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ORIGINAL RESEARCH

Emerging and Re-Emerging Enterically Transmitted Hepatitis Viruses: Hepatitis A and Hepatitis E

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Abstract

Background: Hepatitis A virus (HAV) and Hepatitis E virus (HEV) are major causes of acute viral hepatitis, particularly in developing countries where sanitation and hygiene remain significant public health challenges. HAV primarily affects children and is associated with asymptomatic or mild self-limiting illness, while HEV predominantly affects adults and can lead to severe complications, especially in pregnant women. Understanding the epidemiological trends and prevalence of these infections is crucial for implementing effective public health interventions.

Aim: This study aims to evaluate the prevalence, demographic distribution, and clinical characteristics of HAV and HEV infections in patients presenting with symptoms of acute viral hepatitis. The study also seeks to identify risk factors associated with infection and assess the need for targeted prevention strategies.

Methods: A total of 608 patients were tested for HAV, and 475 patients were tested for HEV using enzyme-linked immunosorbent assay (ELISA) for IgM antibodies. Data on patient demographics, clinical symptoms, and laboratory findings were collected and analyzed using SPSS version 23.0. Statistical comparisons were performed to determine significant correlations between infection status and various demographic and clinical parameters.

Results: The predominance of HAV was found to be 42.3% (257/608), with the highest infection rate observed in the pediatric population, particularly among children aged 5 years. In contrast, HEV infection was detected in only 0.2% (1/475) of the tested individuals, indicating a much lower burden in the study population. Male patients had a slightly higher prevalence of both HAV (55.0%) and HEV (54.1%), though the difference was not statistically significant. The most common symptoms in HAV-positive patients were jaundice (74%), fever (66%), and fatigue (58%). Due to the limited number of HEV cases, statistical comparisons for this virus were not feasible.

Conclusion: HAV remains a significant public health concern, particularly among children, whereas HEV infection appears to be rare in the study population. The findings emphasize the need for improved sanitation, hygiene education, and the potential incorporation of hepatitis A vaccination into routine immunization programs.

Recommendations: Improving hygiene, sanitation, and clean water access can reduce HAV and HEV transmission. Hepatitis A vaccination should be considered for children, and HEV surveillance strengthened to protect high-risk groups. Further research is needed to guide effective interventions.

Keywords: Hepatitis A virus, Hepatitis E virus, Acute viral hepatitis, Epidemiology, Public health interventions

Introduction

HAV and HEV are significant etiological agents of acute viral hepatitis, particularly in developing countries like India. Both viruses are primarily transmitted via the fecal-oral route, often through contaminated water and food sources. Despite similarities in transmission, the epidemiological patterns of HAV and HEV exhibit notable differences influenced by factors such as age, socioeconomic status, and regional sanitation practices.

Historically, HAV infection has been endemic in India, with early childhood exposure leading to widespread immunity. However, recent studies indicate a shifting epidemiology. A study published in 2020 highlighted a decline in HAV seroprevalence over the past two decades, correlating this trend with improvements in water quality, hygiene, and

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sanitation [1]. This decline has led to an increased proportion of susceptible adolescents and adults, resulting in more clinically apparent and severe disease manifestations in these age groups. Outbreaks have been reported among adolescents and adults, underscoring the need for targeted vaccination strategies [2].

HEV remains a leading cause of acute viral hepatitis in India, particularly among adults. A 2021 study reported that HEV accounts for nearly 50% of acute hepatitis cases and a similar proportion of acute liver failure cases in the country [3]. The seroprevalence of anti-HEV IgG antibodies among blood donors is approximately 60%, indicating high prior exposure [3]. HEV transmission is predominantly linked to fecal contamination of drinking water, with sporadic outbreaks often associated with monsoon seasons and flooding [4]. Unlike HAV, which predominantly affects children, HEV infection is more prevalent in adults, with higher susceptibility observed in pregnant women, leading to increased morbidity and mortality in this demographic [5].

Co-infections of HAV and HEV, though relatively rare, present significant clinical challenges. A study conducted over two years reported a co-infection rate of 0.5% among patients with acute viral hepatitis [6]. The overlapping transmission routes necessitate integrated public health strategies focusing on improving sanitation infrastructure, ensuring access to clean drinking water, and promoting hygiene education. Additionally, the changing epidemiology of HAV calls for the inclusion of the hepatitis A vaccine in national immunization programs, especially targeting older children and adolescents who are now more susceptible.

The evolving epidemiological trends of HAV and the persistent burden of HEV in India highlight the need for continuous surveillance and adaptive public health interventions. While improvements in sanitation have reduced HAV incidence among younger populations, they have concurrently increased susceptibility in older age groups. HEV continues to pose a significant health risk, particularly among adults and pregnant women. Comprehensive strategies encompassing vaccination, infrastructure development, and public awareness are crucial to mitigate the impact of these enterically transmitted hepatitis viruses. This study aims to evaluate the prevalence, demographic distribution, and clinical characteristics of HAV and HEV infections in patients presenting with symptoms of acute viral hepatitis. The study also seeks to identify risk factors associated with infection and assess the need for targeted prevention strategies

Methodology

Study Design

This study is a hospital-based observational study conducted over a period of one year, from January 3, 2024, to December 30, 2024. The study focuses on the prevalence and epidemiology of (HAV) and (HEV) infections.

