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STUDY OF HEPAITIS A AND HEPATITIS E VIRUS INFECTION IN ACUTE HEPATITIS PATIENTS

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ABSTRACT

Background: Acute viral hepatitis is a major public health problem worldwide. Hepatitis-A virus (HAV) and Hepatitis E virus (HEV) are two major hepatotropic viruses responsible for enterically transmitted acute viral hepatitis. **Objectives:** To know seroprevalence , clinico-epidemiological factors and co-infection of hepatitis A & hepatitis E virus infection. **Methods:** The study was carried out in the Virology Research & Diagnostic Laboratory (VRDL) under Department of Microbiology IGGMC, Nagpur from January to October 2019. Cases included were children & young adults of both sexes having clinical hepatitis attending OPD and IPD. Blood sample was collected aseptically from each suspected patient. Serum was separated and tested for presence of IgM antibody against HAV and HEV by using Enzyme Linked Immunosorbant assay. **Results:** Out of 184 samples, HAV seropositivity was seen in 13.04 %, HEV seropositivity in 35.32 %. Maximum cases were seen in age group of 0-10 years for HAV and 21-30 years for HEV. Male to female ratio was almost equal for both HAV and HEV. Urban population was most affected Source of water in maximum cases was tap water in urban and well water in rural area. **Conclusion:** Prevalence of HEV infection among the acute viral hepatitis cases is much more common than HAV. HEV being caused by feco-oral route, it is very important to have supply of safe drinking water. Awareness regarding sanitation, hand and food hygiene is the key factor to prevent hepatitis A & E infection.

KEYWORDS

Acute Viral Hepatitis, Hepatitis A, Hepatitis E, Seroprevalence, ELISA

INTRODUCTION

Worldwide, acute viral hepatitis is a major problem and HAV and HEV are the main causes responsible for substantial morbidity and mortality in both developed and developing countries [1] Both viruses are transmitted primarily by the fecal–oral route and cause a disease that is insignifcant without serological testing [2]

India is hyperendemic for hepatitis A and E. HAV is the most common cause of AVH in children, whereas HEV is predominant in adults. Because of the improvement in living standard, the pattern of AVH due to HAV is changing from an asymptomatic or mild infection to an increased incidence of symptomatic or severe disease. HAV is also the most common cause of fulminant hepatitis in children in India and worldwide [3]

HEV has been associated with the large scale of epidemics and outbreaks in various parts of India. It is related to high attack rate and mortality in pregnant women [4]. HEV infection during pregnancy is associated with increased risk of prematurity, abortion, low birth weight, perinatal mortality, fulminant hepatitis, and maternal mortality [2] Though it is a major disease of adults, it can affect children with a similar picture of hepatitis and unlikely cause of fulminant hepatitis in children[5]

Despite it being a major health problem, not many studies in India have explored the prevalence, etiology or clinic-epidemiological profile of the cases. The limiting factor remains the high cost of these diagnostic kits, but serological studies are essential from epidemiological and prognostic point of view. [6] Therefore this study was undertaken to determine the seroprevalence, clinical and epidemiological profile of AVH in central India so that appropriate management and preventive strategies for this part of the country could be planned.

AIMS & OBJECTIVES

1) To Know the seroprevalence of hepatitis A & hepatitis E virus infection in patient of AVH
2) To know the clinico-epidemiological factors associated with them.
3) To know the co-infection of hepatitis A & hepatitis E in patient with AVH.

MATERIAL & METHODS:

The hospital based cross-sectional study was carried out in the Department of Microbiology in Virology Research & Diagnostic Laboratory (VRDL) , at a tertiary care hospital, from January 2019 to October 2019.

Patients of all age group of both sexes who presented with acute hepatitis in whom HAV and HEV was suspected to be the etiology were included in this study. The study was approved by institutional ethics committee and informed written consent was taken from patients. Blood samples were collected and serum was separated as per the standard guidelines [7] and was accompanied by fully filled requisite form with detailed history of patients. Sera samples were tested for IgM anti HAV & IgM anti HEV for detection of acute hepatitis A and acute hepatitis E respectively using commercially available IgM capture Enzyme Linked Immuosorbant Assay kit (Dia.Pro Diagnostic Bioprobes, Italy) in accordance with the manufacturer's instructions. The database was created in MS excel and was analysed.

