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Frequency and Association of Hepatotropic Co-infections in Clinically Suspected Hepatitis Cases: A Comparative Study using Rapid Diagnostic Test (RDT) and RT-PCR

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Abstract: Viral hepatitis remains a major public health concern in India, with Hepatitis A Virus, Hepatitis B Virus, Hepatitis C Virus, and Hepatitis E Virus contributing significantly to acute liver disease. Co-infections among these viruses complicate clinical presentation and diagnosis, particularly when relying on serology-based Rapid Diagnostic Tests (RDTs).To determine the frequency and pattern of hepatotropic viral infections and co-infections in clinically suspected hepatitis cases, and to compare the diagnostic performance of RDTs with Reverse Transcriptase Polymerase Chain Reaction (RT-PCR).A hospital-based cross-sectional study was conducted among 160 clinically suspected hepatitis patients. All participants underwent RDT screening for HAV IgM, HBsAg, anti-HCV, and HEV IgM, followed by RT-PCR for HAV RNA, HBV DNA, HCV RNA, and HEV RNA. Clinical severity was assessed using biochemical parameters. Diagnostic concordance between RDT and RT-PCR was evaluated. HEV was the most common infection detected by both RDT (25.6%) and RT-PCR (25.0%), followed by HBV and HCV. Co-infections were frequent, with 20% dual and 10% triple infections. Severe cases showed significantly higher bilirubin, ALT, AST, INR, and lower platelet counts ($p < 0.001$). RDT-PCR concordance varied across viruses, with poor agreement for HAV and HEV due to IgM cross-reactivity and early-window seronegativity. HEV and HBV are the predominant etiologies of acute viral hepatitis in this population. Co-infections contribute to more severe disease. RDTs show variable reliability and require confirmation with RT-PCR for accurate diagnosis. A combined diagnostic approach is essential for effective clinical management and epidemiological surveillance..

Keywords: Hepatitis, Co-infection, RT-PCR, RDT, HAV, HBV, HCV, HEV.

INTRODUCTION

Viral hepatitis continues to pose a major global public health challenge, contributing substantially to both acute and chronic liver disease across diverse populations. Worldwide, hundreds of millions of individuals live with chronic hepatitis B and C infections, while outbreaks of hepatitis A and hepatitis E remain common in low- and middle-income countries where sanitation infrastructure and access to safe drinking water are inadequate. According to global surveillance data, viral hepatitis remains a leading cause of liver-related morbidity and mortality, accounting for a substantial burden of disease comparable to tuberculosis and HIV in many regions.[1,22,25]

The four major hepatotropic viruses-Hepatitis A virus (HAV), Hepatitis B virus (HBV), Hepatitis C virus (HCV), and Hepatitis E virus (HEV)-differ considerably in their genomic structures, modes of transmission, epidemiological patterns, and long-term clinical outcomes. Nevertheless, all four viruses demonstrate a specific affinity for hepatocytes and induce liver inflammation that may range from mild self-limiting illness to fulminant hepatic failure or chronic liver disease.[2] In developing countries, enterically transmitted viruses such as HAV and HEV are commonly associated with waterborne outbreaks, whereas bloodborne viruses such as HBV and HCV continue to spread through unsafe medical practices, blood transfusions, and perinatal transmission.[3]

In India, viral hepatitis remains a significant public health concern due to factors such as high population density, socioeconomic disparities, inadequate sanitation systems, and variable vaccination coverage. These conditions facilitate the persistent circulation of multiple hepatotropic viruses within the same communities. National public health programs such as the National Viral Hepatitis Control Programme (NVHCP) have highlighted the continuing burden of HBV and HCV infections, while HEV outbreaks are frequently reported in areas with compromised water quality and sanitation infrastructure.[3,17]

Clinically, patients with viral hepatitis often present with nonspecific symptoms including fever, malaise, fatigue, nausea, vomiting, abdominal discomfort, dark urine, pale stools, and jaundice. Because these manifestations overlap across different viral etiologies, the initial clinical differentiation of specific hepatotropic viruses is often difficult without laboratory confirmation.[4] In addition to diagnostic challenges, an increasing body of evidence indicates that hepatotropic viral co-infections are becoming more common in regions where multiple hepatitis viruses circulate simultaneously. Studies have reported various combinations of co-infection, including HAV-HEV, HBV-HEV, HBV-HCV, and even triple viral infections, particularly in endemic areas with overlapping transmission routes.[5]

