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Original Article

Microbiology Section

Prevalence of Hepatitis A Virus and Hepatitis E Virus Infection in the Patients Presenting with Acute Viral Hepatitis in Eastern India: A Cross-sectional Study

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ABSTRACT

Introduction: Enterically transmitted Hepatitis A Virus (HAV) and Hepatitis E Virus (HEV) are the most common cause of Acute Viral Hepatitis (AVH) and a major health concern in developing nations like India. Both viruses cause AVH and are spread predominantly through the faecal-oral pathway, most commonly through contaminated water.

Aim: To estimate the prevalence of HAV and HEV infection in patients presenting with AVH.

Materials and Methods: An analytical cross-sectional study was undertaken in Indira Gandhi Institute of Medical Sciences, Bihar, India. The study was conducted over a period of 24 months from November 2019 to October 2021. All patients presenting with AVH were included as study participants. The blood samples were subjected to test anti-HAV and anti-HEV positivity. Prevalence of HAV and HEV was calculated taking total cases of AVH as denominator. Patients with confirmed infection with HCV, HBV and any other cause of hepatitis were excluded from the study. Templates were generated in an Microsoft excel spreadsheet and analysis of data was done using Statistical Package of the Social Sciences software (SPSS) version 20.0. Quantitative data were presented as frequency and percentages.

Results: A total of 682 patients presented with acute hepatitis. The AVH patients comprised 467 (68.5%) males and 215 (31.5%) females with the mean age 39.6±18.87 years. The current study reports the seroprevalence of 9.19% HAV and 8.35% of HEV. A total of four patients tested positive for coinfection with HAV and HEV. Most of the HAV patients belonged to an age group less than or equal to 12 years 25 (58.1%) and none were more than 60 years. However, none of the HEV patients were children and most of them were aged between 13-60 years 46 (92%). A male preponderance among HAV 31 (65.9%) and HEV 41 (75.9%) was noted.

Conclusion: Low seroprevalence was noted, with infection more common in younger age group and male patients. Further studies and vaccination along with surveillance system strengthening are warranted.

Keywords: *Picornaviridae*, Prevalence, Seasonal variations

INTRODUCTION

Acute Viral Hepatitis (AVH) is a major public health concern in India and throughout the world. All around the nation, cases have been reported [1]. One of the most common causes are enterically transmitted HAV and HEV, which are serious health concerns in developing countries like India. Both viruses are mostly transmitted by the faecal-oral channel, most frequently through contaminated water and both cause acute viral hepatitis [2]. Hepatitis A and E outbreaks and sporadic infections are common all around the world, but in resource constrained countries like India, they are especially associated with dirty water, insufficient sanitation, poor hygiene and inadequate health services. Self-limiting illnesses such as hepatitis A and E can develop into fulminant hepatitis (acute liver failure) [3-5].

The HAV is a non enveloped Ribonucleic Acid (RNA) virus in the genus Hepatovirus of the *Picornaviridae* family that is resistant to heat, acid and ether. Antibodies against HAV (anti-HAV) can be found when serum aminotransferase activity is elevated and faecal HAV shedding is still occurring. In this early antibody response, the IgM class of antibodies predominates. HEV is a single-stranded positive-sense RNA virus belonging to the family Hepeviridae's genus Hepevirus. The IgM and IgG classes both contain HEV antibodies (anti-HEV IgM and anti-HEV IgG), although the former decreases out quickly after an acute infections [6].

The illness caused by HAV or HEV infection is characterised by a rapid onset of fever and other systemic symptoms, which is followed by jaundice a few days later. With no long-term repercussions, the majority of people with acute viral hepatitis recover on their own within a few weeks. A severe form of the disorder known as Acute Liver Failure (ALF), marked by reduced sensorium and a propensity to haemorrhage, may make some people's symptoms worse (coagulopathy). The defining feature is prominent coagulopathy; with International Normalised ratio ≥1.5, with hepatic encephalopathy in absence of any pre-existing liver pathology [7]. Patients with ALF have a high case fatality rate in the absence of liver transplantation, which is either unavailable or prohibitive for the great majority of Indians [7].