OBSERVATIONS & RESULTS

Out of total 184 samples tested for HAV and HEV, 24(13.04 %) were positive for HAV infection and 65 (35.32 %) were positive for HEV infection. Overall positivity of HAV and HEV infection was 89 (48.36 %) .Among the total positive cases, HAV and HEV co-infection was seen in 8 (4.34 %)

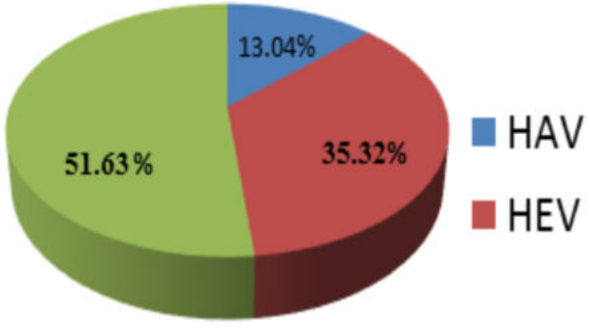

Figure 1. Seropositivity Of Hepatitis A And Hepatitis E Among Acute Hepatitis Patients (N=184)

Table 1: Distribution Of HAV & HEV Positive Cases According To Age Group

Age group	HAV		HEV	
	Number	%	Number	%
1-10	13	54.16	7	10.76
11-20	4	16.66	15	23.07
21-30	5	20.83	20	30.76
31-40	1	4.19	12	18.47
41-50	0	0	6	9.22
51-60	1	4.16	5	7.69
Total	24	100	65	100

Table number 1 shows that in case of HAV maximum proportion of cases were in the age group of 1 to 10 years i.e 13 (54.16%). This was followed by age group of 21 to 30 years i.e 5(20.83%) and age group of 11 to 20 years i.e 4 (16.66%). While out of total 65 cases of HEV maximum were found to be in 21 to 30 year group i.e 20 (30.76%). This was followed by age group of 11 to 20 year i.e 15 (23.07%) and age group of 31 to 40 year i.e 12 (18.47%) . Table 2 shows that there was no significant difference between mean age of patients between two infections.

Table 2 : Comparison Of Mean Age Between HAV & HEV

TEST NAME	Mean	Std. Deviation	P Value
HAV	15.38	13.387	0.57
HEV	27.85	13.996	

Table 3 shows that among HAV infection maximum cases were seen in females i.e 14 (58.33 %) than males 10 (41.67 %) and for HEV infection males were 33 (50.77 %) as compared to females i.e 32 (49.23 %). There was no significant difference in proportion of male and female patients between two groups.

Table 3: Distribution Of HAV & HEV Positive Cases According To Gender

Gender	HAV		HEV	
	Number	%	Number	%
Female	14	58.33	32	49.23
Male	10	41.67	33	50.77
Total	24	100	65	100

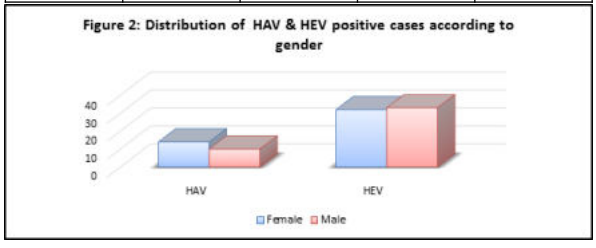

Table 4 shows that out of 24 HAV positive cases, maximum were from rural area 19 (79.17%) while out of 65 HEV positive cases 54 (83.07%) were from urban area. Overall positive cases of AVH were more from urban area i.e 59(66.29%) than rural area i.e 30 (33.70%).There was significant difference between two diseased groups in proportion of patients according to residence (p<0.05).