Such co-infections may significantly alter the natural history of viral hepatitis by intensifying hepatic inflammation, modifying immune responses, and increasing the risk of severe clinical outcomes such as acute liver failure or acute-on-chronic liver failure.[6]

The presence of multiple viral pathogens can also complicate diagnostic interpretation, since serological markers may demonstrate atypical patterns or cross-reactivity between antibodies directed against different hepatotropic viruses.[7]

Rapid diagnostic tests (RDTs) are widely used in many healthcare settings for the detection of HAV IgM, HEV IgM, HBsAg, and anti-HCV antibodies because they provide rapid results and are easy to perform without sophisticated laboratory infrastructure. However, the diagnostic performance of these assays varies considerably depending on factors such as the stage of infection, host immune response, and assay sensitivity.[8] Cross-reactivity between HAV and HEV IgM antibodies and the possibility of early-window seronegativity further reduce the reliability of serology-based rapid tests in certain clinical situations.

In contrast, molecular diagnostic methods such as Reverse Transcription Polymerase Chain Reaction (RT-PCR) provide significantly higher sensitivity and specificity by detecting viral nucleic acids directly, independent of host immune responses.[9] RT-PCR therefore plays a crucial role in confirming early infection, identifying low-level viremia, and detecting mixed infections that may not be apparent through serological testing alone. Despite these advantages, molecular diagnostics remain limited in many resource-constrained settings due to cost, infrastructure requirements, and technical expertise.[10]

Understanding the epidemiology of hepatotropic viral infections, particularly their prevalence, co-infection patterns, and association with clinical severity, therefore requires an integrated diagnostic approach combining serological screening with molecular confirmation. Although several studies have investigated individual hepatitis viruses in India, comprehensive analyses evaluating HAV, HBV,

HCV, and HEV simultaneously in clinically suspected hepatitis cases remain limited.[11,16] Furthermore, comparative assessments of RDT and RT-PCR results within the same patient population are relatively scarce, despite evidence suggesting significant diagnostic discordance between these modalities.

Therefore, the present study was conducted to determine the frequency and pattern of hepatotropic viral infections and co-infections among clinically suspected hepatitis cases and to compare the diagnostic performance of Rapid Diagnostic Tests with RT-PCR. By integrating serological and molecular findings, this study aims to provide a clearer understanding of viral hepatitis epidemiology and diagnostic reliability in a high-burden setting, thereby supporting improved clinical management and surveillance strategies..

MATERIALS AND METHODS

The present study was designed as a hospital-based cross-sectional diagnostic accuracy investigation conducted among clinically suspected cases of acute viral hepatitis attending a tertiary care centre in Central India. A total of 160 consecutive patients presenting with symptoms suggestive of hepatitis-such as jaundice, fever, abdominal pain, vomiting, fatigue, dark urine, or pale stools-were recruited after meeting predefined inclusion and exclusion criteria1. Individuals with known chronic liver disease, previously diagnosed and treated HBV or HCV infection, non-infectious causes of jaundice, or inadequate/hemolysed blood samples were excluded to avoid confounding and ensure diagnostic precision. All participants or guardians provided informed consent in accordance with institutional ethical guidelines, and approval was obtained from the Institutional Ethics Committee prior to study initiation2.

For each enrolled patient, detailed demographic, socioeconomic, and clinical information was collected using a structured proforma to ensure uniformity. This included age, sex, residence, education level, occupation, and socioeconomic status, along with clinical symptoms, risk factor history, and laboratory parameters such as liver function tests (LFTs) and complete blood counts (CBC). Blood samples were collected under aseptic precautions using sterile vacutainers; serum was separated after centrifugation and used immediately for rapid diagnostic test (RDT) analysis, while plasma and aliquoted serum samples were stored at 2-8°C for short-term use or at -20°C for subsequent molecular testing3.

All participants underwent serological testing using validated Rapid Diagnostic Tests for HAV IgM, HBsAg, anti-HCV antibodies, and HEV IgM. These immunochromatographic lateral-flow assays were performed strictly according to manufacturer instructions, with internal procedural controls verified for each batch to ensure assay validity. While RDTs provide rapid, point-of-care results, their performance can be affected by cross-reactivity, prozone effects, or early-window seronegativity, particularly for IgM assays; therefore, they were used as screening tools rather than definitive diagnostics4. In cases where HBsAg tested positive, additional testing for HDV IgM/IgG was performed using delta-virus-specific RDTs to assess possible delta hepatitis, given its known dependency on HBV replication5.