National level data reports that between 2010 and 2013, almost 315 outbreaks of viral hepatitis were reported. In India, HAV causes 10-30% of cases of acute hepatitis and 5-15% of cases of acute liver failure. HEV is the cause of 10-40% of acute hepatitis and 15-45% of acute liver failure in India. Acute HEV has an exceptionally high mortality incidence of 15-25% in third trimester pregnant women. About 10-15% of patients in India with acute and chronic liver failure have superimposed HEV.

With this background, it was deemed necessary to estimate the burden of HAV and HEV in the region of Patna district. Estimation of prevalence is a stepping stone for planning preventive measures. Thus, as per our knowledge, this is the first study in this part of the country to assess the seroprevalence of Hepatitis A and Hepatitis E virus. Thus, we aimed to estimate the prevalence of HAV and HEV infection among patients presenting with AVH.

MATERIALS AND METHODS

A descriptive, cross-sectional study was conducted in the Virology Laboratory of Indira Gandhi Institute of Medical Sciences, Patna, Bihar, India, for a total duration of two years from November 2019 to October 2021) among patients presenting with symptoms suggestive of AVH. The data collection started after Institutional Ethics Committee approval (Letter No 1125/IEC/IGIMS/2019) was taken for conducting the study. Thus, all consecutive patients presenting in the medicine Outdoor Patient Department (OPD) with the complaints of AVH and prescribed for undergoing test for anti-HAV and anti-HEV and willing to participate in the study, were enrolled in the study.

Inclusion criteria: Patients of all age groups presenting with AVH and who gave consent to participate in the study were recruited.

Exclusion criteria: Patients with confirmed infection with Hepatitis C virus, Hepatitis B virus and any other cause of hepatitis were excluded from the study.

Sample size calculation: Based on the national level data, which reports that 10-30% patients and 10-40% patients of AVH are HAV and HEV positive respectively [8]. Assuming 95% of confidence interval and 5% absolute precision (L) and p=40% and using the formula,

$$\frac{Z^2\alpha \times p(1-p)}{L^2}$$

a sample size of 369 was calculated. Consecutive sampling was done and thus, as many patients visiting the health facility in the aforementioned period were included in the study.

Sample Collection and Processing

Data were collected using a pretested semistructured questionnaire comprising socio-demographic characteristics, presenting symptoms, pregnancy status etc. The blood sample (around 4 mL) was collected from peripheral vein. The serum samples of patients were analysed for IgM anti-HAV and IgM anti-HEV for the detection of HAV and HEV infection respectively, using commercially available ELISA (enzyme-linked immunosorbent assay)/ELFA (enzyme-linked fluorescence assay) kits (Vidas HAV IgM and Vidas HEV IgM by Biomerieux), based on the principle of ELFA. Kit instructions were followed properly.

STATISTICAL ANALYSIS

Templates were generated in an Microsoft excel spreadsheet and analysis of data was done using Statistical Package of the Social Sciences (SPSS) software version 20.0. Quantitative data were presented as frequency and percentages. Association between quantitative data was found using the Chi-square test and Analysis of Variance (ANOVA) and the p-value <0.05 was considered statistically significant.

RESULTS

A total of 682 patients presented with acute hepatitis in the OPD of the tertiary care centre during the aforementioned period. Thus, all such consenting patients were enrolled in the study. The AVH patients comprised 467 (68.5%) males and 215 (31.5%) females. Their age ranged from 9 months to 90 years (39.6±18.87 years). The IgM anti-HAV was tested among 511 patients presenting with AVH of which 47 tested positive, resulting in a seroprevalence of 9.19%. Similarly, out of 647 AVH patients tested for IgM anti-HEV, 54 returned a positive result. Thus, the seroprevalence of anti-HEV was 8.35% [Table/Fig-1]. One of the 54 anti-HEV positive patients, was a pregnant woman.

Viral hepatitis	Total acute hepatitis cases	Proportion (%)	95% CI	
			Upper limit	Lower limit
Hepatitis A virus	511	47 (9.19)	0.068364	0.120431
Hepatitis E virus	647	54 (8.35)	0.063319	0.107498

[Table/Fig-1]: Prevalence of Hepatitis A and Hepatitis E virus in patients presenting with acute hepatitis.

