

## Study of etiological spectrum of acute viral hepatitis and prevalence of hepatotropic viruses (A, B, C, D and E) in a tertiary care hospital of Eastern India.

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### Abstract

**Background:** Acute viral hepatitis is a global public health problem, particularly in resource-poor countries. India is known to have a large burden of viral hepatitis. Almost all cases of acute viral hepatitis (AVH) are caused by one of the five viral agents: hepatitis A virus (HAV), hepatitis B virus (HBV), hepatitis C virus (HCV), the HBV-associated delta agent or hepatitis D virus (HDV) and hepatitis E virus (HEV).

**Aims and Objective:** The aim of this study was to know the etiological spectrum of AVH, prevalence of hepatotropic viruses and their co-infections in AVH patients.

**Material and Methods:** This prospective study was conducted during October 2015 to September 2016 in VRDL, ICMR, Department of Microbiology, RIMS, Ranchi. One hundred and eighty three (183) blood samples were taken from patients presented with clinical sign and symptoms of acute viral hepatitis, serum separated and tested for anti-HAV IgM, anti-HEV IgM by ELISA commercial kit and hepatitis B surface antigen (HBsAg), anti-HCV total antibodies (Anti-HCV), by 3<sup>rd</sup> generation CMIA. HBsAg reactive samples were again tested for Anti-HDV IgM by ELISA commercial kit. Data was collected in excel sheets and analysed by SPSS software.

**Results:** The viral aetiology was confirmed in 56.83% of the suspected AVH cases. The prevalence of HAV was higher in children (48%) as compared to adults (9.18%) and the prevalence of HEV was higher in adults (44.89%) as compared to children (4.71%). The prevalence of HBV and HCV in adults were 5.26% and 1.02% respectively. None of the children was positive for HBV and HCV. Maximum number of hepatitis A cases were seen among 0-10 years aged (70 %) followed by 11 -20 years aged (26 %). None of the case of hepatitis A was found in patients older than 30 years of age. Infection with more than 1 virus (co-infection) was detected in 3 cases. HAV and HEV co-infection was found in 2 cases whereas HBV and HEV co-infection was present in 1 case only. Maximum number of cases due to HAV was found in July-August and maximum number of cases due to HEV was detected in March and April.

**Keywords:** Acute viral hepatitis, etiological spectrum, hepatotropic viruses, prevalence

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### I. Introduction

Viral hepatitis is a global public health problem, particularly in resource-poor countries. Inadequate sanitary conditions, lack of awareness and unscrupulous practices of healthcare providers are responsible for large numbers of cases of viral hepatitis in developing countries.<sup>1</sup>

The burden of viral hepatitis in India is not well characterized.<sup>2</sup> India is known to have a large burden of viral hepatitis.<sup>(3-6)</sup>

Acute viral hepatitis is a systemic infection affecting the liver predominantly. Almost all cases of acute viral hepatitis are caused by one of the five viral agents: hepatitis A virus (HAV), hepatitis B virus (HBV), hepatitis C virus (HCV), the HBV-associated delta agent or hepatitis D virus (HDV) and hepatitis E virus (HEV). Commonly HDV infection occurs with HBV, either as a simultaneous co-infection or as a super-infection in a previously HBV-infected individual. Almost all these agents produce clinically similar illness. These range from asymptomatic and inapparent to fulminant and fatal acute infections common to all types.

Hepatitis symptoms are so nonspecific, perfect diagnosis cannot be achieved through history and physical examination alone. Serological tests become mandatory to identify the specific causative agent. Patients presenting with clinical signs and symptoms of hepatitis are specifically tested with a panel that detects hepatitis B surface antigen (HBsAg), hepatitis B core immunoglobulin M (HBc IgM), antibody to HCV (anti-

HCV), hepatitis A immunoglobulin M (anti-HAV IgM) and hepatitis E immunoglobulin M(anti-HEV IgM) to rule out or rule in acute viral hepatitis.<sup>7</sup>

## II. Material And Methods

Our study was a prospective study. One hundred and eighty three (183) blood samples were taken from patients presented with clinical sign and symptoms of acute viral hepatitis (AVH), at our hospital and were referred to the Grade II viral diagnostic and research laboratory, Department of Microbiology, RIMS, Ranchi, all around one year period, from October 2015 to September 2016.