Molecular confirmation using Reverse Transcription Polymerase Chain Reaction (RT-PCR) was carried out for all four major hepatotropic viruses: HAV RNA, HBV DNA, HCV RNA, and HEV RNA. Viral nucleic acid extraction was performed using standardized spin-column kits, followed by real-time amplification using CE-IVD-approved PCR kits capable of detecting specific genomic regions of each virus. Each PCR run included internal controls, positive controls, and negative controls to monitor extraction efficiency, amplification validity, and contamination-free processing. The cycling conditions, fluorescence detection channels, probe chemistries, Ct thresholds, and interpretation criteria adhered strictly to manufacturer guidelines to maintain diagnostic accuracy and reproducibility6. The use of RT-PCR as the reference standard allowed precise identification of early infection, low-level viremia, and co-infections that may not be detected through serological assays.

Infection patterns were categorized based on combined RT-PCR and serological findings, distinguishing mono-infection, dual infection, and triple infection profiles. Clinical severity was assessed using biochemical indicators such as total and direct bilirubin, ALT, AST, ALP, albumin, and INR, along with clinical signs suggestive of acute liver failure or acute-on-chronic liver failure. These parameters were then analysed in relation to infection status to determine severity correlations7.

All data were entered into a validated electronic database to minimize transcription errors. Statistical analysis was performed using SPSS and Microsoft Excel. Descriptive statistics were calculated for demographic and clinical variables. Categorical variables were analysed using the chi-square test, while continuous variables were compared using Student's t-test or Mann-Whitney U test depending on distribution. Diagnostic performance metrics-including sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall accuracy-were calculated for each RDT using RT-PCR as the gold standard. Concordance between RDT and RT-PCR results was assessed using Cohen's kappa coefficient. A p-value < 0.05 was considered statistically significant8.

This comprehensive methodological approach ensured robust evaluation of hepatotropic viral

prevalence, co-infection patterns, and diagnostic performance of RDTs relative to molecular assays, thereby generating clinically and epidemiologically relevant findings within the study population.

RESULTS

A total of 160 clinically suspected hepatitis cases were analysed to determine infection prevalence, co-infection patterns, diagnostic performance of RDT and RT-PCR, and clinical severity associations. The findings are presented below in a structured sequence beginning with demographic characteristics and followed by clinical, biochemical, and virological outcomes.

Table 1. Demographic and Socioeconomic Characteristics of Study Participants (N = 160)

Variable	Category	n (%)
Age group (years)	6-12	16 (10.0)
	13-30	48 (30.0)
	31-50	56 (35.0)
	>50	40 (25.0)
Mean age (years)	-	36.7 ± 14.0
Sex	Male	80 (50.0)
	Female	80 (50.0)
Residence	Urban	96 (60.0)
	Rural	64 (40.0)
Socioeconomic class	Upper	16 (10.0)
	Upper middle	32 (20.0)
	Lower middle	48 (30.0)
	Upper lower	40 (25.0)
	Lower	24 (15.0)

Table 1: *The study population showed equal gender distribution and predominance of adults aged 31-50 years, with most belonging to lower-middle or upper-lower socioeconomic classes.*

Table 2. Clinical Features, Risk Factors, and Comorbidities (N = 160)

Parameter	Category	n (%)
Symptoms	Jaundice	136 (85.0)
	Fever	112 (70.0)
	Fatigue	96 (60.0)
	Abdominal pain	72 (45.0)
	Vomiting	64 (40.0)
	Dark urine	88 (55.0)
	Pale stools	24 (15.0)
Clinical signs	Hepatomegaly	64 (40.0)
	Splenomegaly	24 (15.0)
	Ascites	16 (10.0)
	Icterus	48 (30.0)
Risk factors	Alcohol consumption	48 (30.0)
	Travel/flood exposure	32 (20.0)
	Blood transfusion	13 (8.1)
	Injection drug use	3 (1.9)
Comorbidities	None	112 (70.0)
	Diabetes	16 (10.0)
	Hypertension	13 (8.1)
	Pregnancy	10 (6.3)
	HIV	5 (3.1)

Table 2: *Jaundice was the most common presenting symptom, while alcohol intake and recent travel/flood exposure were the predominant risk factors. Most patients had no major comorbidities.*

Table 3. Comparison of Biochemical and Hematological Parameters in Severe vs Non-Severe Cases