The study began in November 2019 and an increase in patients with AVH was observed. This was followed by a sharp decline from April to August. This decline was due to Coronavirus Disease-2019 (COVID-19) emergence and nationwide lockdowns imposed by Government of India (GOI). A statistically significant seasonal variation in seropositivity of HAV patients (p<0.001) and HEV patients (p-value=0.041) was observed. To analyse the confounding effect of COVID-19 on admission, the months were stratified year-wise and the seasonal variation in 2020 lost its significance for both HAV (p-value=0.205) and HEV (p-value=0.740). However, the seasonal variation of the year 2021 was retained (HAV p-value=0.013 and HEV p-value <0.001). A rising trend in seropositivity was observed from April 2021 (except May 2021) onwards, with maximum seropositivity reported in July 2021 and August 2021 [Table/Fig-2].

Months	HAV (N=47) n, %		HEV (N=54) n, %	
	2020	2021	2020	2021
January	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
February	0 (0.0%)	2 (5.1%)	0 (0.0%)	1 (1.8%)
March	5 (10.6%)	1 (2.1%)	9 (16.6%)	1 (1.8%)
April	0 (0.0%)	5 (10.6%)	2 (3.7%)	1 (1.8%)
May	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
June	0 (0.0%)	1 (2.1%)	2 (3.7%)	1 (1.8%)
July	0 (0.0%)	15 (31.9%)	0 (0.0%)	3 (5.5%)
August	0 (0.0%)	3 (6.4%)	1 (1.8%)	4 (7.4%)
September	0 (0.0%)	10 (21.3%)	2 (3.7%)	5 (9.3%)
October	1 (2.1%)	2 (4.2%)	3 (5.5%)	9 (16.6%)
November	1 (2.1%)	0 (0.0%)	1 (1.8%)	0 (0.0%)
December	0 (0.0%)	0 (0.0%)	4 (7.4%)	0 (0.0%)

[Table/Fig-2]: Seasonal variation in seroprevalence of anti-HAV and anti-HEV patients presenting in the tertiary care centre.

There was a total of four patients who tested positive for both IgM HAV and HEV (coinfection of HAV and HEV). The association between those testing positive and age and gender was analysed. It was observed that the AVH patients testing positive for both HAV and HEV (9.7±3.77 years). were very young compared to those testing positive for only HAV (16.79+16.7 years) and HEV (39.9±15.48 years). Those testing negative either for anti-HAV or anti-HEV were still older presenting with a mean age of 42.3±17.8 years (p<0.001). The age was stratified to assess the distribution of seropositive HAV and HEV patients. Most of the HAV patients belonged to an age group less than or equal to 12 years 25 (58.1%) and none were more than 60 years. However, none of the HEV patients were children and most of them were aged between 13-60 years 46 (92%) (p-value <0.001) [Table/Fig-3].

Male preponderance among HAV 31 (65.9%) and HEV 41 (75.9%) was noted. However, this difference was not found significant (p-value=0.491). Out of four patients testing positive for both IgM HAV and HEV, 02 (50%) each was male and female [Table/Fig-3].

Demographic characteristics	HAV (N=47)	HEV (N=54)	Combined HAV+HEV (N=04)	Test statistics (df)	p-value
Age	16.79 (16.70)	39.9 (15.48)	09.75 (3.77)	31.66 (3,499)	<0.001
Gender					
Male	31 (65.9%)	41 (75.9%)	02 (50.0)	2.2004 (3)	0.491
Female	16 (34.1%)	13 (24.1%)	02 (50.0)		

[Table/Fig-3]: Association of enteric viral hepatitis with age and gender.
*mean (+SD); #ANOVA; $Fisher's exact

DISCUSSION

The current study was undertaken to estimate the proportion of AVH patients testing positive for HAV and HEV and the seroprevalence of 9.19% HAV and 8.35% of HEV were observed.

