

## Seroprevalence of Sporadic Acute Viral Hepatitis With Their Co-Infection At Tertiary Care Hospital

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**Abstracts:** Background: Viral hepatitis is one of the major causes of mortality & morbidity in developing countries. Present study was aimed to know the seroprevalence and co infection of the acute viral hepatitis caused by hepatitis A, hepatitis B, hepatitis C and hepatitis E virus from patient attending one of the largest tertiary care hospitals. Material and Methods: Study was carried out from May 2009 to June 2010 at our hospital. A total of 556 serum samples were tested for HBsAg, antibody for HCV, IgM antibody of HAV and HEV by ELISA method from the patients having clinical signs & symptoms of acute viral hepatitis. Statistical analysis: Chi square test was done and the association was considered to be statistically significant if  $p < 0.05$ . Results: Out of 556 suspected cases of acute hepatitis 281 were positive. Among the total positive cases, IgM anti HAV antibodies was 70 (24.91%), IgM anti HEV antibodies was 141 (50.18 %), HBsAg was 65 (23.13%) and HCV was 5 (1.78 %). Dual infection was seen in 14 (4.98 %) cases with 6 children cases. Among the HAV positive patients, 80% were children, In contrast to that HEV infection (63.1%) and HBsAg infection (61.5%) was common in young adult. HCV infection was found common in adults more than 20 years of age. Overall male was affected more than female. Conclusion: Sporadic HEV infection constitutes significant cause of the acute viral hepatitis. In the light of this result a nationwide survey is recommended to confirm this pattern in the other areas. As vaccine for HEV is not available, prevention in form of improvement of socio - economic and hygienic standards of the population is the better option [ Hetal S et al NJIRM 2012; 3(2) : 1-5]

**Key words:** Hepatitis A virus (HAV), Hepatitis B virus (HBV), Hepatitis C virus (HCV), Hepatitis E virus (HEV), co-infection

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**Introduction:** Viral hepatitis is a major public health problem throughout the world that affects several hundred millions of people. <sup>1</sup> It is a cause of considerable morbidity and mortality, both from acute infection and from chronic sequelae.<sup>2</sup> Acute viral hepatitis is a diffuse necroinflammatory infection of liver along with various systemic manifestations for a maximum duration of six months. The predominant etiological agents are HAV, HBV, HCV, HDV and HEV. Others like HGV, Cytomegalovirus (CMV), Herpes simplex virus, Epstein Barr virus and Yellow Fever virus account for only 1-2 per cent of all hepatitis causing viruses.<sup>3</sup> Till now six major viruses from Hepatitis A Virus to Hepatitis G Virus have been fully characterized, excluding Hepatitis F virus. <sup>4</sup> The epidemic of acute viral hepatitis (AVH) is a public health problem in India and most developing countries. This is mainly due to the poor hygienic and sanitary conditions of living environment, illiteracy and poverty. <sup>5</sup> Hepatitis B and non-A non-B (NANB) hepatitis, respectively are considered to contribute about one-third and

more than half of the acute sporadic cases of the viral hepatitis. <sup>6</sup> HEV accounts for about 50% of cases of sporadic acute hepatitis in India and epidemics have also been reported in Indian subcontinent, sub-Saharan Africa and Mexico. <sup>7</sup> Overall HAV accounts for 25% of clinically evident acute hepatitis worldwide, HBV has infected over 2 billion people worldwide with a carrier of 350 million. <sup>7</sup> It has been estimated that the global prevalence of Hepatitis C virus (HCV) infection is around 2%, with 170 million persons chronically infected with the virus and 3 to 4 million persons newly infected each year. <sup>8</sup> The exact prevalence of hepatitis viruses varies from country to country.

To the date, very few reports have addressed the prevalence of hepatitis A, B, C and E in India. The present study was undertaken to investigate the seropositivity of HBV, HCV, HEV, HAV in patients suspected clinically of having AVH. This will throw some light on the seropositivity of various types of

hepatitis and will try to help to define better preventive and curative measures.

**Material and Methods :** This is retrospective study. All the data were collected from the routine investigations done in our department. A total of consecutive 556 patients presenting with signs & symptoms of acute hepatitis and raised Liver Function Tests were taken as study group at our the largest tertiary care centre hospital in Ahmedabad, Gujarat, India from May 2009 to June 2010.

Three to five millilitres of blood sample was collected aseptically from each patient and centrifuged at 3000 rpm. Serum was separated within four hours of the collection and stored at -20° c in vials for testing by ELISA.