Parameter	Overall Mean ± SD	Severe (n = 32)	Non-severe (n = 128)	p-value
Total bilirubin (mg/dL)	3.20 ± 3.50	8.00 ± 4.20	2.10 ± 1.40	<0.001
Direct bilirubin (mg/dL)	2.00 ± 2.20	5.00 ± 2.80	1.10 ± 0.90	<0.001
AST (IU/L)	220 ± 180	450 ± 200	170 ± 120	<0.001
ALT (IU/L)	280 ± 240	520 ± 300	210 ± 150	<0.001
ALP (IU/L)	180 ± 90	260 ± 140	150 ± 70	0.002
Albumin (g/dL)	3.50 ± 0.60	3.00 ± 0.50	3.70 ± 0.50	<0.001
INR	1.20 ± 0.30	1.80 ± 0.50	1.10 ± 0.20	<0.001
WBC (/µL)	8,200 ± 2,800	9,000 ± 3,200	8,000 ± 2,600	0.080
Platelets (lakh/µL)	2.20 ± 0.90	1.60 ± 0.80	2.40 ± 0.80	<0.001

Table 3: *Severe cases demonstrated markedly higher bilirubin and transaminases, prolonged INR, and significantly reduced platelet counts, indicating greater hepatic dysfunction and inflammatory burden.*

Table 4. RDT Positivity Rates for Hepatotropic Viruses (N = 160)

Virus	RDT Positive (n)	Percentage (%)
HAV IgM	21	13.1
HBsAg	33	20.6
Anti-HCV	27	16.9
HEV IgM	41	25.6

Table 4: *HEV was the most frequently detected virus by RDT, followed by HBV and HCV, reflecting mixed exposure patterns in the population.*

Table 5. RT-PCR Positivity Rates (Reference Standard) (N = 160)

Virus	PCR Positive (n)	Percentage (%)
HAV RNA	16	10.0
HBV DNA	32	20.0
HCV RNA	24	15.0
HEV RNA	40	25.0

Table 5: *HEV RNA positivity was highest, confirming its dominant role in acute viral hepatitis in the study population.*

Table 6. Infection Patterns Based on RDT and PCR Findings (N = 160)

Pattern	Frequency (n)	Percentage (%)
Mono-infection	112	70.0
Dual infection	32	20.0
Triple infection	16	10.0

Table 6: *Nearly one-third of the participants showed mixed viral infections, underscoring the clinical importance of screening for multiple hepatotropic viruses simultaneously.*

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DISCUSSION

The present study provides an integrated evaluation of hepatotropic viral infections among clinically suspected hepatitis cases using both Rapid Diagnostic Tests (RDTs) and Reverse Transcription Polymerase Chain Reaction (RT-PCR). The findings highlight important epidemiological and diagnostic insights relevant to hepatitis-endemic regions such as India. Viral hepatitis continues to represent a significant global health burden, with developing countries experiencing a higher incidence of enterically transmitted hepatitis viruses due to sanitation challenges and limited access to safe water.[1,22]

In the present study, HEV emerged as the most common viral infection detected by both RDT and RT-PCR, followed by HBV and HCV. This observation is consistent with previous studies from South Asia demonstrating that HEV remains a leading cause of acute viral hepatitis in developing regions.[1,16] HEV outbreaks are frequently associated with contaminated drinking water, poor sanitation infrastructure, and seasonal flooding, which facilitate fecal-oral transmission within communities.[3,18] In India, multiple epidemiological investigations have reported HEV as the predominant cause of acute hepatitis, particularly during monsoon seasons and in regions with compromised public health infrastructure.

HBV was the second most frequently detected infection in the present study, which aligns with national estimates indicating that HBV continues to be a major contributor to liver disease burden in India.[3,17] The persistence of HBV transmission is

largely attributed to vertical transmission, inadequate vaccination coverage in certain populations, and unsafe medical or injection practices. Similarly, HCV infection remains an important cause of chronic liver disease in many settings, often associated with blood transfusion exposure or unsafe injection practices.
An important finding of this study is the substantial proportion of co-infections observed among the study participants. Nearly one-third of cases demonstrated dual or triple infections involving different hepatotropic viruses. Similar patterns have been reported in previous studies, where HAV-HEV, HBV-HEV, and HBV-HCV combinations were commonly observed in regions with overlapping viral circulation.[5,19] Such co-infections may intensify hepatic inflammation and modify host immune responses, thereby increasing the risk of severe liver injury.[6] The coexistence of multiple hepatotropic viruses can also complicate clinical diagnosis because overlapping symptoms and atypical serological responses may obscure the identification of the primary etiological agent.