This study also ascertains that the younger age group is more likely to be associated with anti-HAV seropositivity. A similar study was conducted over two years in Mangalore by Joon A et al., [6]. The study reports seropositivity for HAV or HEV of 19.31% and 10.54%, respectively. In this study, patients with acute viral hepatitis had an 11.5% seroprevalence of both HAV and HEV [6]. In a study carried out in eight rural communities in Southeast Bolivia, Bartoloni A, et al., reported seropositivity of 97% of IgG anti-HAV [9]. Of 64.7% those in this group were under the age of five years. The seropositivity of 7.8% of HEV was reported in the same study. This finding corroborates with the current study. Similarly, the median age of patients with positive anti-HEV was 37 years [9]. According to a study by Yun H et al., the overall prevalence of HAV was 63.80% (55.21% of those affected were in their 20s and 95.92% of those affected were in their 30s, p-value=0.01) and that of HEV was 9.40% (5.21% of those affected were in their 20s and 7.14% were in their 30s, p-value=0.01) [10]. Chandra NS et al., and colleagues performed a study at Calcutta Medical College that involved analysing samples from 285 individuals with acute hepatitis for HBsAg, HEV, and HCV. According to the study, among all viral indicators, serum positivity for HEV was highest. This demonstrates Calcutta's HEV endemicity [11]. Vaidya SR et al., conducted an analysis of a sewage sample from the city of Pune for enteric viral markers in the years 1999-2000. According to this investigation, the total prevalence in raw sewage was 10.98% (9/82, HEV) and 24.42% (21/86, HAV) [12]. This signifies that the seropositivity of HEV (8.35%) estimated in the current study is more or less similar to previous studies.

A systematic review of 500 articles on the prevalence of anti-HAV found that while South Asia was reported to have high prevalence rates, new research, particularly from India, points to a declining incidence rate. As a result, in recent decades, patterns in South Asian countries have altered from intermediate rates to low prevalence rates [13].

The [Table/Fig-4] presents the comparison of seroprevalence of HAV and HEV reported in various studies. A study conducted in Rohtak, Haryana reports that the HEV IgM ELISA test was positive on 138 individuals with an overall seroprevalence rate of 138 (44.9%) and HAV antibodies were detected in 109 subjects, with the seroprevalence of HAV was 34 (31.1%) [14]. An analysis was done on the laboratory surveillance data produced between 2014 and 2017 by a network of 51 virology laboratories. A total of 24,000 patients were tested for HAV and HEV; 3,017 (12.6%), 3,865 (16.1%), and 320 (1.3%) patients tested positive for both HAV and HEV [15].

Reference studies	Place of study	Year of publication	HEV prevalence	HAV prevalence
Joon A et al., [6]	Mangalore	2015	10.54%,	19.31%
Vaidya SR et al., [12]	Pune	2002	10.98%	24.42%
Rawat S et al., [14]	Rohtak, Haryana	2019	44.9%	31.1%
Murhekar MV et al., [15]	Aggregated data from IDSP	2018	12.6%	16.1%
Present study	Patna, Bihar	2022	8.35%	9.18%

[Table/Fig-4]: Comparison of prevalence of Hepatitis A and Hepatitis E virus disease in various studies [6,12,14,15].

Thus, the seropositivity of HAV (9.19%) reported in the current study was less compared to the aforementioned studies. This could be due to fewer patients of AVH attending the healthcare system due to COVID-19. Additionally, the studies report IgG positivity of serum to anti-HAV and anti- HEV while in present study IgM anti-HAV and anti-HEV were assessed. Thus, this evidence suggests that HAV and HEV are sporadic and endemic worldwide, with recurrent cycles of infections. Similarly wide variations in seroprevalence are also observed. Strengthening the surveillance system in enhancing reporting of enteric viral infections could help generate a more realistic picture.

