



Case Report

65

East-West Med. Col. J. Vol. 13, No. 1 January 2025

CO-INFECTION OF HEPATITIS A AND HEPATITIS E VIRUSES IN OUTPATIENTS IN DHAKA, BANGLADESH: A CASE SERIES

Siddique MAB¹, Nafisa T², Akram A³, Resma TI⁴, Akter T⁵

Article history:

Received: 22 October 2024

Accepted: 1st December 2024

Keywords: HAV; HEV, Feco oral; ViralHepatitis; Transmission.

Abstract:

Hepatitis E Virus (HEV) and Hepatitis A Virus (HAV) infections continue to pose substantial global health concerns, especially in areas of insufficient sanitation and hygiene standards. This case series investigates the seroprevalence of Hepatitis A Virus (HAV) and Hepatitis E Virus (HEV) among two patients attending OPD of National Institute of Laboratory Medicine and referral center, Dhaka, Bangladesh. The findings underscore the importance of considering multiple hepatitis viruses in the diagnostic evaluation of patients with acute hepatitis symptoms, particularly in regions with variable prevalence rates for these pathogens.

EWMCJ Vol. 13, No. 1, January 2025: 65-68

Introduction

Feco-orally transmitted Hepatitis remains a significant communicable disease in Bangladesh, serving as an indicator of poor sanitization, especially in rural and semi-urban areas ¹. It can cause a variety of health problems, some of which can be fatal. Hepatitis A, B, C, D, and E are the five main viruses that cause hepatitis. ¹ Acute hepatitis in pregnancy, acute chronic liver failure (ACLF) in Bangladesh, and other deadly illnesses are still mostly caused by HEV. Even though people with HEV illness typically recover completely; clinical research indicates that pregnant women who contract HEV and their unborn children frequently pass away. ²

Hepatitis A virus (HAV) is found worldwide and is a common infection that results in approximately 1.4 million new cases annually on a global scale. HAV is a non-enveloped virus with a size of 27 nanometers, known for its resistance to heat, acid, and ether. It

falls under the RNA virus category in the Hepatovirus genus, belonging to the Picornaviridae family. ² The presence of anti-HAV antibodies in human sera during acute illness is associated with elevated serum liver enzyme levels, and the shedding of HAV in feces continues. Initially, IgM antibodies are elevated, typically lasting for a few months (usually 6-12 months). However, during the recovery phase, IgG class antibodies become the predominant type. It's important to note that Hepatitis A is a self-limiting infection and does not progress to chronic liver disease. ³

On the other hand, Hepatitis E virus (HEV) is prevalent in Asia, Africa, and Central America. HEV belongs to the Hepevirus genus in the Hepeviridae family, characterized by a non-enveloped structure and a single-stranded positive-sense RNA. Antibodies to HEV, including anti-HEV IgM and anti-HEV IgG, can be identified, but the former decreases rapidly post-

1. Md. Abu Baker Siddique, Senior Medical technologist, Department of virology, National Institute of Laboratory Medicine and referral center, Dhaka, Bangladesh.
2. Dr. Tasnim Nafisa, Medical officer, Department of Virology, National Institute of Laboratory Medicine and Referral Center, Dhaka, Bangladesh.
3. Dr. Arifa Akram, Assistant professor, Department of virology, National Institute of Laboratory Medicine and referral center, Dhaka, Bangladesh.
4. Dr. Tania Islam, Assistant professor, Department of virology, National Institute of Laboratory Medicine and Referral Center, Dhaka, Bangladesh.
5. Tanzila Akter, Medical Technologist, Department of virology, National Institute of Laboratory Medicine and Referral Center, Dhaka, Bangladesh.