The biochemical findings of this study further support the clinical significance of viral co-infection. Patients categorized as severe cases demonstrated significantly higher levels of bilirubin, ALT, AST, and INR along with reduced platelet counts compared with non-severe cases. These findings are consistent with previous reports indicating that elevated bilirubin and coagulopathy serve as important indicators of hepatic dysfunction and disease severity in acute viral hepatitis.[13,14] Co-infected individuals are particularly vulnerable to rapid clinical deterioration because simultaneous viral replication may amplify inflammatory responses within the liver.

Another key aspect of the present study is the comparison between RDT and RT-PCR diagnostic results. Although RDTs offer rapid and convenient screening for viral hepatitis markers, their diagnostic accuracy varies depending on the virus and the stage of infection.[8] The results of this study demonstrated variable concordance between RDT and RT-PCR findings, with the lowest agreement observed for HAV and HEV IgM assays. This observation is consistent with previous studies reporting that IgM-based serological tests may produce false-positive or false-negative results due to cross-reactivity or delayed antibody production.[7,24]

HEV IgM assays in particular have been shown to demonstrate considerable variability in sensitivity and specificity across different commercial kits.[8,9] Some patients who tested positive by RDT did not show detectable viral RNA by RT-PCR, suggesting possible false-positive IgM reactions or resolving infections. Conversely, several RT-PCR-positive cases lacked detectable IgM antibodies, likely reflecting the early phase of infection before the development of measurable antibody responses.[9] These discrepancies highlight the limitations of relying solely on serological assays for definitive diagnosis in acute hepatitis.

In contrast, RDTs for HBsAg and anti-HCV antibodies showed relatively better concordance with RT-PCR results in this study. This may be attributed to the more stable antigen-antibody interactions associated with these markers compared with IgM-based assays.[10] Molecular diagnostic methods such as RT-PCR offer superior sensitivity and specificity by directly detecting viral nucleic acids, thereby enabling early diagnosis even before the development of detectable antibodies.[9,15]

The ability of RT-PCR to detect low-level viremia and mixed viral infections is particularly valuable in clinical settings where co-infections are suspected. Molecular assays have been widely recognized as the reference standard for viral hepatitis diagnosis because they allow precise identification of viral genetic material independent of host immune responses.[11,20] In addition, multiplex PCR techniques capable of detecting multiple hepatotropic viruses simultaneously are increasingly being utilized to improve diagnostic efficiency in acute hepatitis cases.[21]
The public health implications of these findings are considerable. The predominance of HEV infection observed in this study suggests persistent gaps in sanitation and water quality, emphasizing the need for improved infrastructure and hygiene interventions.[3,25] Strengthening vaccination programs for HBV and expanding screening strategies for HBV and HCV are also essential components of viral hepatitis control initiatives.[17] Furthermore, the high frequency of co-infection observed underscores the importance of screening for multiple hepatotropic viruses rather than relying on single-virus testing strategies in endemic regions.

Overall, the results of this study demonstrate that while RDTs remain valuable tools for rapid screening, they should not be used as the sole diagnostic method in clinically suspected hepatitis cases. A combined diagnostic approach incorporating both serological tests and molecular confirmation provides the most reliable strategy for identifying hepatotropic viral infections and co-infections. Such an integrated diagnostic framework can improve clinical decision-making, enable early treatment interventions, and strengthen epidemiological surveillance in regions with a high burden of viral hepatitis.

CONCLUSION

The study demonstrates that HEV and HBV are the predominant causes of acute viral hepatitis in the study population, with a considerable proportion of patients exhibiting dual or triple co-infections. Co-infected individuals showed significantly greater biochemical severity, underscoring the clinical relevance of multi-virus screening. RDTs, while useful for rapid initial assessment, displayed variable concordance with RT-PCR-particularly for HAV and HEV-highlighting the essential role of molecular testing for accurate diagnosis. Integrating RDT screening with RT-PCR confirmation is therefore crucial for reliable detection, improved patient management, and strengthened surveillance in hepatitis-endemic settings.

COMPLIANCE WITH ETHICAL STANDARDS

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Conflict of Interest

The authors declare that they have no conflict of interest regarding the publication of this paper.

Ethical Approval

This study was conducted in accordance with the ethical standards of the institutional research committee and with the Declaration of Helsinki. Ethical approval was obtained from the Institutional Ethics Committee of Jawaharlal Nehru Medical College and Acharya Vinoba Bhave Rural Hospital, Datta Meghe Institute of Higher Education and Research (Deemed to be University) Sawangi (Meghe), Wardha,
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Informed Consent

Informed consent was obtained from all individual participants included in the study (or from legally authorized representatives where applicable).