All were tested for IgM anti-HAV antibodies (ELISA, Immunovision, India – use HAV specific immuno-dominant recombinant antigen – with sensitivity >99% and Specificity 98%), IgM anti-HEV antibodies (ELISA, Smart Test, Israel – use HEV specific synthetic antigens encoding for conservative and immunodominant determinants – with sensitivity and specificity >= 98%), HBsAg (Advanced ELISA, Morepen, India – a sandwich immunoassay which uses immobilised specific monoclonal antibodies to HBsAg with sensitivity 0.5 ng/ml and specificity 99.9% ) and HCV antibodies (Microlisa - 3<sup>rd</sup> generation ELISA, J.Mitra, India - use structural and non-structural antigen of HCV-with sensitivity 100% and Specificity 99.73%). All tests were carried out using procedures as per the manufacturers' instruction and conducted uniformly for all samples using same standards in the same laboratory. Any doubtful results or equivocal results were tested once again by ELISA.

**Statistics:** The Chi-square test was used to study the association. The association was considered to be statistically significant if  $p < 0.05$ .

**Result:** Out of 556 suspected cases of acute hepatitis, 281(50.54%) were positive. Among which, the total positive cases for IgM anti-HAV was 70 (24.91 %), IgM anti-HEV was 141 (50.18 %), HBsAg was 65 (23.13 %) and anti-HCV was 5 (1.78 %). Percentage prevalence of the positive acute hepatitis cases with their clinical profile are shown in Table 1.

**Table:1 Distribution of the hepatitis with clinical profile**

Group	HAV IgM positive (N=70) (24.91%)	HEV IgM Positive (N=141) (50.18%)	HBsAg Positive (N=65) 23.13%	HCV Ab Positive (N=05) (1.78%)
Jaundice	70	141	65	05
Fever	37	82	21	00
Pruritus	22	53	17	00
Pain in Abdomen	17	43	9	00
Vomiting	40	85	32	00
Hepatic encephalopathy	00	02	01	00

Dual infection was seen in 14 (4.98%) cases. Table 2 shows percentage of seropositivity of hepatitis co infected cases.

**Table:2 : Seropositivity of combine hepatitis cases.**

Combine hepatitis	Number positive (N=281)	Percentage (N=281)
HAV+HEV	5	1.78%
HAV+HBV	5	1.78%
HEV+HBV	4	1.42%
Total	14	4.98%

Table 3 shows the distribution of different Hepatitis positive cases according to age. Studying the age range of 281 patients with acute hepatitis showed that highest percentage (80%) of HAV infection was present in paediatric age group (age ≤ 12 years), in contrast to that, HEV infection found highest (63.1%) in adult age group (between 21-40 yrs.) HBV infection also found highest (61.5%) in adult age group (between 21-40 yrs.) Out of 5 HCV positive cases, 4 (80%) were detected in more than 20 years of age and only 1(20%) positivity rate was seen in children less than 12 years.

Table 4 shows sex wise distribution of the patients infected with acute hepatitis. Over all male sex suffered higher than female.

**Table:3 : Distribution of different Hepatitis positive cases according to age.**

	0-12 yrs	13-20 yrs	21-40 yrs	> 40 yrs	Total
HAV IgM	56 (80%)	02 (2.9%)	07 (10%)	05 (7.1%)	70 (24.91%)
HEV IgM	10 (7.0%)	22 (15.6%)	89 (63.1%)	20 (14.1%)	141 (50.18%)
HBsAg + HCV Ab	07+01 (10.7%+20%)	04+00 (6.1%)	40+02 (61.5%+40%)	14+02 (21.5%+40%)	65+05 (23.13%+1.78%)
Total cases	74	78	138	41	281 (100%)

\*(P&lt;0.05)

**Table: 4 Gender distributions of different hepatitis positive cases.**

Tests	Male	Female	Total
HAV IgM positive	30 (42.85%)	40 (57.15%)	70
HEV IgM positive	96 (68.08%)	45 (31.92%)	141
HBsAg+HCV positive	40+03 (61.53%+60%)	25+02 (38.47%+40%)	65+5
Total positive	169 (60.14%)	112 (39.86%)	281

\*(P&lt;0.05)

**Discussion:** In about half the patients (50.54%), no viral marker was detected; these patients may have been infected with other hepatitis viruses or may not have undergone seroconversion. Testing for viremia in these cases would have been helpful.<sup>4</sup>

As shown in the table 1, in our study, viral hepatitis E (50.18%) was found to be the most frequent cause of acute viral hepatitis followed by hepatitis A (24.91%), hepatitis B (23.13%) and hepatitis C (1.78%). Tandon *et al*, 1984; Nanda *et al*, 1994; Nejdard *et al*, 1994; and Tan *et al*, 1995 reported 44 - 84% HEV in acute viral hepatitis.<sup>9-12</sup> Studies from different parts of India have reported 15-32% HAV infection, 1.8-57% HBV infection, and 0-12.5% HCV infection in acute viral hepatitis.<sup>13-15</sup> Our study is well correlated with these studies.