An AVH case is defined as a person having an acute illness typically presenting with acute jaundice, dark urine, anorexia, malaise, extreme fatigue and right upper quadrant tenderness. Biochemical markers include increased urine urobilinogen and >2.5 times the upper limit of serum alanine aminotransferase.<sup>8</sup>

Written informed consents were taken from patients or guardians, in case patient was a child or was not able to give consent. The study was approved by the institutional ethics committee

Blood samples were collected, serum separated and tested for hepatitis B surface antigen (HBsAg) and anti-HCV total antibodies (Anti-HCV) by 3<sup>rd</sup> generation ARCHITECT Chemiluminescent microparticle immunoassay (CMIA). Anti-HAV immunoglobulin M (anti-HAV IgM), and anti-HEV immunoglobulin M (anti-HEV IgM) were also tested by the Enzyme Linked Immunosorbent Assay (ELISA) commercial kit{DIA.PRO SESTO SAN GIOVANI (MILANO) – ITALY}. All HBsAg reactive sera were again tested for anti-HDV immunoglobulin M (anti-HDV IgM) by ELISA commercial KIT (DSI S.R.L).

Relevant clinical information was collected from clinical case sheets that included history of jaundice, physical signs and symptoms. Data collected was fed in the Microsoft Excel and analysis was done using SPSS version 24. P < 0.05 was taken as statistically significant.

Inclusion Criteria: The samples from hospitalised and OPD patients of both sexes and all ages with acute onset of jaundice and other symptoms suggestive of acute viral hepatitis were included in the study.

Exclusion Criteria: Known alcoholics and patients on hepatotoxic drugs were excluded from the study.

## III. Results

In the present study, 183 cases of acute viral hepatitis (AVH) were considered.

The viral aetiology was confirmed in 104 (56.83%) cases while in 79 (43.17%) cases, no hepatitis virus could be detected.(Table 1)

**.Table 01: Distribution of viral aetiology confirmed cases and viral aetiology not confirmed cases among AVH cases.**

Total number of AVH cases	Viral aetiology confirmed		Viral aetiology not confirmed	
	n	%	n	%
183	104	56.83%	79	43.17%

Out of 183 cases, 98 (53.55%) were adults and 85 (46.45%) were children. (Table 02)

**Table 02: Distribution of AVH cases among adult and children.**

Total number of AVH cases	Adults		Children	
	n	%	n	%
183	98	53.55%	85	46.45%

Males (66.38%) outnumbered females (36.61%). (Table 03)

**Table 03: Distribution of AVH among male and female.**

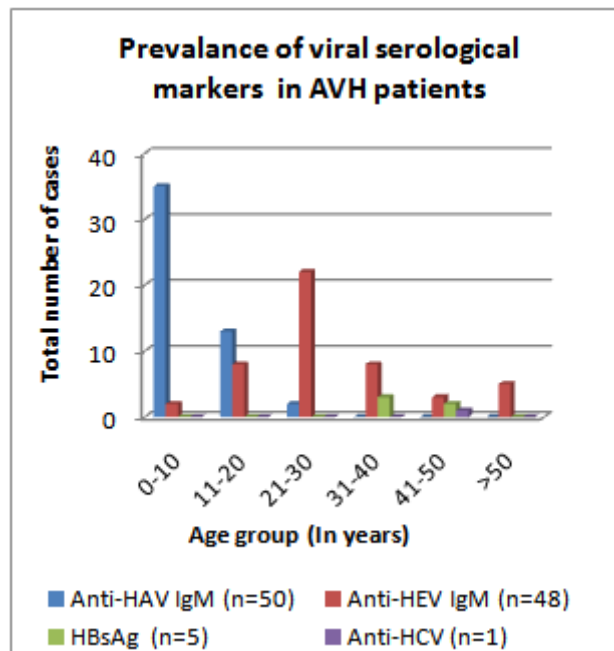
Total number of AVH cases (n)	Male		Female	
	n	%	n	%
183	116	63.39%	67	36.61%