Authors Contribution

Mr. Asim conceived and designed the study, performed laboratory work, analyzed the data, and prepared the original manuscript draft. Dr. Pratibha supervised the study and critically reviewed the manuscript. Mrs. Deepali and Mr. Abhijeet assisted in laboratory investigations and data collection. Dr. Nandkishore provided academic guidance and departmental support during the study. Dr. Sarita provided mentorship and contributed to critical revision of the manuscript. All authors read and approved the final manuscript.

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REFERENCES

1. World Health Organization. Global Hepatitis Report. Geneva: WHO; 2022.
2. Khatoon F, et al. Epidemiology of Viral Hepatitis in South Asia: A Review. J Clin Diagn Res. 2020;14(8):1-6.
3. Kumar A, et al. Burden of Hepatitis E and Waterborne Outbreaks in India. Indian J Med Res. 2019;150(5):477-486.
4. Singh R, et al. Clinical Profiles of Acute Viral Hepatitis in Tertiary Hospitals. Trop Gastroenterol. 2021;42(3):168-175.
5. Gupta E, et al. Co-infections Involving HAV, HBV, HCV, and HEV: Emerging Trends in India. J Med Virol. 2018;90(5):843-850.
6. Verma N, et al. Impact of Mixed Hepatitis Infections on Disease Severity. Hepatol Int. 2020;14(1):120-127.
7. Aggarwal R. Serological Cross-Reactivity in HAV and HEV Diagnosis. Hepatol Res. 2018;48(2):123-131.
8. Tripathi P, et al. Limitations of IgM-Based Rapid Diagnostic Tests in Acute Hepatitis. J Clin Microbiol. 2019;57:e01345-18.
9. Dutta S, et al. Diagnostic Challenges of HEV IgM Assays. J Viral Hepatitis. 2019;26(9):1004-1011.
10. Narayanasamy K, et al. Comparative Evaluation of HBsAg and Anti-HCV Rapid Tests. Indian J Pathol Microbiol. 2017;60(3):406-412.
11. Mishra S, et al. Diagnostic Concordance Between Serology and PCR in Viral Hepatitis. Int J Infect Dis. 2021;112:120-127.
12. Borkakoty B, et al. Ct-Value Patterns and Clinical Severity in HEV Infection. J Clin Virol. 2020;129:104469.
13. Khanna R, et al. Acute Liver Failure in Viral Hepatitis: HEV and HBV as Major Drivers in India. Liver Int. 2018;38(3):482-489.
14. Bernal W, et al. Prognostic Markers in Acute Liver Injury: Role of INR and Bilirubin. Hepatology. 2017;65(1):266-277.
15. Jothikumar N, et al. RT-PCR Methods for HAV, HBV, HCV, and HEV. J Virol Methods. 2018;253:1-7.
16. Sharma A, et al. Prevalence of Hepatotropic Viruses in Clinically Suspected Hepatitis. Indian J Med Microbiol. 2020;38(4):501-507.

17. National Viral Hepatitis Control Programme (NVHCP). Operational Guidelines. Ministry of Health & Family Welfare, Govt. of India; 2021.
18. Aggarwal R, Jameel S. Hepatitis E Virus: Epidemiology, Diagnosis, and Treatment. Nat Rev Gastroenterol Hepatol. 2018;15(5):304-316.
19. Soni R, et al. Mixed Viral Hepatitis in Northeastern India: A Molecular Assessment. Virus Res. 2019;273:197741.
20. Kumar R, et al. Clinical Significance of RT-PCR in Acute Hepatitis. J Med Microbiol. 2021;70(2):001318.
21. Singh J, et al. Evaluation of Multiplex PCR Panels for Acute Viral Hepatitis. Clin Microbiol Infect. 2022;28(7):1012-1019.
22. Centers for Disease Control and Prevention. Viral Hepatitis Surveillance. CDC, Atlanta; 2022.
23. Sharma M, et al. Hepatitis E in Pregnancy: Systematic Review. J Clin Exp Hepatol. 2020;10(5):481-492.
24. Chauhan A, et al. False Positivity in HAV and HEV Rapid Tests: A Comparative Study. Diagn Microbiol Infect Dis. 2019;95(3):114-120.
25. WHO. Guidelines for the Prevention and Control of Viral Hepatitis in LMICs. Geneva: WHO; 2021