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Original Research Article

HEPATITIS E AS A LEADING CAUSE OF ACUTE VIRAL HEPATITIS: SEROPREVALENCE IN A TERTIARY CARE COHORT

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ABSTRACT

Background: Hepatitis E virus (HEV) is a major cause of acute viral hepatitis in developing countries, with significant public health implications due to its waterborne transmission and potential for outbreaks. Despite improvements in sanitation, HEV remains underdiagnosed, especially in tertiary care centers where patients often present with acute hepatitis of unknown etiology. Understanding the seroprevalence of HEV among clinically suspected cases is essential for guiding diagnostic strategies and public health interventions.

Materials and Methods: This cross-sectional observational study was conducted in the Department of Medicine from January 2024 to December 2024. A total of 180 patients with clinical suspicion of acute viral hepatitis were enrolled. Serum samples were tested for anti-HEV IgM antibodies using enzyme-linked immunosorbent assay (ELISA). Demographic, clinical, and biochemical data were collected. Statistical analysis was performed using chi-square and Student's t-test, with $p < 0.05$ considered significant.

Results: Of 180 patients, 35 (19.4%) were seropositive for HEV. The mean age of HEV-positive patients was 32.6 ± 10.8 years, and seropositivity was most common in the 21–40 years age group (42.9%). No significant differences were observed with respect to age, gender, or residence, although a numerical predominance was noted in rural areas (71.4%). Clinical symptoms, including jaundice and fatigue, were common in both groups, but none showed statistical significance. Biochemical analysis revealed significantly higher ALT (632.5 ± 211.3 U/L vs. 418.6 ± 187.9 U/L, $p = 0.001$) and AST (588.7 ± 198.5 U/L vs. 402.1 ± 176.4 U/L, $p = 0.002$) levels in HEV-positive patients, while bilirubin and alkaline phosphatase levels did not differ.

Conclusion: HEV accounted for nearly one-fifth of acute viral hepatitis cases in this cohort. Elevated transaminase levels were the most consistent biochemical feature, while clinical and demographic factors did not show significant associations. These findings support the inclusion of HEV IgM testing in diagnostic panels for acute hepatitis and highlight the importance of preventive strategies such as safe water access and community awareness in endemic regions.

Keywords: Hepatitis E virus, acute viral hepatitis, seroprevalence, ELISA, tertiary care, India.

INTRODUCTION

Acute viral hepatitis (AVH) continues to be a major cause of morbidity across the globe, with developing countries bearing a disproportionate share of the burden.[1] The disease is characterized by inflammation of the liver caused by hepatotropic viruses, most commonly hepatitis A, B, C, and E. Among these, hepatitis E virus (HEV) has emerged as a significant pathogen in both sporadic and epidemic cases of AVH, particularly in Asia and

Africa, where environmental and socioeconomic factors favor its transmission.[2]

HEV is a non-enveloped RNA virus transmitted predominantly through the fecal–oral route. Contaminated drinking water remains the principal source of infection, and outbreaks are often associated with flooding, breakdowns in sanitation infrastructure, or seasonal water scarcity.[3] The global distribution of HEV shows that large populations are exposed to risk, and the infection has been implicated in millions of symptomatic cases annually.[4] Despite improvements in hygiene and public health measures, the virus continues to circulate widely and causes repeated outbreaks in endemic regions.

The clinical course of HEV infection is typically acute and self-limiting, but the spectrum of disease is broad. Patients commonly present with fever, anorexia, malaise, nausea, jaundice, and deranged liver function tests, features that are indistinguishable from other causes of AVH.[5] In most individuals, recovery occurs within weeks; however, severe complications can arise in certain high-risk groups. Pregnant women represent the most vulnerable population, with infection during the third trimester associated with acute liver failure, high maternal mortality, and poor fetal outcomes.[6] Similarly, individuals with underlying chronic liver disease or those who are immunocompromised may experience a more aggressive course.