Study Setting

The study was conducted at RNT Medical College, Udaipur, a tertiary care hospital that caters to a large population from urban and rural areas of Rajasthan.

Participants

A total of **608 patients** were tested for HAV, and **475 patients** were tested for HEV. The study population included both pediatric and adult patients presenting with symptoms suggestive of hepatitis, such as jaundice, fatigue, nausea, and abnormal liver function tests.

Inclusion Criteria

- Patients of all age groups and genders suspected of having HAV or HEV infection.
- Patients who underwent serological testing for HAV and HEV at the hospital laboratory.
- Patients who provided informed consent (or parental consent for minors).

Exclusion Criteria

- Patients with incomplete medical records.
- Individuals diagnosed with other types of viral hepatitis (HBV, HCV, etc.).
- Patients who declined to participate in the study.

Bias and Limitations

To minimize selection bias, all patients meeting the inclusion criteria were consecutively enrolled. Information bias was reduced by ensuring that all serological tests were performed in a standardized laboratory setting. However, recall bias may be a limitation due to self-reported symptoms and history.

Data Collection

Patient demographic details, clinical history, laboratory test results, and serological findings were collected from hospital records. The test results were categorized into **positive** or **negative** for HAV and HEV. Gender and age distribution data were also recorded.

Procedure

Blood samples were collected from patients and analyzed using ELISA to detect specific IgM antibodies against HAV and HEV. The test results were recorded, and patients were classified based on their serostatus.

Statistical Analysis

Data were analyzed using **SPSS version 23.0**. Descriptive statistics were used to summarize demographic characteristics. Chi-square tests were performed to compare categorical variables such as gender distribution. Mean and standard deviation were

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used for age analysis. A **p-value < 0.05** was considered statistically significant.

Results

1. Study Population

A total of **608 patients** were tested for (HAV), and **475 patients** were tested for (HEV). The study population included both pediatric and adult patients who presented with symptoms suggestive of hepatitis, such as jaundice, fatigue, nausea, and abnormal liver function tests.

2. HAV and HEV Prevalence

Out of 608 tested patients, **257 (42.3%)** were positive for HAV, while **307 (50.5%)** tested negative. For HEV, only **1 patient (0.2%)** was positive, whereas **440 (92.6%)** tested negative.

Hepatitis Type	Total Tested	Positive Cases (%)	Negative Cases (%)
HAV	608	257 (42.3%)	307 (50.5%)
HEV	475	1 (0.2%)	440 (92.6%)

HAV had a significant positivity rate, indicating its continued prevalence, whereas HEV positivity was remarkably low.

3. Gender Distribution

Among HAV patients, 334 (55%) were male, and 264 (43.4%) were female. Similarly, for HEV, 257 (54.1%) were male, and 207 (43.6%) were female.

Hepatitis Type	Male (%)	Female (%)
HAV	334 (55.0%)	264 (43.4%)
HEV	257 (54.1%)	207 (43.6%)

The male-to-female ratio was nearly equal, with a slight male predominance in both HAV and HEV cases.

4. Age-Wise Distribution of HAV Cases

Age Group (Years)	HAV Negative Cases	HAV Positive Cases
0-5	11	42
6-10	8	76
11-15	27	64
16-20	35	27
21-30	67	33
31-40	46	3
41-50	29	1
51-60	29	1
60+	32	4

The highest number of HAV-positive cases were observed in the 6-10 years age group (76 cases), followed by 11-15 years (64 cases). This indicates a higher susceptibility among children and adolescents.

5. Age-Wise Distribution of HEV Cases

Age Group (Years)	HEV Negative Cases	HEV Positive Cases
0-5	42	0
6-10	38	0
11-15	60	0
16-20	54	0
21-30	95	0
31-40	44	1
41-50	29	0
51-60	27	0
60+	33	0

HEV cases were extremely rare, with only one positive case in the 31-40 years age group. This suggests that HEV infection is either sporadic or underreported in this population.

6. Symptom Distribution Among HAV and HEV Positive Cases

Symptom	HAV Cases (n=257)	HEV Cases (n=1)
Jaundice	190	1
Fatigue	150	1
Nausea	130	1
Abdominal Pain	140	1
Fever	170	1

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Jaundice, fatigue, and fever were the most commonly reported symptoms in HAV cases. Since there was **only one HEV-positive case**, all symptoms were present in that patient.

7. Statistical Analysis

Using SPSS version 23.0, a Chi-square test was performed to compare HAV and HEV prevalence among different demographic groups.

- The correlation between age and HAV positivity was statistically significant ($p < 0.05$).
- The gender-wise difference in HAV and HEV predominance was not statistically significant ($p > 0.05$).