The cost of HAV infection in communities and nations is significantly influenced by the average age of infections [13]. In countries with high endemicity, nearly all children develop the condition at a young age, when the asymptomatic infection is most prevalent. As a result, the incidence decreases. The infection rates steadily decline and a high-to-low endemicity epidemiological shift is observed. The chance of infection then rises with age and symptomatic viral hepatitis develops in older adults [16]. Endemicity is classified as high if 90% of children are immune by age 10, middle if 50% are immune by age 15, and low if 50% are immune by age 30 [12]. Moreover, it has also been reported that high-income countries located primarily in Europe, North America, and Australia, and they are also found in parts of the Middle East and East Asia, including Japan and the Republic of Korea have very low levels of HAV endemicity (<50% of population), while high levels of endemicity (>90% of population) are reported from low-income regions like sub-Saharan Africa, South and Southeast Asia, and parts of Central America, Central Asia, the Middle East, and Oceania [17]. Middle-income regions of society reports both intermediate and low levels of endemicities [18,19].

A previous study reports that young people were more likely to have these conditions [6]. Likewise, present study also ascertains that the seropositivity of HAV was greater among children (58.1%) and adults (34.9%). The seropositivity of HEV was not observed among children till the age of 12 years. Mohanavalli B et al. collected serum samples from 185 kids in Royapatti, Chennai. The analysis of age-wise seropositivity showed that the 10-12 year old age group had the highest levels of HAV-IgG positivity [20]. In the current investigation, anti-HAV was reported at an average age of 16.8 years.

Contrary to HAV, the mean age of presentation of HEV patients was 39.9 years. Similar findings were demonstrated by various studies. The peak anti-HEV prevalence (33%) was reported in the age group of 26-35 years [21].

Joon A et al. noticed that males were more likely than females to have HAV and HEV (68% and 31% respectively) [6]. In corroboration with previous studies, male preponderance was seen in seropositivity over females for both HAV and HEV (65.9% and 75.9% respectively) in the present study. This implies that young boys are exposed to viral infections more than their female counterparts because they spend more time in outdoor activities.

However, in contrast to present findings that enteric hepatitis is commonly seen in young age, a seroprevalence research carried out in the Iranian province of Sari shows that the younger age group (1-5 years) had the lowest prevalence (5.2%) and the older age group (15-25 years) had the highest prevalence (82.0%) [22]. Seropositivity was considerably greater in females, rural locations, and older age groups.

The HAV and HEV are transmitted through the faecal-oral route through contaminated water. Therefore, the peak incidence in July for HAV and August for HEV was observed in present study as well. The disease was most prevalent at the end of the monsoon season and the onset of winter as reported by Joon A et al., and a systematic review, on the other hand, found that there is no clear-cut seasonal trend for viral hepatitis, despite the fact that data points to a peak in the spring and summer [6,23].

Limitation(s)

Although, the study was well-planned but because of the insurgence in COVID-19 cases, a drastic fall in patients other than COVID-19 was seen. This eventually, decreased the cases of AVH and thus could have had a negative response on estimation of seroprevalence also.

CONCLUSION(S)

The present study concludes that the HAV mainly infects children of age less than 12 years while the hepatitis E virus infects the

older population. The seropositivity is more common among males. Measures should be taken to improve the sanitary conditions, especially during the monsoon and winter seasons. Vaccination for HAV among children should be promoted to enhance their immunity against enteric viruses. The surveillance system should be strengthened to increase reporting of these infections. Analytical studies are warranted to ascertain the epidemiology of viral infections and other related factors should also be explored in its causation.