Although HEV accounts for a considerable proportion of acute hepatitis cases, it remains under-recognized in clinical practice. In many healthcare systems, the diagnostic focus is directed toward hepatitis A and B, while HEV is frequently overlooked due to limited awareness or restricted availability of routine diagnostic testing.[7] This underdiagnosis has implications not only for patient care but also for public health, as unrecognized HEV cases may contribute to ongoing community transmission.

Furthermore, the epidemiology of HEV varies widely across geographic regions. Reported prevalence rates differ depending on population characteristics, environmental factors, and study methodologies.[8] This variability makes it essential to generate local data that can reflect the true burden of HEV in different clinical settings.

Against this background, evaluating the seroprevalence of HEV among clinically suspected AVH cases in tertiary care centers is crucial.

MATERIALS AND METHODS

Study Design and Setting

This was a hospital-based, cross-sectional observational study conducted in the Department of Medicine of a tertiary care teaching hospital. The study was carried out over a period of twelve months, from January 2024 to December 2024. The hospital caters to a diverse population from both urban and rural backgrounds, making it a suitable setting to evaluate the seroprevalence of hepatitis E virus (HEV) among patients with clinically suspected acute viral hepatitis (AVH).

Study Population

All patients presenting to the Department of Medicine with clinical suspicion of AVH were screened for eligibility. Clinical suspicion was based on the presence of acute onset jaundice, malaise, fatigue, anorexia, nausea, right upper quadrant discomfort, or dark-colored urine, along with elevated liver enzymes.

Inclusion Criteria

- Patients aged ≥18 years with clinical features suggestive of acute viral hepatitis.
- Willingness to provide informed consent.

Exclusion Criteria

- Patients with known chronic liver disease, autoimmune hepatitis, drug-induced hepatitis, or metabolic liver disorders.
- Patients unwilling or unable to provide informed consent.

Sample Size

A total of 180 consecutive patients fulfilling the eligibility criteria were enrolled during the study period. The sample size was estimated considering the expected prevalence of HEV in clinically suspected AVH cases and allowing for statistical precision.

Data Collection

Detailed demographic and clinical information was obtained using a structured proforma, including age, sex, residence (urban/rural), occupation, risk factors, and clinical presentation. Venous blood samples were collected under aseptic precautions at the time of admission for laboratory investigations.

Laboratory Investigations

All serum samples were tested for the presence of anti-HEV IgM antibodies using a commercially available enzyme-linked immunosorbent assay (ELISA) kit, as per the manufacturer's instructions. Standard biochemical investigations, including liver function tests (serum bilirubin, alanine aminotransferase [ALT], aspartate aminotransferase [AST], and alkaline phosphatase), were also performed. Results were interpreted based on reference ranges defined by the institutional laboratory.

Statistical Analysis

Data was entered into Microsoft Excel and analyzed using Statistical Package for the Social Sciences (SPSS) version 26.0. Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were summarized as frequencies and percentages. Comparisons between HEV seropositive and seronegative groups were performed using Student's t-test for continuous variables and chi-square test for categorical variables. A p-value <0.05 was considered statistically significant. Confidence intervals (95% CI) were reported where applicable.

Ethical Considerations

The study was conducted following approval from the Institutional Ethics Committee. Written informed consent was obtained from all participants after providing a detailed explanation of the study objectives and procedures. Confidentiality of patient information was strictly maintained throughout the study.