Address of Correspondence: Dr Arifa Akram, Assistant professor & Head, Department of virology, National Institute of Laboratory Medicine and referral center, Dhaka, Bangladesh. E mail: drbarna43@gmail.com Phone: +8801816296249

acute infection, reaching low levels within six months. Currently, routine serologic testing for HEV infection is not widely available.⁴ Numerous studies on sporadic acute hepatitis and fulminant liver failure in the mentioned regions have linked 20-60% of cases to HEV infection. Pregnant women experiencing these conditions tend to have higher rates of HEV infection compared to non-pregnant individuals. Despite this, the seroprevalence rates indicating prior exposure to HEV are relatively low, ranging from 10-40% in most studies.⁴

A nationwide study conducted in Bangladesh on the seroprevalence of Hepatitis A and Hepatitis E Virus revealed that out of 998 participants, 19% (191/998) tested positive for HAV, and 10% (103/998) tested positive for HEV.⁵ The median age for HAV-positive patients was 12 years, while for HEV-positive patients, it was 25 years. The prevalence of HAV was notably higher among females, accounting for 24.9%, whereas HEV was more prevalent among males, with a rate of 11.2%. The study found the highest occurrence of HAV among children, while HEV was most commonly observed in the 15–60 years age group, with a prevalence of 12.4%.⁵

HAV and HEV co-infection was reported in developing countries such as India⁶, Mexico⁷, Egypt⁸, and Venezuela⁹, but it is not common in developed countries.¹⁰ Drug use, homelessness, unavailability of the HAV vaccine, blood donation, and immunosuppression could be risk factors for HAV co-infection with HEV or other viral hepatitis.^{11,12} The outcomes of HAV–HEV co-infection are not well explored. HEV diagnosis is not routinely performed in several developing countries and there is no common in vitro or in vivo model system to study this co-infection.¹⁰

Hepatitis E Virus (HEV) and Hepatitis A Virus (HAV) infections remain significant global health challenges, particularly in regions with inadequate sanitation and hygiene standards.¹³ Both viruses are responsible for acute hepatitis, and their prevalence varies across populations and geographic locations.¹⁴ While studies on HEV and HAV have been conducted, there is a paucity of research specifically investigating the prevalence and co-infection rates using Enzyme-Linked Immunosorbent Assay (ELISA) tests. Investigating the co-infection rates of HEV and HAV can provide insights into the clinical implications and guide appropriate diagnostic and therapeutic strategies.¹⁴

Despite the significance of HEV and HAV infections, there is a gap in the literature regarding the simultaneous detection and differentiation of these viruses. Co-infection with multiple hepatitis viruses can complicate clinical outcomes and pose challenges for healthcare providers. This report therefore aims to investigate outpatients who are advised for HAV and/or HEV ELISA tests at the National Institute of Laboratory Medicines and Referral Center (NILMRC).

Case Presentation:

Case-1: A 30 years Female presented to the healthcare facility with complaints of fever, vertigo, vomiting, yellow discoloration of the skin (jaundice), and low blood pressure. Her symptoms began with the sudden onset of fever, followed by persistent vomiting and dizziness. She noticed a yellowish tint to her skin, prompting her to seek medical attention. Her medical history did not reveal any pre-existing liver conditions or known risk factors for hepatitis.

On physical examinations, Jaundice was evident in the yellow discoloration of the skin and sclera. On abdominal Examination, Mild hepatomegaly was found. She has mild Vertigo but no focal neurological deficits were identified.

Case -2: A 30 years male presented to the healthcare facility with complaints of fever, generalized weakness, loss of appetite, yellow discoloration of the skin (jaundice), concentrated urine, and dark-colored urine. He reported the sudden onset of fever associated with generalized weakness and a noticeable loss of appetite. He also observed yellow discoloration of his skin and noticed concentrated and dark-colored urine, prompting him to seek medical attention. There was no significant past medical history or known risk factors for liver diseases.

On physical Examination, there was fever, generalized weakness, fatigue, and icteric (yellow discoloration of the skin and sclera). Abdominal Examination revealed mild hepatomegaly. There were no neurological impairments.

