminases >5 times the upper limit of normal.

- Fever in absence of chronic liver disease or past history of jaundice.

Exclusion criteria:

- History of chronic liver disease or past history of jaundice with duration of illness more than 6 months.

- Acute fatty liver of hepatitis or alcoholic hepatitis or intrahepatic cholestasis.

All the serum samples obtained from the subjects (study and control group) were tested for the presence of anti-hepatitis A virus (HAV) IgM and anti-hepatitis E virus (HEV) IgM using commercially available enzyme-linked immunosorbent assay kits (ELISA; Biokit®, Barcelona, Spain). Informed consent and institutional review board approval was taken from ethics committee for the study bearing protocol number MIC 07/312.

We used SPSS Ver. 10.0 (SPSS Inc. Chicago, Illinois) for the statistical analysis. The means of continuous variables were compared using the Student's t-test and categorical variables were compared using the Chi square test and the Fisher's exact test, as appropriate. A p value of less than 0.05 was considered to be significant.

## RESULTS

The study group was divided age wise i.e. 0-10 years, 11-20 years, 21-30 years, 31-40 years and >40 years. The study group comprised of 362 males and 238 females. The overall male to female ratio was 1.5:1 and thus a male preponderance was seen in study group. The control group (n=200) comprised of 121 males and 79 females with overall male to female ratio of 1.5:1. The mean age in the study group was 20.2 ± (SD) 15.2 years while in the control group it was 19.65±14.8 years. The difference between the mean age of study and control group was not statistically significant (p=0.46).

Overall 71 (11.8%) cases were positive for enterically transmitted viral hepatitis in the study group while 9 (4.5%) were positive in control group (p=0.007). HAV infection was seen in 50 (8.3%) cases in the study group while 4 (2%) cases were seen in the control group (p=0.002). HEV infection was seen in 21 (3.5%) cases in the study group while 5 (2.5%) cases were seen in the control group (p=0.735; Table 1).

**Table 1.** Comparison of the overall seroprevalence of acute viral hepatitis A and E between the study and control groups \*

Serological markers	Study Group, n=600 (%)			Control Group n=200 (%)			p-value
	Male	Female	Total	Male	Female	Total	
Anti-HAV IgM	32 (8.8)	18 (7.5)	50 (8.3)	3 (2.4)	1 (1.2)	4 (2)	0.002
Anti-HEV IgM	13 (3.4)	8 (3.3)	21 (3.5)	5 (4.1)	0	5 (2.5)	0.735
Total	45 (7.5)	26 (4.3)	71 (11.8)	8 (4)	1 (0.5)	9 (4.5)	0.007

\*Data presented as n (%).

On observing age wise seropositivity of HAV, it was found that maximum seropositivity of anti-HAV IgM was in 0-10 years of age group in the study group (16.8%) followed by 11-20 years (7.2%) and 21-30 years (4.6%). When compared to controls the anti-HAV IgM seropositivity was significantly higher in the study group in 0-10 years of age group ( $p=0.002$ ). There was decrease in seroprevalence of HAV with an increase in age (Table 2).

**Table 2.** Comparison of distribution of hepatitis A virus seropositivity by age between the study and control groups \*

Age groups	Study Group n/N (%) (N=600)	Control Group n/N (%) (N=200)	p-value
0-10 years	36/214 (16.8)	2/71 (2.8)	0.002
11-20 years	8/110 (7.2)	2/36 (5.5)	0.434
21-30 years	6/130 (4.6)	0/43	0.418
31-40 years	0/67 (0)	0/43	-
> 40 years	0/71 (0)	0/43	-
Total	50/600 (8.3)	4/600 (2)	0.002

\*Data presented as n/N (%), n/N: number of test positive/number of tested.

## DISCUSSION

Enterically transmitted acute viral hepatitis is a global public health concern associated with substantial morbidity and mortality.<sup>9-10</sup> In our study, HAV was the major cause of feco-orally transmitted viral hepatitis. Seroprevalence of anti-HAV IgM recorded by different authors in and around Delhi in recent years is between 2.3% to 11.4%.<sup>11-15</sup> Kar et al. found the seropositivity of anti-HAV IgM in 113 patients with acute viral hepatitis as 3.5%.<sup>11</sup> Das et al. reviewed 75 patients with acute viral hepatitis and found the overall infective pathology attributed to HAV as 5%.<sup>12</sup> Our findings were comparable with the recent studies and we found that the seroprevalence of acute HAV infection as 8.3%. This high incidence could be

On observing age wise seropositivity of HEV it was found that maximum seropositivity of anti-HEV IgM was in the 21-30 years (10.7%) age group in the study group followed by 31-40 years (2.9%), 11-20 years (2.7%) and 0-10 years (0.9%; Table 3). In the control group the maximum seropositivity of HEV was seen in the 31-40 years (4.5%) age group followed by 0-10 years (2.8%), 11-20 years (2.7%) and 21-30 years (2.3%). Anti-HEV IgM seropositivity was significantly higher in the study group in 21-30 years of age group then that of controls (10.7% vs. 2.3%;  $p=0.002$ ; Table 3).