Parenterally transmitted hepatitis viruses (HBV and HCV) are of major interest and given more importance because of the associated high

frequency of sequelae such as liver cirrhosis and hepatocellular carcinoma. In our study low prevalence of HCV as a cause of AVH were due to the high prevalence of hepatitis B and enterically-transmitted hepatitis viruses (HAV and HEV) in Asia and Africa. The rates of HCV vary from 1.2% in Hong Kong, 2% in Moscow, 3% in India, 9.6% in Japan and as high as 14 in Taiwan.<sup>16</sup> It is possible that more cases of acute HCV might have been detected if the acute phase sera were tested for HCV RNA. This test is not readily available or applicable to clinical use.

The commonest clinical finding was jaundice (100%) followed by vomiting and fever. Ravindra kaur et al also found icterus as a commonest finding and was 93.06%.<sup>17</sup>

Dual infection occurred in the occurrence of infections with more than one virus is well known but the clinical significance is not fully understood. Many Study carried out in India indicated a significant occurrence of fulminant hepatic failure in children infected simultaneously by two or more hepatotropic viruses.<sup>16</sup> In our study dual infection was seen in 14 (4.98%) cases. Out of fourteen cases, six were children, among which 3 children were dually infected with HAV and HEV, 2 were infected with HAV and HBV and only 1 was infected with HEV and HBV.

The age distribution of the cases showed that adults in age group of 21 years to 40 years were maximally infected (63.1%) with HEV and only 7.00% of children below 12 years were infected with it. It is not well known why this infection is common in adults; this could be because anicteric hepatitis or subclinical infection is common in children under 9 years of age in endemic hepatitis. An alternative explanation could be that HEV is maintained in the community as a sporadic infection; thus, HEV is acquired early in life, making infants and children immune to another attack.<sup>18</sup> Other probable explanation is that adults consume more food, exposed to different food and drinks in comparison to children. This leads the adults more vulnerable to this infection through contaminated food and water. Added factor may include rainy season, flood, contaminated water supply but extensive studies are needed involving large population from different geographical areas from different

countries to establish these factors.<sup>7</sup> Though HEV and HAV have a common route of transmission, in our study HAV infection was the predominant form in individuals less than 12 years (80%) and only 10.00% of the adults were affected. Low prevalence of anti HAV IgM in adult population may be due to seroconversion of HAV early in childhood and subsequent acquisition of immunity to HAV to adults population. HAV is considered a childhood disease in developing countries.<sup>18, 19</sup> HBV and HCV infection was mainly found in adult population in our study. A study carried out by Nandi B et al found the same result.<sup>20</sup> Comparison of the relative frequencies of the various forms of AVH in the age groups revealed statistically significant differences ( $p < 0.05$ ).

Majority of the cases came in summer and Monsoon seasons at our setup and there is a male preponderance, with seropositivity of 60.14%. Male to female ratio in total positive cases was 1.5:1.<sup>4</sup> Comparison of the frequencies of the various forms of hepatitis in males and females revealed a statistically significant difference ( $p < 0.05$ ).

**Conclusion:** HRV In conclusion, present study indicates high seroprevalence of HEV infection in acute viral hepatitis cases than other hepatitis viruses at our set up. HEV serological markers are common among the adults, in contrast to HAV which show high prevalence in children. Co infections were present in many cases including children. So, more attention should be given to children dually infected with co infected viruses as it may cause acute hepatic failure and fulminant hepatic failure in children. Males are more affected than female and majority of the cases are found in summer and rainy seasons. In the light of these results a nationwide survey is recommended to confirm this pattern in other area also.

We further recommend that high risk groups be identified and evaluated for their anti-HAV status and anti-HBsAg status as they are candidates for HAV and HBV vaccination and more attention should be paid to the prevention of HEV and HCV as no vaccine is available for both at present. For HEV infection, prevention in form of improvement of socio - economic and hygienic standards of the population is the better option. A high disease

burden of viral hepatitis and related chronic liver disease in India, calls for the setting up of a hepatitis registry and formulation of government supported prevention and control strategies. There is a need to educate general population regarding HBV and HCV infection and risks associated with inappropriate therapeutic injections. Hepatitis B vaccine should be administered to all new born regardless of maternal HBsAg status. Inclusion of HBV vaccination in the expanded programme of immunization is essential to reduce the HBV disease burden

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