RESULTS

Table 1: Demographic characteristics of study participants

Variable	HEV Positive (n=35)	HEV Negative (n=145)	Total (n=180)	p-value
Total patients	35	145	180	–
Mean age (years)	32.6 ± 10.8	34.1 ± 11.2	33.5 ± 11.0	0.318
Male : Female ratio	22:13	86:59	108:72	0.642
Urban residence	10 (28.6%)	59 (40.7%)	69 (38.3%)	0.259
Rural residence	25 (71.4%)	86 (59.3%)	111 (61.7%)	0.259

Table 2: Clinical presentation of patients with acute viral hepatitis

Symptom	HEV Positive (n=64)	HEV Negative (n=116)	p-value
Jaundice	32 (91.4%)	121 (83.4%)	0.356
Fatigue/Malaise	27 (77.1%)	102 (70.3%)	0.554
Anorexia	24 (68.6%)	91 (62.8%)	0.655
Nausea/Vomiting	22 (62.9%)	84 (57.9%)	0.734
Abdominal pain	16 (45.7%)	66 (45.5%)	1.000

Table 3: Biochemical parameters of study groups

Parameter	HEV Positive (n=64)	HEV Negative (n=116)	p-value
Total bilirubin (mg/dL)	8.3 ± 3.1	7.9 ± 2.9	0.397
ALT (U/L)	632.5 ± 211.3	418.6 ± 187.9	0.001*
AST (U/L)	588.7 ± 198.5	402.1 ± 176.4	0.002*
Alkaline phosphatase (U/L)	311.4 ± 112.6	298.2 ± 106.9	0.536

Table 4: Age-wise distribution of HEV seropositivity

Age group (years)	HEV Positive (n=35)	HEV Negative (n=145)	p-value
<20	4 (11.4%)	15 (10.3%)	1.000
21–40	15 (42.9%)	42 (29.0%)	0.167
41–60	10 (28.6%)	39 (26.9%)	1.000
>60	5 (14.3%)	20 (13.8%)	1.000

Table 5: Comparison of residence with HEV seropositivity

Residence	HEV Positive (n=64)	HEV Negative (n=116)	p-value
Urban	10 (28.6%)	59 (40.7%)	0.259
Rural	25 (71.4%)	86 (59.3%)	0.259

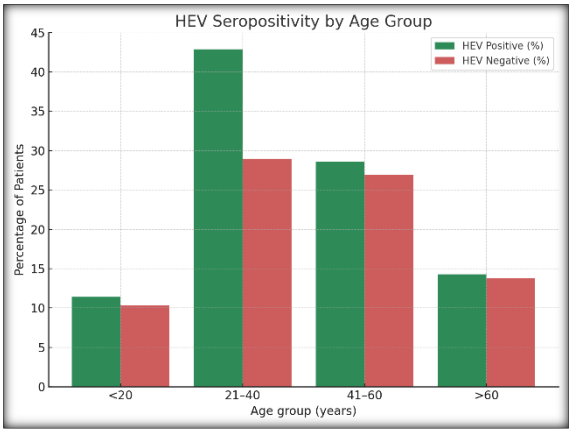

Figure 1: HEV seropositivity according to age

A total of 180 patients with clinically suspected acute viral hepatitis were evaluated, of whom 35 (19.4%) were seropositive for hepatitis E virus (HEV). The mean age of HEV-positive patients was 32.6 ± 10.8 years, while that of HEV-negative patients was 34.1 ± 11.2 years, with no significant difference ($p = 0.318$). The overall male-to-female ratio remained 1.5:1, and gender distribution did not differ significantly between groups ($p = 0.642$).

Residence pattern showed that 71.4% of HEV-positive cases were from rural areas compared to 59.3% of HEV-negative cases, whereas 28.6% of positives were from urban settings versus 40.7% of negatives. However, this difference was not statistically significant ($p = 0.259$).

Clinical presentation was broadly similar across groups. Jaundice was the most common symptom, reported in 91.4% of HEV-positive and 83.4% of HEV-negative patients ($p = 0.356$). Fatigue was seen in 77.1% and 70.3% respectively ($p = 0.554$). Other symptoms such as anorexia, nausea/vomiting, and abdominal pain showed no significant intergroup differences (all $p > 0.05$).

