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Original Research Article

Prevalence and co-infection of acute hepatitis A virus and hepatitis E virus infections in patients with acute viral hepatitis

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ABSTRACT

Background: Viral hepatitis constitutes a significant global health burden, with hepatitis A virus (HAV) and hepatitis E virus (HEV) causing approximately 1.34 million deaths annually. This study aimed to determine the prevalence of acute HAV and HEV infections, evaluate co-infection patterns, and assess liver dysfunction among suspected acute viral hepatitis cases.
Methods: This cross-sectional study was conducted from July 2023 to July 2024 at a tertiary care hospital. A total of 165 patients with clinically suspected acute viral hepatitis were included. Serum samples were tested for IgM antibodies against HAV and HEV using ELISA. Clinical severity was assessed using standardized grading criteria.
Results: Among 165 patients with suspected acute viral hepatitis, HAV IgM seropositivity was 23.6% (39/165), HEV IgM seropositivity was 10.9% (18/165), and co-infection rate was 2.4% (4/165). HAV mono-infections comprised 21.2% (35/165) and HEV mono-infections 8.5% (14/165). Co-infected patients were significantly younger (mean age 15.8±4.2 years) compared to HAV (30.2±13.8 years) and HEV (25.6±11.4 years) mono-infections ($p=0.042$). Severe disease occurred in 50% of co-infected patients compared to <9% in mono-infections. Seasonal clustering was highly significant ($p < 0.001$) with 47.2% of cases during monsoon period.
Conclusions: This study demonstrates significant HAV and HEV disease burden with young adults being most susceptible. Co-infected patients showed more severe clinical presentation requiring enhanced monitoring. Seasonal clustering emphasizes the environmental influence on transmission patterns.

Keywords: Acute infection prevalence, Acute viral hepatitis, Co-infection, Hepatitis A virus, Hepatitis E virus, Seasonal variation

INTRODUCTION

Viral hepatitis constitutes one of the leading causes of morbidity and mortality globally, with hepatitis A and E viruses collectively causing substantial disease burden through fecal-oral transmission. The World Health Organization reports that viral hepatitis caused approximately 1.34 million deaths globally in 2015, matching tuberculosis mortality.[1] India bears a disproportionate burden of enterically transmitted viral hepatitis, with HAV seroprevalence exceeding 90% among adults and HEV causing recurrent large-scale outbreaks.[2,3]

These pathogens demonstrate epidemiological transition patterns, shifting from high childhood endemicity toward adult susceptibility as sanitation improves.[4,5] The relationship between HEV and pregnancy merits particular attention, with case-fatality rates among pregnant women ranging from 15-30% compared to 0.5-4% in the general population.[6,7]

Despite extensive research, significant knowledge gaps remain regarding current acute infection prevalence patterns, co-infection rates, and clinical presentations of HAV and HEV infections.[8,9] This study aims to determine the prevalence of acute HAV and HEV infections in

patients with acute viral hepatitis, assess co-infection prevalence, and evaluate clinical presentations.

METHODS

Study design and setting

A cross-sectional study was conducted from July 2023 to July 2024 at the Department of Microbiology at a tertiary care centre after obtaining approval from the Institutional Ethics Committee. The study aimed to determine acute infection prevalence patterns, clinical presentations, severity assessment, and seasonal distribution of HAV and HEV infections in patients with acute viral hepatitis.

Study population

A total of 165 patients with clinically suspected acute viral hepatitis from Medicine, Pediatrics, Gastroenterology, and Obstetrics & Gynecology departments were included after obtaining informed consent. Patients with chronic viral hepatitis, liver cirrhosis, non-infective jaundice, and neonatal jaundice were excluded.

Clinical data collection and severity assessment

Comprehensive clinical assessment was performed for all patients including demographic characteristics (age, gender), presenting symptoms (jaundice, fever, abdominal pain, nausea/vomiting, fatigue), and clinical presentation patterns. Age was recorded as both categorical groups and continuous variable for statistical analysis.