**Table 3.** Comparison of distribution of hepatitis E virus seropositivity by age between the study and control groups \*

Age groups	Study Group n/N (%) (N=600)	Control Group n/N (%) (N=200)	p-value
0-10 years	2/214 (0.9)	2/71 (2.8)	0.080
11-20 years	3/110 (2.7)	1/36 (2.7)	0.770
21-30 years	14/130 (10.7)	1/43 (2.3)	0.042
31-40 years	2/67 (2.9)	1/22 (4.5)	0.094
> 40 years	0/79 (0)	0/28 (0)	-
Total	21/600 (3.5)	5/200 (2.5)	0.735

\*Data presented as n/N (%), n/N: number of test positive/number of tested

attributed to a constant increase in the population of Delhi. The increase in this population load leads to more than one third of the people residing below the poverty line with poor sanitation and low socioeconomic status. Water shortage, poor standard of living, fecal contamination of food and water are responsible for increased susceptibility for infection.

The seroprevalence rate of IgM anti HAV in apparently healthy population in our study was 2% (Table 1). There is paucity of data regarding the prevalence of IgM anti HAV in the general population. However, several authors have studied the pattern of anti-HAV IgG in healthy population.<sup>16,17</sup> On studying the trends of HAV infection in different age groups, it was found that as the age increased,

the seropositivity of HAV decreased so that none of the cases were positive in >30 years of age groups. Thus our study implied that HAV infection was the commonest cause of enterically transmitted acute viral hepatitis in childhood. Similar trends in age wise seropositivities of Hepatitis A virus were seen by Poddar et al.<sup>18</sup> who reviewed 197 children in less than 14 years of age group with acute viral hepatitis and found the prevalence of IgM anti HAV as 64.5%. Their finding was supported by the fact that population comprised only of children less than 14 years of age and HAV infection was predominantly seen in childhood. Kaur et al.<sup>14</sup> have also analyzed age wise seropositivity of HAV infection and they found that percentage positivity of anti-HAV IgM declined between childhood (3.1%) and adulthood (1.7%). Such trends showing a high incidence of HAV infection in less than 10 years of age is attributed to the fact that viral hepatitis A is predominantly an infection of childhood. The high prevalence rate in children is attributed to their susceptibilities to infection due to poor hygiene, overcrowding and poor sanitary conditions, when there is abundant shedding of HAV in the faeces. In the control group, maximum seropositivity was seen in 11-20 years of age group (5.5%) followed by 0-10 years group (2.8%). Some recent studies of Delhi have shown that epidemiological transition of HAV in India and concluded that the peak age of seroprevalence is shifting from 1st decade of life to 2nd and 3rd decades.<sup>13,19</sup> HAV infection is a vaccine preventable disease but in India, vaccination against HAV is still not included in the universal immunization program and also there are no recommended HEV vaccination strategies till date. Thus, target oriented measures should be undertaken and vaccination program should be consolidated for HAV.

The seroprevalence rate of anti-HEV IgM in our study was 3.5% while in the control group it was 2.5% (Table 1). No outbreak of acute hepatitis E was reported during the study period. Although some authors have shown that the high prevalence rates of anti-HEV IgM in and around Delhi during the recent years, our study showed comparatively low prevalence rates as compared to others.<sup>14</sup> This could be probably due to the fact that there was no outbreak of hepatitis reported during the course of our study. Secondly, our hospital is mainly a pediatric institution and more than 50% of the patients studied belonged to the pediatric age group. As HEV infection is most common in young adults and less number of adults was included in our study, this could be another reason for low prevalence rates of HEV in our study. Delhi is an endemic zone for HEV

and outbreaks have occurred from time to time.<sup>20,21</sup> HEV is widespread due to problems associated with increased size of population, population migration, poor sanitation and poor standards of living leading to increased susceptibilities to infection. Epidemics and point source outbreaks are common in rainy season when flooding leads to sewage contamination of drinking water.<sup>22</sup> Our study implied that HEV is predominantly an infection of adults. Many authors have shown similar results.<sup>23,24</sup> Mishra et al. studied 569 hospitalized patients suspected of acute viral hepatitis and recorded high seroprevalence rates in adults as compared to adolescents and children i.e. 5% in adults versus 12% in children.<sup>20,23</sup> Among the seropositive individuals, male preponderance was also noted similar to our results. The reason for increased trends of HEV infection with increased age could be due to the fact that symptomatic HEV infection is most common in young adults aged 15-40 years and is uncommon in children. Although HEV infection is frequent in children, it is mostly asymptomatic and anicteric, in children under nine years of age in endemic hepatitis. Similar trends were recorded by Tandon et al. who showed that HEV was more common in adults as compared to children.<sup>24</sup> HEV infection is usually a self-limiting disease with low rate of fulminant hepatic failure. However, when the infection occurred in pregnancy, the consequences are particularly disastrous. In our study, the only 15 pregnant women were recorded and none of them had seropositivity against HEV (data not shown).

In conclusion, both HAV and HEV infection are common causes of enterically transmitted acute viral hepatitis in the region and hence, it is recommended that measures for public awareness regarding the spread, better sanitation facilities, safe drinking water and proper collection, treatment and disposal of sewage should be undertaken to limit spread. We recommend that the vaccination programs should be intensified.

**Competing interest and funding:** The author declares no competing interest and funding.

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