Biochemical analysis revealed significantly higher transaminase levels in HEV-positive patients. Mean ALT was 632.5 ± 211.3 U/L in positives compared to 418.6 ± 187.9 U/L in negatives ($p = 0.001$). Similarly, AST was 588.7 ± 198.5 U/L versus 402.1 ± 176.4

U/L (p = 0.002). Total bilirubin (8.3 ± 3.1 vs. 7.9 ± 2.9 mg/dL; p = 0.397) and alkaline phosphatase (311.4 ± 112.6 vs. 298.2 ± 106.9 U/L; p = 0.536) did not differ significantly.

Age distribution demonstrated that HEV seropositivity was most frequent in the 21–40 years group (42.9%), followed by 41–60 years (28.6%), >60 years (14.3%), and <20 years (11.4%). However, differences across age strata were not statistically significant (all p > 0.05).

Overall, HEV accounted for nearly one-fifth of AVH cases, with elevated transaminase levels being the most significant biochemical feature, while demographic and clinical associations were not statistically significant.

DISCUSSION

Hepatitis E virus (HEV) is an important etiological agent of acute viral hepatitis in endemic regions, particularly in South Asia. In the present study, HEV accounted for 19.4% of clinically suspected AVH cases in a tertiary care hospital. Although lower than some previously reported figures, this finding highlights that HEV remains a considerable contributor to the burden of acute hepatitis in referral centers, where diagnostic focus often continues to be directed toward hepatitis A and B.

The age distribution in this study showed that HEV seropositivity was most frequent among young adults aged 21–40 years (42.9%), followed by those aged 41–60 years (28.6%). Similar patterns have been documented in other Asian cohorts, where HEV infection disproportionately affects young and middle-aged adults, likely reflecting increased occupational and environmental exposure.[11,12] Unlike hepatitis A, which commonly affects children, or hepatitis B, which may progress to chronic infection, HEV tends to cluster among adults in economically productive age groups, adding to its public health impact.

In contrast to earlier reports, rural residence was not found to be a statistically significant determinant of HEV positivity in this cohort, although a numerical predominance was observed (71.4% of positives were rural residents). This suggests that while sanitation and water supply remain important risk factors, the distinction between urban and rural exposure may be narrowing in some regions due to changing living conditions or improved infrastructure.

Biochemical analysis demonstrated that alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels were significantly higher in HEV-positive patients compared to seronegatives, confirming the hepatocellular injury pattern typically associated with HEV infection.[14,15] However, total bilirubin and alkaline phosphatase levels did not differ significantly, in line with the observation that cholestatic changes are not characteristic features of this infection.

The clinical presentation of HEV in this study was non-specific and overlapped with other viral hepatitides. Jaundice, fatigue, anorexia, and nausea were common, but none of these parameters were statistically different between HEV-positive and negative groups. This emphasizes the inability of clinical features alone to distinguish HEV from other causes of AVH and reiterates the importance of laboratory-based serological confirmation.[16]

The study has several clinical implications. First, although the prevalence was lower than in some prior studies, the contribution of HEV to acute hepatitis underscores the need to include HEV IgM testing in the diagnostic workup of suspected cases, especially in endemic regions. Second, markedly elevated transaminases may serve as a biochemical clue to HEV infection in the absence of clear epidemiological risk factors. Finally, preventive measures aimed at ensuring safe water supplies and raising community awareness remain essential for reducing transmission and disease burden.

CONCLUSION

This study demonstrates that hepatitis E virus (HEV) accounted for 19.4% of acute viral hepatitis cases in a tertiary care setting. The infection was most common among young adults, particularly in the 21–40 years age group, although age-related differences were not statistically significant. Rural residence showed a numerical predominance but did not emerge as a significant determinant. Elevated transaminase levels were the most consistent biochemical feature associated with HEV infection, while clinical manifestations were largely indistinguishable from other viral hepatitis. These findings emphasize the importance of incorporating routine HEV IgM testing into the diagnostic evaluation of acute hepatitis. Strengthening preventive strategies, including access to safe drinking water and public health education, remains vital in reducing the disease burden in endemic areas.

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Conflicts of Interest

The authors declare no conflicts of interest related to this work.

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