Clinical severity was assessed using a standardized grading system based on clinical presentation and laboratory abnormalities. Mild disease was defined as jaundice with minimal symptoms, ALT/AST <5× upper limit of normal (ULN), bilirubin <5 mg/dL. Moderate disease included jaundice with moderate symptoms, ALT/AST 5-10× ULN, bilirubin 5-10 mg/dL. Severe disease was characterized by jaundice with severe symptoms, ALT/AST >10× ULN, bilirubin >10 mg/dL, or complications.

Laboratory methods

Approximately 5 ml of blood sample was collected aseptically from suspected cases of acute viral hepatitis by venepuncture. The serum was separated by centrifugation and collected in a serum vial. The specimen was properly labelled with the serial number, name of the patient and date of collection.

All 165 acute viral hepatitis suspected cases were tested for the detection of HAV and HEV IgM antibodies by Enzyme Linked Immunosorbent Assay (ELISA) using commercial IgM 'Capture' ELISA for HAV and Indirect sandwich ELISA for HEV. Tests were performed and calculations were done according to the manufacturer's instructions.

Liver function tests including alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin, and alkaline phosphatase (ALP) were performed for all patients. ALT/AST ratios were calculated to assess predominant patterns of liver injury.

Seasonal analysis

Cases were categorized by season of presentation: monsoon (July-September), post-monsoon (October-December), winter (January-March), and summer (April-June) to assess temporal clustering patterns.

Statistical analysis

Results obtained were analysed statistically using Statistical Package for the Social Sciences (SPSS). Categorical variables were expressed as frequencies and percentages with Wilson 95% confidence intervals for prevalence estimates. Continuous variables were expressed as mean ± standard deviation after testing for normal distribution.

For categorical variables, Fisher's exact test was used for comparisons between groups, particularly when expected cell frequencies were small. Chi-square test was applied for overall distribution analysis and seasonal pattern assessment. For continuous variables, one-way ANOVA was used for comparing means across groups, followed by post-hoc analysis when significant. The p values of less than 0.05 were considered statistically significant.

RESULTS

Among 165 patients with clinically suspected acute viral hepatitis, 53 (32.1%, 95% CI: 25.4-39.4%) tested positive for HAV or HEV acute IgM seropositivity. Overall HAV IgM seropositivity was 23.6% (39/165) and HEV IgM seropositivity was 10.9% (18/165). HAV mono-infections predominated with 35 cases (21.2%), followed by HEV mono-infections with 14 cases (8.5%), and co-infections with 4 cases (2.4%) (Table 1, Figure 1).

Table 1: Prevalence and demographic characteristics of acute hepatitis A virus and hepatitis E virus infections.

Parameter	HAV mono-infection	HEV mono-infection	Co-infection	Total positive
Cases, N (%)	35 (21.2)	14 (8.5)	4 (2.4)	53 (32.1)
95% CI*	15.7-28.1	5.1-13.7	0.9-6.1	25.4-39.4
Male gender (%)	21/35 (60.0)	9/14 (64.3)	2/4 (50.0)	32/53 (60.4)

Continued.

Parameter	HAV mono-infection	HEV mono-infection	Co-infection	Total positive
Age groups in years (%)				
<20	7/35 (20.0)	4/14 (28.6)	3/4 (75.0)	14/53 (26.4)
21-30	11/35 (31.4)	5/14 (35.7)	1/4 (25.0)	17/53 (32.1)
31-40	9/35 (25.7)	4/14 (28.6)	0/4 (0.0)	13/53 (24.5)
>40	8/35 (22.9)	1/14 (7.1)	0/4 (0.0)	9/53 (17.0)
Mean age ± SD (years)	30.2±13.8	25.6±11.4	15.8±4.2	28.1±13.2
Clinical severity† (%)				
Mild	8/35 (22.9)	6/14 (42.9)	0/4 (0.0)	14/53 (26.4)
Moderate	24/35 (68.6)	7/14 (50.0)	2/4 (50.0)	33/53 (62.3)
Severe	3/35 (8.6)	1/14 (7.1)	2/4 (50.0)	6/53 (11.3)

