

Original Research Article

Clinico-epidemiological profile of hepatitis A virus and hepatitis E virus co-infection in pediatric age group: a hospital based retrospective study

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ABSTRACT

Background: Hepatitis-A virus (HAV) and Hepatitis E virus (HEV) are two major hepatotropic viruses of great public health importance in the developing countries like India. Both HAV and HEV are enterically transmitted and there are speculations that their co-infection might be associated with a more severe clinical course and increased rate of mortality. The objective of this study is to determine the prevalence, clinical features and biochemical parameters of Hepatitis A and Hepatitis E co-infection in hospitalized patients at a tertiary care centre in Uttarakhand.

Methods: It is a retrospective study, covering a period of 4years and conducted in Himalayan Institute of Medical Sciences, SRHU Jolly Grant, Dehradun. Records of the patients with Hepatitis A and Hepatitis E co-infection were retrieved and analyzed.

Results: Out of total 125 patients of acute viral hepatitis, 13 patients had HAV and HEV co-infection. 100% of the patients with co-infection presented with complaints of fever and jaundice, followed by 76.92% with vomiting, 69.23% with pruritis, 61.53% with pain in abdomen and 23.07% with altered sensorium. Mean Bilirubin, ALT, AST were 8.69 ± 7.27 mg/dl, 2030.69 ± 1726.93 IU/L and 1880.07 ± 1881.11 IU/L respectively. Average duration of stay was 8.2 days. Encephalopathy was seen in 2 patients. However, no mortality was reported.

Conclusions: Co-infection of HAV and HEV is not rare in pediatric age group. Knowledge about this will be of immense help for planning of future vaccination strategies and for better sanitation program in developing countries like India.

Keywords: Co-infection, Hepatitis A, Hepatitis E, Public health

INTRODUCTION

Acute viral hepatitis is a major public health problem worldwide.¹⁻⁶ Hepatitis A, B, C and E are the four major hepatotropic viruses causing viral hepatitis. Hepatitis D virus or Hepatitis Delta virus is not included in this group as it can propagate only in the presence of Hepatitis B virus and is now considered to be a sub viral satellite.⁷ HAV and HEV are the most common cause of acute viral hepatitis occurring throughout the year, affecting mainly the pediatric age group. Absence of natural immunity,

lack of awareness and the socioeconomic conditions like poor sanitation and contaminated water make the children susceptible to infection by both the viruses.

HAV is a non-enveloped RNA virus of the genus Hepatovirus and family Picornaviridae. HEV is also a non-enveloped RNA virus of the genus Hepevirus and family Hepeviridae. Both HAV and HEV are primarily spread via the faeco-oral route. In developing countries like India with vast areas of sub-optimal hygiene and sanitary conditions, HAV and HEV infection has

assumed endemic proportions.⁸ HAV mainly affects children whereas HEV is more common among young adults.⁹⁻¹² Both HAV and HEV usually cause self-limiting disease although fulminant hepatitis can develop in either of these.¹³⁻¹⁵

High fatality has especially been noted in pregnant females who contracted HEV infection particularly in the second and third trimester.¹⁶ Co-infection with multiple hepatotropic viruses has been reported in various studies on acute viral hepatitis with a prevalence rate varying from 7-24%.^{17,18} There has been speculation that this co-infection may increase the severity of the disease and such patients may have a poorer prognosis.¹ This study was therefore undertaken to determine the prevalence and clinico-epidemiological profile of HAV and HEV co-infection in patients with acute viral hepatitis.

The aim is to study the clinico-epidemiological profile of patients admitted with Hepatitis A and Hepatitis E co-infection in pediatric age group and to determine the prevalence of hepatitis A and E co-infection in patients admitted with acute viral hepatitis.

METHODS

This is a retrospective study conducted in Department of pediatrics at Himalayan Institute of Medical Sciences, Swami Rama Himalayan University, Jolly Grant, Dehradun, over a period of 4 years from January 2014 to December 2017.

Inclusion criteria

- Age group 0 years to 18 years
- Patients with both anti HAV IgM and anti HEV IgM positive status.

Exclusion criteria

- Other causes of acute viral hepatitis or any other co-infection.

Case records of all the patients admitted from January 2014 till December 2017 with acute viral hepatitis, were retrieved. Clinico-epidemiological data and laboratory parameters of the patients were noted and analyzed.