The prevalence of HAV was higher in children (48%) as compared to adults (9.18%)( p= < 0.001). On the other hand, a much larger proportion of adults were positive for HEV (44.89%) as compared to children (4.71%) (p= < 0.001). The prevalence of HBV and HCV in adults were 5.26% and 1.02% respectively. No child was detected as positive for HBV and HCV.(Table 04)

**Table 04: Prevalence of causative agents of acute viral hepatitis (AVH)**

Aetiology	Total (n=183)		Children (n=85)		Adults (n=98)	
	n	%	n	%	n	%
Hepatitis A virus (HAV)	50	27.32%	41	48%	09	9.18%
Hepatitis B virus (HBV)	5	2.73%	00	-	5	5.26%
Hepatitis C virus (HCV)	01	0.54%	00	-	01	1.02%
Hepatitis D virus (HDV)	00	-	00	-	00	-
Hepatitis E virus (HEV)	48	26.22%	04	4.71%	44	44.89%
Viral aetiology not confirmed or non ABCDE	79	43.16%	40	47.05%	39	39.79%
Co-infection of HAV-HEV	02	1.09%	02	2.35%	00	-
Co-infection of HBV and HEV	01	0.54%	0	-	01	1.02%

Infection with more than 1 virus (co-infection) could be detected in 3 cases only. HAV and HEV co-infection was found in 2 cases whereas HBV and HEV co-infection was present in 1 case only. (Table 04) Maximum number of HAV cases were seen among 0-10 years aged (70 %) followed by 11 -20 years age (26 %). No case of HAV was found in patients older than 30 years of age. (Fig. 01)



**Figure1. Age wise prevalence of hepatotropic viral markers in AVH patients.**

Seasonal variation of hepatitis A Virus (HAV) and hepatitis E virus (HEV) was also observed. Although cases due to HAV and HEV are seen throughout the year, maximum number of cases due to HAV was found in July-August and maximum number of cases due to HEV was detected in March and April. (Fig. 02)

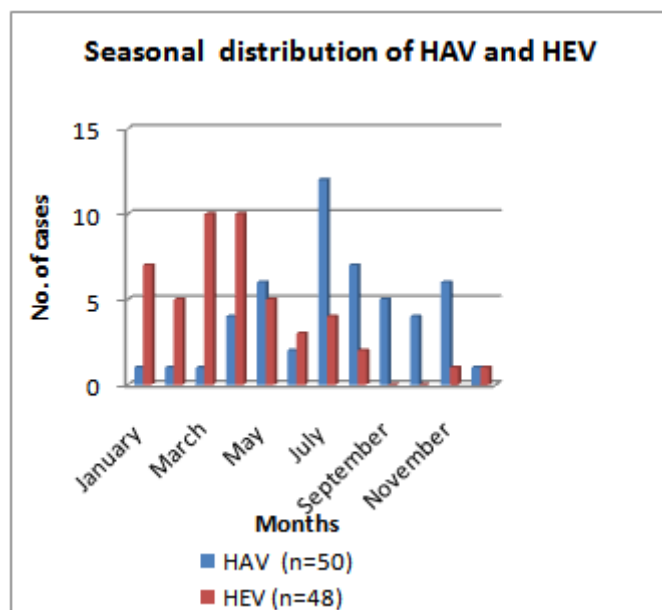


Figure.2: Seasonal distribution of HAV and HEV

All patients had icterus (jaundice) at the time of enrolment in the study. Fever (52.5%), abdominal pain and right upper quadrant tenderness (50.9%), vomiting (33%), nausea (28.6%) anorexia (27.8%), and malaise (25.7%), were the most common clinical signs and symptoms, in order of frequency. (Fig. 3)