Table 4: Distribution Of HAV & HEV Positive Cases According To Area Of Dwelling

Residence	Diagnosis			
	HAV (n= 24)		HEV (n= 65)	
	Number	%	Number	%
Urban	05	20.83	54	83.07
Rural	19	79.17	11	16.93
Total	24	100	65	100

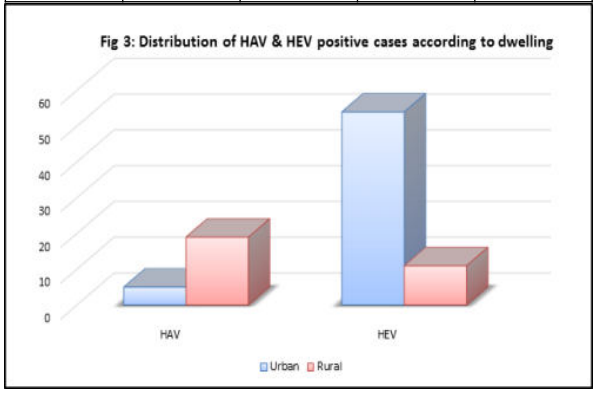

Table 5 shows that out of 24 cases of HAV maximum cases were seen in month of April 5(20.84%). This was followed by 4 each (16.67 %) in the month of February and July. Out of total 65 cases of HEV, maximum cases were seen in month of March i.e 22 (33.85%) followed by 10(15.38%) cases in the month of June and 9(13.84%) cases in the month of July. In the month of March there was significant difference in proportion of patients between two groups (P<0.05).

Table 5: Distribution Of HAV & HEV Positive Cases According To Months

Month	TEST NAME				P value
	HAV		HEV		
	Number	%	Number	%	
JAN	2	8.33	4	6.16	0.65
FEB	4	16.67	4	6.16	0.20
MARCH	2	8.33	22	33.85	0.016
APRIL	5	20.84	7	10.77	0.29
MAY	2	8.33	3	4.61	0.60
JUNE	2	8.33	10	15.38	0.50
JULY	4	16.67	9	13.84	0.74
AUG	3	12.5	4	6.16	0.38
SEPT	0	0	2	3.07	-
Total	24	100	65	100	-

Table 6 shows that in case of HAV infection most common symptoms were found to be jaundice, nausea/vomiting, fever, arthro-myalgia and abdominal pain present in 19 (79.16%), 12 (50%), 11(45.83%), 10(41.66%) and 8 (33.30%) cases respectively While in case of HEV infection most common symptoms were jaundice, nausea/vomiting and abdominal pain present in 51(78.46%), 17(26.15%) and 16(24.61%) cases respectively. HAV cases with fever, nausea/vomiting and arthro-myalgia were significantly more as compared to HEV cases having similar complaints (p<.05)

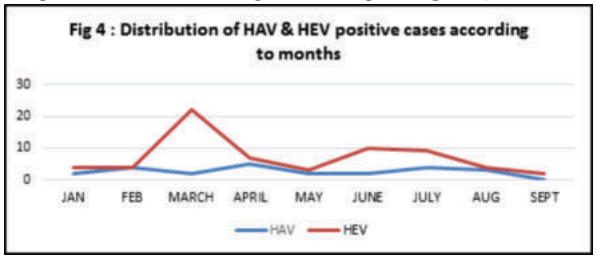

Table 6: Distribution Of HAV & HEV Positive Cases According To Clinical Features

Clinical features	Diagnosis				P Value
	HAV (n= 24)		HEV (n= 65)		
	Number	%	Number	%	
Jaundice	19	79.16	51	78.46	0.45
Fever	11	45.83	7	10.76	<0.01
Abdominal Pain	8	33.30	16	24.61	0.58
Nausea/vomiting	12	50	17	26.15	<0.01
Weight loss	0	0	3	4.61	0.26
Diarrhoea	2	8.33	0		0.024
Pruritis	2	8.33	8	12.30	0.75
Arthro-myalgia	10	41.66	5	7.69	<0.01
Encephalopathy	0	0	0	0	-
Ascites	0		2	3.07	0.51
Asymptomatic	1	4.16	13	20	0.024

Table 7 shows that out of total 24 HAV cases, 15(62.50%) gave history of washing their hand without soap which was found to be the major the major risk factor and this was significantly more as compared to HEV cases (p<0.05). Out of total 65 HEV cases ,38 (58.46%) used tap water for drinking which was found to be the major risk factor in this group and this was significantly more as compared to HAV cases (p<0.05).