Statistical analysis

Result analysis was done using statistical software SPSS 22. Qualitative data were expressed in percentage, while quantitative data were expressed in mean±SD.

RESULTS

A total of 125 patients were diagnosed with Acute Viral Hepatitis during the study period. Out of 125, 96 patients were HAV IgM positive, 6 patients were HEV IgM positive with 2 patients having equivocal levels of HEV

IgM, 8 patients were HBsAg positive and 13 patients had co-infection of both Hepatitis A and E (Table 1). The prevalence of HAV and HEV co-infection was 10.4%. There were 16 patients with acute viral hepatitis in whom Anti HEV IgM was not done, so the prevalence could actually have been higher than this.

Table 1: Distribution of patients.

Patient	Number
Acute viral hepatitis	125
Hbs Ag positive	8
Anti HAV IgM positive	96
Anti HEV IgM positive	6
Equivocal Anti HEV IgM	2
Anti HAV IgM and Anti HEV IgM positive	13

Out of 13 enrolled patients, 8 (61.5%) were males and 5 (38.5%) were females. The maximum number of patients 6 (46.15%) were in the age group 0-5 years. Of these 4 were male and 2 females. Only 2 (15.38%) patients were more than 16 years of age and both were male. Age wise distribution of the patients is given in Table 2.

Table 2: Age wise distribution of patients with HAV and HEV co-infection.

	Number (%)	Male	Female
0-5 years	6 (46.15%)	4	2
6-10 years	2 (15.38%)	1	1
11-15 years	3 (23.07%)	1	2
16 years and above	2 (15.38%)	2	0

All 13(100%) patients admitted with co-infection had complaints of fever and jaundice. 8(61.5%) and 10(76.9%) of the patients also complained of pain in abdomen and vomiting respectively. Pruritis was present in 9(69.2%) of patients.

Hepatomegaly was the most common clinical finding seen in 11(84.6%) of the patients, whereas both hepatomegaly and splenomegaly was seen in 4(30.7%) patients. 3(23.07%) of the patients had features of stage II-III hepatic encephalopathy and 1(7.6%) of which required assisted ventilation for 5 days (Table 3).

Ultrasound abdomen was done in 7 patients and the most common ultrasound finding was coarse liver echotexture with circumferential gall bladder thickening. The peak level of bilirubin noted was 30.51mg/dl, while peak transaminases level i.e. ALT and AST was 5,592 IU/L and 5,657 IU/L respectively. Maximum PT (sec), INR and APTT (sec) noted were 33.5, 3.34, 52.3 respectively. Deranged coagulation profile was associated with clinically significant bleeding in 3 patients who were also transfused with FFP. The duration of hospital stay varied from 4 to 16 days, with an average duration of stay of 8.2 days.

No mortality was seen in present study.

Table 3: Clinico- laboratory findings of the patients with hepatitis A and E co-infection.

Clinico-laboratory findings	Number of patients
Fever*	13 (100)
Icterus*	13 (100)
Pain in abdomen*	8 (61.5)
Vomiting*	10 (76.9)
Bleeding*	3 (23.07)
Pruritis*	9 (69.2)
Altered sensorium*	3 (23.07)
Hepatomegaly*	11 (84.6)
Hepatosplenomegaly*	4 (30.7)
Encephalopathy*	3 (23.07)
Ventilator requirement*	1 (7.6)
Mortality	0
Duration of stay (avg. days)	8.2
T. Bilirubin [#]	8.6±7.27
ALT [#]	2030.69±1726.93
AST [#]	1880.07±1881.11
PT (sec) [#]	20.06±7.3
INR [#]	1.78±0.851
APTT (sec) [#]	37.74±8.72

*n(%) #mean±SD

DISCUSSION

HAV and HEV are the most common cause of acute viral hepatitis occurring throughout the year.¹⁹ Various studies from the Indian subcontinent have shown high prevalence rates ranging from 31-67% for HAV and 16-66% for HEV in children.^{1,4-6,13,18,20-24} In present study the prevalence of HAV and HEV was 76.8% and 4.8% respectively and the prevalence rate of HAV and HEV co-infection was 10.4%. Anti HEV IgM was not done in 16 patients with acute viral hepatitis.