*Wilson 95% confidence intervals; †Clinical severity based on laboratory abnormalities and clinical presentation; Fisher's exact test for age distribution: p = 0.021; One-way ANOVA for mean age: p=0.042

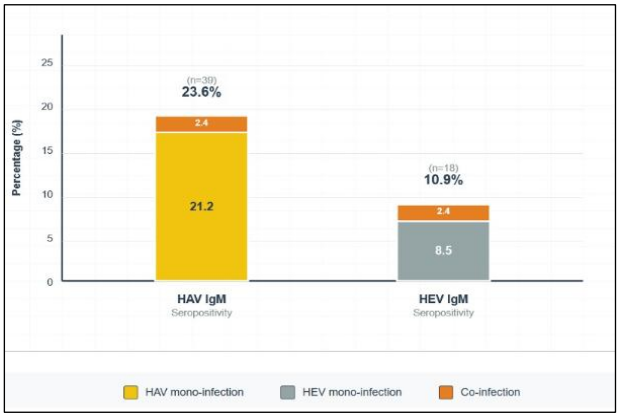

Figure 1: Overall IgM seropositivity of hepatitis A virus and hepatitis E virus among patients with suspected acute viral hepatitis.

Stacked bar chart showing overall IgM seropositivity rates for hepatitis A virus (HAV) and hepatitis E virus (HEV) among 165 patients with suspected acute viral hepatitis. Left bar shows HAV IgM seropositivity (23.6%, n=39) comprising mono-infections (21.2%, yellow) and co-infections (2.4%, orange). Right bar shows HEV IgM seropositivity (10.9%, n=18) comprising mono-infections (8.5%, gray) and co-infections (2.4%, orange). Orange segments represent the same 4 co-infected patients positive for both viruses. Total IgM seropositivity was 32.1% (53/165). IgM antibodies detected using ELISA. HAV = hepatitis A virus; HEV = hepatitis E virus; IgM = immunoglobulin M.

Clinical severity assessment revealed important differences among infection groups. Co-infected patients demonstrated significantly more severe disease, with 50% presenting with severe disease compared to 8.6% for HAV and 7.1% for HEV mono-infections. Moderate disease was most common in HAV mono-infections (68.6%), while HEV mono-infections showed the highest proportion of mild disease (42.9%). None of the co-infected patients had mild disease.

Liver function abnormalities were prevalent across all infection categories, with no statistically significant differences observed between HAV and HEV mono-infections for individual parameters. However, co-infected patients consistently demonstrated universal abnormalities (100%) across all tested liver function parameters, compared to 82.9% for HAV and 64.3% for HEV mono-infections showing all parameters abnormal (Table 2).

Clinical presentations were similar across infection types, with jaundice being nearly universal (96.2% overall). Fever was more frequent in HEV mono-infections (71.4%) compared to HAV mono-infections (54.3%), though this difference was not statistically significant (p=0.33). All co-infected patients presented with fever (Table 3).

Seasonal distribution analysis revealed highly significant temporal clustering (χ^2 = 19.08, p<0.001), with 47.2% of all cases occurring during the monsoon period compared to only 9.4% during winter months. This seasonal pattern was consistent across all infection types (Table 4).

Table 2: Liver function abnormalities in viral hepatitis infections.

Parameter	HAV mono-infection (n=35)	HEV mono-infection (n=14)	Co-infection (n=4)	P value†
ALT/AST ratio >1 (%)	30 (85.7)	11 (78.6)	4 (100.0)	0.68
Total bilirubin elevated (%)	34 (97.1)	12 (85.7)	4 (100.0)	0.15
ALP elevated (%)	31 (88.6%)	10 (71.4)	4 (100.0)	0.24
All parameters abnormal (%)	29 (82.9)	9 (64.3)	4 (100.0)	0.29

†Fisher's exact test for HAV vs HEV comparisons; Co-infection group not included in statistical comparisons due to small sample size (n=4)

Table 3: Clinical presentations of HAV mono-infection, HEV mono-infection and their co-infection.