Table 7 : Distribution Of HAV & HEV Positive Cases According To Risk Factors

Risk Factor	HAV (n=24)		HEV (n=65)		P value
	Number	%	Number	%	
Hand washing without soap	15	62.50	12	18.46	<0.001
Consumption unpasteurized milk	3	12.5	1	1.54	0.06
Handling of domestic animals	0	0	1	1.54	0.73
Source of water supply (Tap Water)	2	8.33	38	58.46	<0.001
Consumption of food outside home frequently	2	8.33	3	4.61	0.60

Consumption of uncooked or un-boiled food	2	8.33	10	15.38	0.50

DISCUSSION

In present study out of total 184 samples tested for HAV and HEV infection, Overall positivity was found to be 89 samples (65 HEV + 24 HAV) i.e 48.36 %. In a study conducted by AS Al-Naaimi et al (2012) [8], total 2,692 cases were labeled as acute viral hepatitis cases and a positive hepatitis viral marker (A, B, C and E) was found in 1,332 cases (49.5%). This result is somewhat similar with present study. Priyadarshini et al Rajesh K (2017)[9] studied 1045 suspected cases of AVH and found that 339 had a positive viral marker (32.44%).Our result was comparatively higher than this study.

65 were found to be positive for HEV with seropositivity rate of 35.32 % and HAV were positive in 24 samples with seropositivity rate of 13.04 while HAV and HEV co-infection was seen in 8 cases (4.34 %). Pranav Kumar Sharma et al (2016)[6] in their study found that out of a total of 90 AVH subjects maximum seropositive were due to hepatitis E i.e 35 (38.9%). This is comparable with the present study. In a study by Radhakrishnan S et al in 2000 [10] from CMC, Vellore 381 patients were tested. HAV IgM was present in 51(13.3%) which is similar with present study. Sarangi G (2019) [11] studied 499 laboratory-confirmed fecal– oral-transmitted viral hepatitis cases and out of these 271 (54.3%) were HAV cases, 217 (43.5%) were HEV cases which is much higher than our study. Ashraful Islam Khan (2020) [12] studied total of 998 suspected hepatitis patients and found that 191(19%) were HAV seropositive and 103(10%) were HEV seropositive. Our findings of HEV infection are higher as compared to this study.

Different studies on acute viral hepatitis caused by HAV and HEV have reported varying prevalence of these viruses. The prevalence of HAV varies from 1.7% to 67 % and HEV from 16.3 % to 66.3 % [11]

- In HAV infection maximum positive cases were seen in females i.e 14 (58.33 %) and males were 10 (41.67 %) while in case of HEV infection males were 33 (50.77 %) compared to females i.e 32 (49.23 %).Pregnant women are at increased risk of complications in HEV infection [13] In our study, IgM anti-HEV positivity was seen in two pregnant female but it did not lead to any fatal maternal and fetal outcome. Male to female ratio is almost equal i.e 1:1 for both the infection. There was no significant difference in proportion of male and female patients between two type of infections ($p>0.05$).
- Study by Sarangi G (2019) [11] 271/499 were positive HAV cases and among this females were 137(52.3%) and males were 134 (41.5%). For HEV infection out of 217/499 positive cases 141(43.7%) were males and 76(29%) were females. This study showed a slightly higher female preponderance for HAV & HEV infection which is comparable with our study.

As far as age is concerned , out of 24 positive cases of HAV infection, maximum proportion of cases were seen in the age group of 1 to 10 years While out of total 65 cases of HEV, maximum positivity was found to be in 21-to-30-year age group. Mukherjee Raja (2018) [1] found HAV was predominant in the age group of 0-10 years (18/52-34.61%) and HEV infection was seen in all age groups with maximum prevalence in 21-30 years (8/13-61.53%). Study by Maninder Kaur (2017)[2] 21–30 years age group (25/65 -38.46%) was identified as the most susceptible group for HEV infection while HAV predominated in younger age groups. These findings are similar to our study findings.