HAV infection is acquired early in life with various community based studies demonstrating the presence of anti- HAV antibodies in nearly 80% of children by the age of 5 years.^{25,26} Although seroprevalence of HEV infection is shown to be higher in adults than children, studies such as those by Sarkar et al and Patel et al have shown increasing seroprevalence of HEV infection in children 1-5 years of age.^{5,27} They suggested a possibility of asymptomatic HEV infection in early childhood which has led to their under diagnosis. They have also suggested a possibility of under diagnosis of HEV infection in symptomatic young children due to the presence of some other acute co-infection like HAV.

The most common age group affected in present study was 0-5 years (46.15%) followed by 11-15 years (23.07%). The youngest patient in present study was a 3year old female child. In a study by Arora D et al conducted in Malwa region of Punjab, HAV and HEV co-infection was found in 5 (7.5%) of the patients with 4 patients less than 20years of age.²⁸ Monica A et al, found seroprevalence of HAV and HEV co-infection to be

5.2%. The most common age group affected was <15 years.²⁹

In a study by Pandaya N et al, co-infection was found in a 7 year old patient. However, it was also reported that prevalence of HAV was more in pediatric age group of 0-5years whereas, prevalence of HEV infection was more seen in the age group of 16-20years.³⁰

In the present study, 61.5% of the patients affected were male while 38.5% were female, which was similar to the study by Monica A et al.²⁹

Joon et al, also reported 33 (11.5%) cases of HAV and HEV co-infection between age group of 9 to 35 years with higher male preponderance.³¹ The higher incidence in males could be due to the greater outdoor mobility of this sex resulting in their greater exposure to contaminated food and water.

Fever, jaundice, vomiting followed by abdominal pain were the most common presenting complaints of the patients in the present study. 3(23.07%) patients presented with complaints of altered sensorium and were diagnosed with hepatic encephalopathy stage II-III. However, only 1(7.6%) patient, had ventilator requirement for 5days.

Kumar et al, Poddar et al and Arvind et al in their study have concluded that hepatitis due to co-existing HAV and HEV and other combinations did not result in a more severe illness when compared to hepatitis due to a mono virus infection.³²⁻³⁴ Arvind et al postulated a phenomenon of mutual viral suppression or viral restitution occurring in multiple viral infection as a probable explanation for this decreased severity. The high level of AST and ALT reported by Kumar et al in their patients was attributed to increased immune mediated viral clearance or increased cytopathic effect of dual infection with HAV and HEV.³²

In present study the peak level of bilirubin noted was 30.15mg/dl, while peak ALT and AST levels were 5592IU/L and 5657IU/L respectively. Maximum PT (sec), INR and aPTT (sec) noted was 33.5, 3.34 and 52.3 respectively. Bleeding manifestations in the form of melena was seen in 3(23.07%) patients and required FFP transfusion. Co-infection with HAV and HEV did not seem to adversely affect the prognosis of present patients as all patients improved with symptomatic management and there was no mortality. However, this data was not compared to the prognosis of patients with a mono-virus infection and further studies in this regard are suggested by the authors.

The establishment of clinical diagnosis of co-existence of HAV and HEV viruses as a cause of viral hepatitis is difficult and cannot be differentiated from mono-infection but the laboratory diagnosis either by serology or polymerase chain reaction (PCR) can be a useful tool in the diagnosis of simultaneous presence of both the

viruses.^{34,35} Treatment is supportive with serial monitoring of the signs of acute liver failure and in rare cases, liver transplant is the end treatment.

Transmission of the disease can be interrupted by proper food hygiene, improved sanitation and public education.³⁶ HAV vaccine is protective but coverage is poor because of high cost and lack of awareness. None of the patients in present study had received HAV vaccine.

The greatest limitation of present study is its small sample size. There were 16 patients with positive anti HAV IgM who were not evaluated for HEV co-infection. A complete evaluation of all the case could have resulted in demonstrating a higher prevalence of co-infection. Also, the study population was hospitalized children in a tertiary care center, so the clinical profile may not be generalized to the community.

CONCLUSION

It is evident from present study that co-infection with HAV and HEV is not infrequent. With similar mode of transmission and symptomatology, clinical diagnosis is difficult to establish, thus timely diagnosis by serology and PCR may help in the management. With increasing urbanization and overcrowding, supply of safe drinking water and safe sewage disposal has been adversely affected in many parts of our country. Despite great efforts by public/private agencies and the medical fraternity, immunization coverage is still abysmal in many areas. Improvement of food, personnel hygiene and periodic surveillance of HAV and HEV infection in pediatric age group will be of immense help in planning future vaccination strategies and helping in creating awareness and better sanitation programs in our country.

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