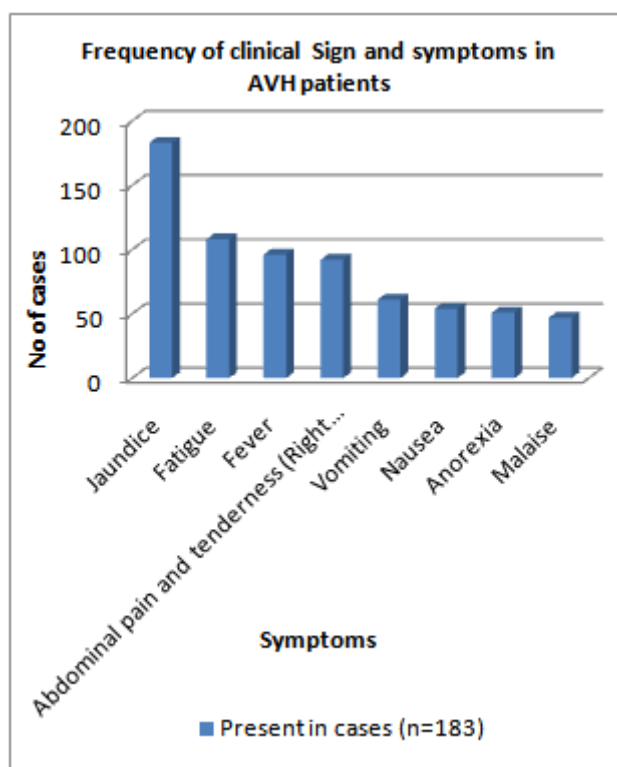


Figure. 3: Frequency of clinical sign and symptoms In AVH patients.

Association between parameters were studied using chi-square test at appropriate level of significance. Association was considered to be statistically significant if  $< 0.05$ .

#### IV. Discussion

The aim of our study was to determine the etiological spectrum of acute viral hepatitis, to know the prevalence of hepatotropic viruses (A, B, C, D and E) and to know their co-infection. Age dependent prevalence and seasonal variation of HAV and HEV were also observed.

Table 3 shows the comparison of several studies on AVH from India highlighting varying prevalence of HAV (9.18%), HBV(5.26%) and HCV (1.02%), whereas among children, prevalence of HAV (48%) was the highest followed by HEV (4.71%). No cases of HBV (0%) and HCV (0%) were identified as a cause of acute jaundice in children. The result of the present study correlates with the finding of other similar studies. (Table-5)

**Table 5: Comparison of different studies on prevalence of causative agents of acute viral hepatitis in India.**

Place and year of study	No. of case-s	India.				Study popula-tion
		HAV %	HBV %	HCV %	HEV %	
Chand-igarh (2007)	685	17.5	7.3	2.8	38.6	10-70 yrs
New Delhi (2010)	74	8.1	12.3	10.6	25.3	Adults
Luckn-ow (2013)	124	26.61	23.3	12.9	27.4	Adults
	143	27.27	9.79	11.8	6.99	Childre-n
Jaipur (2012)	736	4.3	10.8	2	48.3	10-65 yrs
Dibru-garh (2013)	591	33.0	4.74	6.43	20.47	> 13 yrs
Ranch-i (2016)	183	27.32	2.73	0.54	26.22	All ages
	98	9.18	5.26	1.02	44.89	Adults
	85	48	0	0	4.71	Childre-n

In the present study, HEV was the leading cause of AVH in adults, which is similar to some previous studies in north India. Prevalence of HEV was found to be maximum in 21-30 years age group (fig.1) (45%) which is also similar to other studies.<sup>9,10</sup>

High prevalence of HEV indicates that HEV infection should not be considered rare and its presence should be actively investigated, especially in pregnant women because HEV infection may lead to fulminant hepatitis. Additional studies are needed to detail the incidence and severity of this illness in pregnant women in this part of our country.

In the present study, prevalence of HAV is high in children as compared to adults; also suggest that the adults become immune due to infection in childhood. A previous study<sup>11</sup> found that all children by age of 16 years had antibodies against hepatitis A. Indian seroprevalance studies also revealed that 90-100% of population acquires anti-HAV antibody and becomes immune by adolescence. The present study also shows the same type of trends. It will be interesting to know the seroprevalance of protective antibody (anti-HAV IgG) in our population to know the immune status against HAV in adults.