We have observed that out of 24 HAV seropositive cases, maximum i.e 19 (79.17%) were from rural area and 5(20.83%) were from urban area while out of 65 HEV positive cases 54 (83.07%) were from urban area and remaining 11 (16.93%) were from rural area. There was statistically significant difference between two diseased group according to residence ($p<0.05$). Study by Sarangi G et al (2019) [11] found that Hepatitis E cases was more in urban area 121(62.1%) as compared to HAV which were common in rural area 217(55.6%) . This could be due to improper drainage system in the towns and cities leading to sewage contamination of drinking water and may be due to the poverty, overcrowding, and inadequate sanitation seen in most villages. In a study by Pranav Kumar Sharma et al (2016)[6] the rural vs urban distribution of cases was 47.77% and 52.23% respectively. The difference can be attributed to difference in methodologies, a small sample size and also the fact that the Western countries are already low endemic areas for Viral Hepatitis and thus can show higher endemicity in urban regions. These findings were similar to our study findings.

- Maximum HAV positive cases were seen in month of April i.e 5 (20.84%) and for HEV, maximum cases were seen in month of March i.e 22 (33.85%). There was significant difference in proportion of positivity of HAV and HEV infection in the month of March($P<0.05$).

Fares A (2015)[14] Based on data from 28 studies, irregular, cyclical patterns were observed for acute viral hepatitis, with most prominent peaks were shown in spring and summer for hepatitis A. Nidhi S. Chandra (2014) [15] in their study total 285 patients screened for hepatotropic viral markers. Although patients were identified in every month throughout the year, the incidence of HEV infection was highest from March to May. These findings were exactly similar with our study findings. Analysis of seasonal trend in study by Sarangi G et al (2019) [11] showed outbreaks of HAV & HEV occurred throughout the year with peaks in the winter and beginning of the summer season.

In case of HAV infection most common symptoms were jaundice, nausea/vomiting, fever, arthro-myalgia and abdominal pain present in 19 (79.16%),12 (50%),11(45.83%), 10(41.66%) and 8 (33.30%) positive cases respectively. In case of HEV infection most common symptoms were jaundice, nausea/vomiting and abdominal pain present in 51(78.46%), 17(26.15%) and 16(24.61%) positive cases respectively. HAV cases with fever, nausea/vomiting and arthro-myalgia were significantly more as compared to HEV cases having similar complaints ($p<.05$). Hye Won Oh (2017)[16]conducted study in which they identified Jaundice was the most common symptom among patients with HEV (56.5%) and HAV (71.4%) similar to our study. In study by Mukherjee Raja (2018)[1] commonest symptoms complained by the patients were anorexia (96.59%), malaise (95.45%), hepatic enlargement (96.59%) and jaundice (75%). The least common symptom was abdominal distension (38.64%) and liver tenderness (36.36%). So, jaundice is not common symptom and this is contradictory to our study findings.

- Major risk factor for HAV infection was hand washing without soap and for HEV infection drinking tap water without purification. Among HAV seropositive, 15 (62.50%) gave history of washing their hand without soap and this was statistically significantly as compared to 12(18.46%) HEV cases ($p<0.05$). While in case of HEV ,38/65 (58.46%) used tap water for drinking and this was significantly more as compared to HAV cases 2(8.33%) ($p<0.05$). Geofrey Amanya et al (2017) [17] in their study did bivariate (simple) analysis found that HEV was associated with drinking untreated water ,not cleaning their utensils, unsanitary (open) defecation practices, reported frequent travels, “never” washed hands with soap after visiting the latrine , never using soap to wash their hands before eating, which is comparable with risk factors in our study.

CONCLUSION

The study has a few inherent shortcomings as it was conducted among subjects recruited from the hospital and not from the community. The sample size was relatively small due to logistic constraints. The methodology included consecutive patients who fulfilled the inclusion criteria and there was no specific sampling frame for the same in order to ensure better representativeness. With similar mode of transmission and symptomatology, clinical diagnosis is difficult to establish, thus timely diagnosis by serology and molecular diagnostic techniques may help in the management.

High risk groups should be identified and evaluated for their anti-HAV status, as they are candidates for HAV vaccination & more attention should be paid to the prevention of HEV, as no vaccine is available for HEV at present. Improvement in food habits, personnel hygiene, safe supply of drinking water and periodic surveillance will be of immense help in planning future infection control strategies and help in creating awareness and better sanitation programs in our country.

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