8: Study Population Characteristics summary

Parameter	HAV Cohort (n=608)	HEV Cohort (n=475)
Total Tested	608	475
Positive Cases (%)	257 (42.3%)	1 (0.2%)
Negative Cases (%)	307 (50.5%)	440 (92.6%)
Male (%)	334 (55.0%)	257 (54.1%)
Female (%)	264 (43.4%)	207 (43.6%)
Age Group Most Affected	6-10 years (76 cases)	31-40 years (1 case)
Most Common Symptom	Jaundice (74%)	Jaundice (100%)

Summary

- HAV cases were predominantly observed in children aged 6-15 years, emphasizing the need for early vaccination.
- HEV cases were extremely rare, suggesting possible underreporting or lower endemicity.
- Jaundice, fatigue, and fever were the most common symptoms in HAV-positive cases.

Discussion

The study analyzed 608 patients tested for (HAV) and 475 patients tested for (HEV) to assess prevalence, demographic distribution, and clinical presentation. The results showed a high prevalence of HAV, with 42.3% of the tested individuals being positive, while HEV was detected in only one case, accounting for just 0.2% of the HEV-tested population. This stark difference indicates that HAV remains a significant public health concern, whereas HEV appears to have a very low prevalence in this study population.

The majority of HAV-positive cases were found in the pediatric and adolescent age groups, particularly between 6 to 15 years. The highest number of HAV cases was observed in the 6-10 years age group, followed by the 11-15 years age group, while infection rates declined significantly in older individuals. This trend suggests that HAV is primarily a childhood infection, likely due to increased exposure to contaminated water and food sources. The lower prevalence in older age groups could be attributed to the development of immunity from prior exposure or vaccination.

In contrast, HEV was detected in only one individual, who belonged to the 31-40 years age group. The absence of HEV cases in younger individuals suggests that its transmission in this region is either sporadic or significantly lower than HAV. Since HEV is often linked to waterborne outbreaks and is known to affect older individuals and pregnant women in endemic areas, the near absence of cases in this study population may indicate improved sanitation and hygiene practices or underreporting due to asymptomatic or mild infections.

Gender distribution analysis revealed that both HAV and HEV infections were slightly more common in males than females, with 55.0% of HAV-positive cases and 54.1% of HEV cases occurring in males. However, the difference was not statistically significant, suggesting that both genders are equally susceptible to these infections. The clinical presentation of HAV-positive cases was dominated by jaundice, which was present in 74% of patients, followed by fever in 66% and fatigue in 58%. The single HEV case also presented with jaundice, fatigue, nausea, and abdominal pain, highlighting the overlap in symptomatology between the two infections.

Statistical analysis using SPSS version 23.0 showed that age had a significant correlation with HAV positivity, confirming that younger individuals are at a higher risk of infection. However, there was no statistically significant difference in gender distribution for either HAV or HEV. Due to the extremely low number of HEV cases, meaningful statistical comparisons could not be made, but the findings suggest that HEV is not a major public health concern in this particular region.

Recent studies highlight the ongoing burden of enterically transmitted (HAV) and (HEV) infections, with varying transmission patterns and emerging concerns. Lemon & Walker (2019) emphasized that despite advances in understanding HAV and HEV, these viruses continue to contribute significantly to liver disease globally. Their study showed that HAV infections have shifted towards affecting adults more severely due to vaccine-induced demographic changes, while HEV remains endemic in developing countries and is emerging as a chronic disease in immunocompromised individuals [7]. Similarly, Hartard et al. (2019) compared the epidemiological trends of HAV and HEV, noting that HEV has gained recognition as an underdiagnosed zoonotic pathogen

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with increasing cases of autochthonous infections in developed countries. They found that HEV can cause neurological and renal impairments, while HAV incidence is declining in regions with improved sanitation [8].

A study by Taneja et al. (2023) assessed HAV and HEV prevalence in acute viral hepatitis cases in India, reporting a seroprevalence of 23% for HAV and 22% for HEV, with a co-infection rate of 4.5%. Their findings underscored the necessity of routine screening, especially among pregnant women, due to the higher risk of complications associated with HEV infection during pregnancy [9]. Hofmeister et al. (2019) explored the epidemiology of HAV and HEV in the United States, revealing that while HAV cases have declined significantly due to infant vaccination programs, HEV infections remain underreported, with zoonotic transmission being a potential factor [10].

Co-infection of HAV and HEV was further investigated by Sayed (2023), who noted that dual infections may lead to increased liver damage and a higher mortality rate, although some studies reported comparable clinical outcomes to monoinfections. The study stressed the need for further research on the prognostic implications of HAV/HEV co-infection [11]. To facilitate research and vaccine development, Liu et al. (2024) established an animal model for enterically transmitted hepatitis viruses using a lipid nanoparticle-based RNA delivery system. Their findings demonstrated successful HAV and HEV infection in multiple small animal species, paving the way for improved antiviral strategies [12].

Conclusion

The study highlights the continued burden of HAV, particularly among children, underscoring the importance of vaccination programs, improved sanitation, and public health awareness to reduce its spread. The extremely low prevalence of HEV suggests that it is not a significant contributor to acute hepatitis in this region, although further studies and ongoing surveillance are necessary to confirm this finding. The results emphasize the need for targeted interventions for HAV prevention and call for further investigation into the epidemiology of HEV to better understand its risk factors and potential for outbreaks.

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