Recently some studies from India have reported an increase in symptomatic cases of HAV among older populations, so as to substantiate epidemiological shift.<sup>12,13</sup> In contrast, a decrease in the proportion of adult patients with acute hepatitis in lower and middle income group patients in the same city was also observed.<sup>14</sup> The present study (involved mainly low and middle socio-economic group) shows very less percentage of adults (only 9%) are infected with HAV as compared to children (48%). Prevalence of HAV is still higher in children as compared to adults in our population. That suggest, in our population most of the adults are having protective antibodies due to HAV infections during childhood. Also, HAV is not showing any epidemiological shifts in our population.

Hepatitis A infection during childhood often is asymptomatic and unrecognized, and typically confers Lifelong immunity. With increasing age at time of infection, symptomatic cases become more common.<sup>15</sup> The high prevalence of HAV among children and low prevalence in adults in our study indicates immunity in adults. So, mass vaccination against HAV may not be required in this part of the country. The study of sero-prevalence of protective antibodies against HAV, will further confirm, the need of mass vaccination.

As present study shows that, both HAV and HEV are the leading causes of acute viral hepatitis and these infections are associated with poor hygiene and, in particular, the lack of clean drinking water and inadequate sanitation. So, addressing the public health problems associated with the enteric transmission of viral hepatitis will require implementing stronger measures to prevent fecal contamination of food and water.

In the present study, the prevalence of HBV among AVH patients was only 2.73 % in all age population and 5.26 % among adults. NO case of acute HBV hepatitis was found in children. This is similar to one study from the same state (2.45%)<sup>16</sup> and less than some other studies from North India,<sup>17,18</sup> and near to one study.<sup>19</sup> {table 5}

HCV prevalence (1.02%) was found to be lower in adults as compared to other studies from India (2.03-10.6% in adults and 1.1 to 3.1 in children) {table5}. No case of acute HCV hepatitis was found in children in the present study. This data may signify that the prevalence of HCV is either low or it less often presents as acute viral hepatitis although the background data from our population is not available.

HDV infection is not very common in India. We do not have any background data on HDV among AVH patients from our country. In the present study also, no cases of HDV was found.

For prevention of blood-borne hepatitis (HBV, HDV, HCV), education and awareness about preventive measures like safe injection practices, safe blood transfusion, prevention of Mother-to-child transmission, Safe sex practices will decrease the transmission of blood-borne hepatitis. Vaccine against hepatitis B is already available and included recently in the national immunisation program schedule. So, maximum vaccination coverage in children and in those who are at risk will reduce the transmission of HBV.

In the present study, 3 (1.63%) out of 183 cases were positive for co-infection with more than one viruses. HAV-HEV co-infection was present in 2 cases (1.09%) and HBV-HEV co-infection was present in 1 case.(Table 4) These findings are similar with one study (2%)<sup>19</sup> and less than the other.<sup>20</sup>

Kaur R. Et al<sup>21</sup> reported that in cases of co-infection with more than one virus, no clinical differences is reported when compared to AVH due to single virus but others opine that mixed HAV and HEV infection usually lead to severe complications in developing countries like India.<sup>22</sup>. As follow up of the cases were not done in the present study, further follow up study is needed to see the outcome in AVH patients with co-infections of more than one hepatotropic viruses.

As co-infection of more than 1 virus was present in some cases of AVH, it mandates the screening of all hepatotropic viruses (A to E) in patients presenting with acute viral hepatitis.

HAV and HEV infections are endemic in eastern India and infections occur throughout the year. In the present study also both HAV and HEV were seen throughout the year. Maximum cases of HAV were seen in July-August that is during monsoon and maximum number cases due to HEV were seen in March-April that is during summer.(fig. 2) Previous studies have found either no seasonal peaks<sup>23</sup> or peak in summer and monsoon months of the year which is similar to the present study.

All patients had icterus and jaundice at the time of enrolment in the study. Fever, abdominal pain and right upper quadrant tenderness, vomiting, nausea, anorexia and malaise, were the most common sign and symptoms, in order of frequency.(fig. 3)

## V. Conclusion

To conclude, AVH is a significant problem in this part of our country. The study shows, HEV is more prevalent among adults whereas HAV is more prevalent among children and adolescents. The prevalence of HBV and HCV in AVH patients are less in this region.

Presence of Co-infection of more than 1 hepatotropic viruses in AVH patients mandates the screening for all hepatotropic viruses in AVH patients.

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