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REFERENCES

[1] Irshad M, Mohammad Ahmad Ansari SS, Kumar Joshi Y. Viral hepatitis in India: A report from Delhi. GJHS. 2010;2(2):96.
[2] Vitral CL, da Silva-Nunes M, Pinto MA, de Oliveira JM, Gaspar AMC, Pereira RCC, et al. Hepatitis A and E seroprevalence and associated risk factors: A community-based cross-sectional survey in rural Amazonia. BMC Infectious Diseases . 2014;14(1):458.
[3] Acharya SK, Madan K, Dattagupta S, Panda SK. Viral hepatitis in India. Natl Med J India. 2006;19(4):203-17.
[4] World Health Organization. Hepatitis A. https://www.who.int/news-room/fact-sheets/detail/hepatitis-a.
[5] World Health Organization. Hepatitis E. https://www.who.int/news-room/fact-sheets/detail/hepatitis-e.
[6] Joon A, Rao P, Shenoy S, Baliga S. Prevalence of Hepatitis A virus (HAV) and Hepatitis E virus (HEV) in the patients presenting with acute viral hepatitis. Indian Journal of Medical Microbiology. 2015;33:S102-05.
[7] Akamatsu N, Sugawara Y, Kokudo N. Acute liver failure and liver transplantation. Intractable Rare Dis Res. 2013;2(3):77-87.
[8] Viral Hepatitis-The Silent Disease Facts and Treatment Guidelines. Directorate General of Health Service, Ministry of Health & Family Welfare Government of India. guideline_hep20158117187417.pdf.
[9] Bartoloni A, Bartalesi F, Roselli M, Mantella A, Caceres Arce C, Paradisi F, et al. Prevalence of antibodies against hepatitis A and E viruses among rural populations of the Chaco region, south-eastern Bolivia. Tropical Medicine & International Health. 1999;4(9):596-01.
[10] Yun H, Lee HJ, Cheon D, Chu C, Oh KW, Kim YT, et al. Seroprevalence of hepatitis A and E viruses based on the Third Korea National Health and Nutrition Survey in Korea. Osong Public Health Res Perspect . 2011;2(1):46-50.
[11] Chandra NS, Ojha D, Chatterjee S, Chattopadhyay D. Prevalence of hepatitis E virus infection in West Bengal, India: A hospital-based study. Journal of Medical Microbiology. 2014;63(7):975-80.
[12] Vaidya SR, Chitambar SD, Arankalle VA. Polymerase chain reaction-based prevalence of hepatitis A, hepatitis E and TT viruses in sewage from an endemic area. Journal of Hepatology. 2002;37(1):131-36.
[13] Jacobsen KH, Wiersma ST. Hepatitis A virus seroprevalence by age and world region, 1990 and 2005. Vaccine. 2010;28(41):6653-57.
[14] Rawat S, Gill P, Gupta T, Malhotra P, Parmar A. Prevalence of hepatitis A virus and hepatitis E virus in the patients presenting with acute viral hepatitis in Rohtak, Haryana, India. International Journal of Research in Medical Sciences. 2019;7:1792.
[15] Murhekar MV, Ashok M, Kanagasabai K, Joshua V, Ravi M, Sabarinathan R, et al. Epidemiology of hepatitis A and hepatitis E based on Laboratory Surveillance Data-India, 2014-2017. Am J Trop Med Hyg. 2018;99(4):1058-61.
[16] Luyten J, Beutels P. Costing infectious disease outbreaks for economic evaluation: A review for hepatitis A. Pharmaco Economics. 2009;27(5):379-89.
[17] World Development Indicators 2007. The World Bank. 2007. 426. 18. WHO_.pdf [Internet]. [cited 2022 Sep 14].
[18] Hutin Y, Low-Beer D, Bergeri I, Hess S, Garcia-Calleja JM, Hayashi C, et al. Viral hepatitis strategic information to achieve elimination by 2030: Key elements for HIV program managers. JMIR Public Health Surveill. 2017;3(4):e91.
[19] Indian Pediatrics- Editorial. [cited 2022 Jun 22].
[20] Mohanavalli B, Dhevahi E, Menon T, Malathi S, Thyagarajan SP. Prevalence of antibodies to hepatitis A and hepatitis E virus in urban school children in Chennai. Indian Pediatrics. 2003;40:328-31.
[21] Arankalle VA, Tsarev SA, Chadha MS, Alling DW, Emerson SU, Banerjee K, et al. Age-specific prevalence of antibodies to hepatitis A and E viruses in Pune, India, 1982 and 1992. Journal of Infectious Diseases. 1995;171(2):447-50.
[22] Alian S, Ajami A, Ghasemian R, Yadegarinia D. 754 Age-specific seroprevalence of hepatitis A in Sari, northern Islamic Republic of Iran. East Mediterr Health J [Internet]. 2011 Oct 1 [cited 2022;17(10):754-58.
[23] Fares A. Seasonality of hepatitis: A review update. J Family Med Prim Care. 2015;4(1):96-100.

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