Clinical feature	HAV mono-infection (n=35) (%)	HEV mono-infection (n=14) (%)	Co-infection (n=4) (%)	Total (n=53) (%)
Jaundice	33 (94.3)	14 (100.0)	4 (100.0)	51 (96.2)
Fever	19 (54.3)	10 (71.4)	3 (75.0)	32 (60.4)
Abdominal pain	28 (80.0)	11 (78.6)	4 (100.0)	43 (81.1)
Nausea/vomiting	31 (88.6)	12 (85.7)	4 (100.0)	47 (88.7)
Fatigue	35 (100.0)	14 (100.0)	4 (100.0)	53 (100.0)

Fisher's exact test for HAV vs HEV comparisons: Fever p = 0.33, other symptoms p>0.05

Table 4: Seasonal distribution and temporal patterns.

Season	HAV mono-infection (n=35) (%)	HEV mono-infection (n=14) (%)	Co-infection (n=4) (%)	Total (n=53) (%)
Monsoon (Jul-Sep)	16 (45.7)	7 (50.0)	2 (50.0)	25 (47.2)
Post-monsoon (Oct-Dec)	11 (31.4)	4 (28.6)	1 (25.0)	16 (30.2)
Winter (Jan-Mar)	3 (8.6)	1 (7.1)	1 (25.0)	5 (9.4)
Summer (Apr-Jun)	5 (14.3)	2 (14.3)	0 (0.0)	7 (13.2)

Chi-square test for overall seasonal distribution: $\chi^2 = 19.08$, df = 3, $p<0.001$

DISCUSSION

The present study provides important insights into the epidemiological patterns of hepatitis A and E viruses in a tertiary care hospital setting. The findings contribute to the limited surveillance data available for these enterically transmitted viral infections, which remain significant public health challenges in developing countries.[1,2]

Our acute HAV infection prevalence of 23.6% demonstrates consistency with contemporary research. Anitha et al documented a 22% prevalence rate in their retrospective analysis,[10] while Gopinath et al established an equivalent 22% prevalence.[11] This alignment indicates consistent endemic HAV transmission patterns within hospital-based populations across regions.

The acute HEV infection prevalence of 10.9% aligns with Palewar et al, who established a similar 8.5% prevalence through their 3-year retrospective analysis, supporting consistent HEV prevalence patterns across comparable healthcare environments.[12] However, regional variations exist, with Kalita et al reporting higher 28.04% HEV prevalence, indicating geographical differences in transmission patterns.[13]

Our co-infection rate of 2.4% corresponds with Samaddar et al, who established a similar 2.07% dual infection rate, while Bansal et al recorded 1.6%.[14,15] These aligned findings indicate predictable occurrence rates of concurrent infections in endemic regions.

The predominance of young adults in the 21-30 years age group for both infections reflects epidemiological transition, where improved sanitation has increased adult vulnerability by reducing childhood exposure.[4,16] This pattern aligns with Joon et al, who reported predominant infections among young adults.[17] The absence of significant gender differences contrasts with some studies showing male predominance, possibly reflecting regional variations or healthcare-seeking behaviors.[14,17]

The biochemical findings demonstrate characteristic hepatocellular injury patterns typical of acute viral hepatitis. The universal abnormalities observed in co-infected patients, with 100% showing elevated parameters across all liver function tests, suggest additive inflammatory effects and more severe hepatic dysfunction. This corresponds with Sarguna et al, who documented universal liver function abnormalities in outbreak investigations.[19]

The seasonal clustering during monsoon months, with 47.2% of cases occurring during July-September period, reflects typical transmission patterns for enterically transmitted viruses. This correlates with periods of increased water contamination and compromised sanitation conditions during heavy rainfall. The pattern has important implications for public health preparedness and resource allocation during high-risk periods.

CONCLUSION

This study demonstrates significant HAV and HEV disease burden with young adults being most susceptible. Co-infected patients showed more severe clinical presentation requiring enhanced monitoring. Seasonal clustering emphasizes the environmental influence on transmission patterns.

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Ethical approval: The study was approved by the Institutional Ethics Committee (IEC/2023/MIC/07)

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