Table-I
Laboratory Findings of both cases

Parameters	Case 1	Case 2
Serum Bilirubin	7.57 mg/dL	4.9 mg/dL
Alanine Aminotransferase (ALT)	375 U/L	520 U/L
IgM ELISA for HAV	Positive	Positive
IgM ELISA for HEV	Positive	Positive

Discussion:

The presented cases of concurrent acute Hepatitis A (HAV) and Hepatitis E (HEV) infections in our two patients highlight the clinical complexity and importance of recognizing dual viral infections in patients with acute hepatitis. The literature indicates that in Bangladesh, the rates of HEV positivity varied between 10.5% and 50.3%, while HAV positivity rates ranged from 5.6% to 39.8% and co-infection rates varied from 2-8 %.^{6,15,16}

Co-infection with HAV and HEV is a relatively uncommon phenomenon, and understanding the clinical implications, diagnostic challenges, and potential complications is crucial for effective management. In a study done by A Joon P Rao *et al.*, 11.5% of tested groups were found to have HAV & HEV coinfection.¹⁷ Similarly, a study done by Samaddar A *et al.* also found an HAV-HEV co-infection rate of about 2.07%.¹⁸ In our study, the prevalence is 2.1% which is likewise Samaddar A *et al.*¹⁸

While it is commonly stated that the prognosis is generally unaffected by co-infection, with most cases showing improvement through symptomatic therapy, there have been case reports emphasizing complications such as hepatic encephalopathy in individuals with co-infection.¹⁸ Our study also resembles previous findings where patients recovered with Palliative care. In our study, patient-1, shows relatively less severe symptoms than patient-2, who had a severe fever and generalized weakness for 15 days, but none of the patient's developed encephalopathy or any other neuropathy except mild vertigo in patient 1.

Few reports suggest that co infection can lead to severe conditions like hepatic encephalopathy etc whereas Radhakrishnan *et al.*, found that prognosis after symptomatic treatment is unaffected by the presence of one or two infections which complies with our current study.¹⁹ We found that both patients recovered with symptomatic treatment and did not develop any neuropathy or other severe complications that abide by the previous study of Radhakrishnan *et al.*¹⁹

Due to the prevalent feco-oral mode of transmission and the heightened emphasis on personal and food hygiene in society, it is imperative to conduct regular surveillance to monitor the exposure patterns of Hepatitis A (HAV) and Hepatitis E (HEV). Ensuring a

secure water supply and proper sewage disposal is crucial in this regard.

Conclusion

These case series underscore the importance of considering co-infection with HAV and HEV in patients presenting with acute hepatitis. Increased awareness among healthcare professionals, combined with comprehensive diagnostic approaches, is essential for accurate diagnosis, appropriate management, and public health interventions to prevent further transmission.

Conflict Of Interest:

None to disclose

References:

1. Ribeiro BB, Dos Santos MA, Freire TG, et al.: Characteristic of viral hepatitis deaths in Brazil in the year 2021. International Seven Journal of Health Research. 2023, 14:78-90. 10.56238/isevjhv2n2-003
2. World Health Organization. Hepatitis A vaccines: WHO position paper. Weekly Epidemiological Record= Relevé épidémiologique hebdomadaire. 2000, 75:38-44.
3. Braunwald E, Fauci AS, Kasper DL, Hauser SL, Longo DL, Jameson JL: Harrison's principles of internal medicine. In Harrison's principles of internal medicine-15th edition. 2001. <https://biblioteca.uazuay.edu.ec/buscar/item/74596>.
4. Joon A, Rao P, Shenoy SM, 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 Feb 1;33:S102-5.
5. Khan AI, Salimuzzaman M, Islam MT, Afrad MH, Shirin T, Jony MH, Alam MA, Rahman M, Flora MS, Qadri F. Nationwide hospital-based seroprevalence of hepatitis A and hepatitis E virus in Bangladesh. Annals of Global Health. 2020;86(1).
6. Arora NK, Nanda SK, Gulati S, Ansari IH, Chawla MK, Gupta SD, Panda SK: Acute viral hepatitis types E, A, and B singly and in combination in acute liver failure in children in north India. Journal of medical virology. 1996, 48:215-21. 10.1002/(SICI)1096-9071(199603)48:33.0.CO;2-B
7. Copado-Villagrana ED, Anaya-Covarrubias JY, Viera-Segura O, Trujillo-Ochoa JL, Panduro A, José-Abrego A, Roman S, Fierro NA. Spatial and temporal distribution of hepatitis A virus and hepatitis E virus among children with acute hepatitis in Mexico. Viral Immunology. 2021 Nov 1;34(9):653-7.
8. Hyams KC, McCarthy MC, Kaur M, et al.: Acute sporadic hepatitis E in children living in Cairo, Egypt. Journal of medical virology. 1992, 37:274-7. 10.1002/jmv.1890370407
9. García CG, Sánchez D, Villalba MC, et al.: Molecular characterization of hepatitis E virus in patients with acute hepatitis in Venezuela. Journal of medical virology. 2012, 84:1025-9. 10.1002/jmv.23277

10. Sayed IM. Dual infection of hepatitis A virus and hepatitis E virus—What is known?. *Viruses*. 2023 Jan 20;15(2):298.
11. Hofmeister MG: Preventable Deaths During Widespread Community Hepatitis A Outbreaks—United States, 2016–2022. *MMWR. Morbidity and Mortality Weekly Report*. 2023, 72:
12. Fontana S, Ripellino P, Niederhauser C, et al.: Epidemiology of HEV Infection in Blood Donors in Southern Switzerland. *Microorganisms*. 2023, 22:11. 10.3390/microorganisms 11102375
13. Rahman S, Khan M, Karim F: HEV infection as an aetiological factor for acute hepatitis: experience from a tertiary hospital in Bangladesh. *Journal of health, population, and nutrition*. 2009, 27:14. 10.3329/jhpn.v27i1.3314
14. Mahtab MA, Rahman S, Khan M, Karim MF. Hepatitis E virus is a leading cause of acute-on-chronic liver disease: experience from a tertiary centre in Bangladesh. *Hepatobiliary & pancreatic diseases international: HBPD INT*. 2009 Feb 1;8(1):50-2.
15. Kayesh ME, Kohara M, Tsukiyama-Kohara K: Epidemiology and Risk Factors for Acute Viral Hepatitis in Bangladesh: An Overview. *Microorganisms*. 2022, 15:2266.
16. Kalita D, Paul M, Deka S, Badoni G, Gupta P: Simultaneous infection of Hepatitis A and Hepatitis E viruses amongst acute viral hepatitis patients: A hospital-based study from Uttarakhand. *Journal of Family Medicine and Primary Care*. 2020, 9:6130. 10.4103/jfmpc.jfmpc_1373_20
17. Samaddar A, Taklikar S, Kale P, Kumar CA, Baveja S. Infectious hepatitis: A 3-year retrospective study at a tertiary care hospital in India. *Indian journal of medical microbiology*. 2019 Apr 1;37(2):230-4.
18. PARK JH, KIM BS, LEE CH, KIM SY, SEO JH, HUR CJ: A case of coinfection of Hepatitis A and E virus with hepatic encephalopathy. *Korean Journal of Medicine*. 2011, 101:5.
19. Radhakrishnan S, Raghuraman S, Abraham P, Kurian G, Chandy G, Sridharan G: Prevalence of enterically transmitted hepatitis viruses in patients attending a tertiary—care hospital in south India. *Indian journal of pathology & microbiology*. 2000, 1:433-6

©2025 Akram A.; This open-access article is distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Peer-Review History:

The peer review history for this paper can be accessed here: <https://ewmch.com/review/>