# VIRAL INFECTIONS: CHARACTERISTICS OF HEPATITIS VIRUSES AND LABORATORY DIAGNOSIS OF THE DISEASES THEY CAUSE

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**Abstract:** Background: Viral hepatitis, primarily caused by hepatotropic viruses (HAV, HBV, HCV, HDV, and HEV), represents a major global public health problem, leading to acute and chronic liver disease, cirrhosis, and hepatocellular carcinoma (HCC). Objective: To analyze the key virological characteristics of the five main hepatitis viruses and to describe the contemporary laboratory diagnostic methods used for their identification and clinical management. Methods: A narrative review was conducted based on peer-reviewed literature and international guidelines from databases such as PubMed, Scopus, and WHO reports. Results: Each hepatitis virus exhibits distinct structural, genomic, and transmission characteristics. HAV and HEV cause acute, self-limiting enterically-transmitted infections. HBV, HCV, and HDV (a defective virus requiring HBV) cause parenterally transmitted chronic infections. Laboratory diagnosis relies on a combination of serological assays detecting specific viral antigens and antibodies (e.g., HBsAg, anti-HCV) and molecular methods (PCR, qPCR) for viral nucleic acid detection, quantification, and genotyping. Conclusion: Accurate differential diagnosis of viral hepatitis is critical for appropriate patient management. A stepwise laboratory algorithm utilizing serology for initial screening followed by molecular confirmation and monitoring is the cornerstone of modern diagnostics.

**Keywords:** hepatitis viruses, HAV, HBV, HCV, HDV, HEV, laboratory diagnosis, serology, PCR, viral hepatitis

## Introduction

Viral infections affecting the liver, collectively termed viral hepatitis, are among the most common infectious diseases worldwide. The term "hepatitis viruses" typically refers to five distinct, primarily hepatotropic human

pathogens: Hepatitis A virus (HAV), Hepatitis B virus (HBV), Hepatitis C virus (HCV), Hepatitis D virus (HDV, or delta agent), and Hepatitis E virus (HEV). Despite sharing the liver as a primary target, these viruses belong to different viral families, exhibit unique morphological and genomic characteristics, and have different routes of transmission and clinical outcomes. While HAV and HEV typically cause acute, self-limiting infections, HBV, HCV, and HDV often establish chronic infections that can progress to cirrhosis and hepatocellular carcinoma (HCC). Accurate and timely laboratory diagnosis is essential to distinguish between these etiologies, guide treatment decisions, implement public health measures, and prevent transmission. This article reviews the fundamental characteristics of the five hepatitis viruses and describes the laboratory methods used for their diagnosis.

**Methods**

A narrative review was conducted by searching electronic databases including PubMed, Scopus, Google Scholar, and the World Health Organization (WHO) website. The search period covered publications from 2000 to 2025. Keywords used included: "hepatitis A virus", "hepatitis B virus", "hepatitis C virus", "hepatitis D virus", "hepatitis E virus", "laboratory diagnosis", "serology", "PCR", "viral hepatitis", "liver function tests", and "molecular diagnostics". Inclusion criteria: peer-reviewed original articles, systematic reviews, meta-analyses, and clinical guidelines in English. Exclusion criteria: case reports, non-English papers, and studies focusing solely on treatment without diagnostic data. Data were synthesized thematically into sections covering the virology and laboratory diagnosis for each virus.

**Results**

The five main hepatitis viruses differ significantly in their taxonomy, structure, genome, transmission, and clinical outcome. These characteristics are summarized in Table 1.

Table 1. Comparative Virological and Epidemiological Characteristics of Hepatitis Viruses.

Feature HAV HBV HCV HDV HEV

Family Picornaviridae Hepadnaviridae Flaviviridae Deltaviridae Hepeviridae

Genus Hepatovirus Orthohepadnavirus Hepacivirus Deltavirus Orthohepevirus

Genome ssRNA (+) dsDNA (partial) ssRNA (+) ssRNA (-) (circular) ssRNA (+)

Virion size 27-32 nm 42 nm (Dane particle) 50-80 nm 35-37 nm 32-34 nm

Envelope No (non-enveloped) Yes (enveloped) Yes (enveloped) Yes (enveloped, from HBV) No (non-enveloped)

Transmission Fecal-oral Blood, sexual, perinatal Blood, sexual (less) Blood, sexual, perinatal Fecal-oral

Chronicity No Yes (5-10% adults) Yes (70-80%) Yes (co/super-infection) No (except in immunocompromised)

Oncogenic potential No Yes (HCC) Yes (HCC) Yes (HCC) No

Laboratory Diagnosis of Viral Hepatitis

Laboratory diagnosis integrates liver function tests (biochemistry), serological markers (antigens and antibodies), and molecular detection (viral nucleic acids).

Biochemical Markers (Liver Function Tests)

Elevated serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) are sensitive indicators of hepatocyte injury but are non-specific. ALT elevation often precedes jaundice in acute hepatitis. In chronic hepatitis, ALT levels may fluctuate. Elevated bilirubin indicates cholestasis or severe hepatic dysfunction.

Hepatitis A Virus (HAV) Diagnosis

Acute HAV infection is diagnosed by detecting IgM anti-HAV antibodies in serum. These appear at symptom onset and persist for 3-6 months. IgG anti-HAV indicates past infection or vaccination and confers lifelong immunity. HAV RNA can be detected in blood and stool by RT-PCR during the acute phase but is rarely needed for routine diagnosis.

Hepatitis B Virus (HBV) Diagnosis

HBV diagnosis relies on a panel of serological markers (Figure 1, conceptual).

HBsAg (Hepatitis B surface antigen): First marker to appear; indicates active infection (acute or chronic).

Anti-HBs: Indicates recovery and immunity (post-infection or post-vaccination).

Anti-HBc (total and IgM): IgM anti-HBc indicates acute or recent infection. Total anti-HBc indicates past or current infection.

HBeAg: Marker of high viral replication and infectivity.

Anti-HBe: Indicates transition to low replication phase (seroconversion).

HBV DNA (quantitative PCR): Measures viral load; essential for monitoring chronic hepatitis B, guiding antiviral therapy, and assessing treatment response.

Hepatitis C Virus (HCV) Diagnosis

Anti-HCV antibodies (EIA/CLIA): Screening test. Cannot distinguish acute from chronic, past from current infection.

HCV RNA (qualitative or quantitative PCR): Confirmatory test for active infection. Quantitative HCV RNA (viral load) is used to monitor treatment response. HCV genotyping (1-6) is required before initiating direct-acting antiviral (DAA) therapy.

Hepatitis D Virus (HDV) Diagnosis

HDV is a defective virus that requires the HBsAg for packaging and transmission. Diagnosis should be considered in all HBsAg-positive patients with severe or rapidly progressive liver disease.

Anti-HDV antibodies (total and IgM): Screening test.

HDV RNA (RT-PCR): Confirmatory test for active HDV replication and is the gold standard for diagnosis.

Hepatitis E Virus (HEV) Diagnosis

IgM anti-HEV: Indicates acute or recent infection.

IgG anti-HEV: Indicates past infection.

HEV RNA (RT-PCR): Detected in blood and stool during acute phase; essential for diagnosis in immunocompromised patients who may not mount an antibody response.

Diagnostic Algorithms and Clinical Correlation

A practical diagnostic approach begins with measuring serum ALT and detecting IgM anti-HAV for suspected acute hepatitis. If negative, HBsAg and IgM anti-HBc are tested. If HBsAg is positive, testing for anti-HDV and HBV DNA is indicated. For chronic hepatitis, anti-HCV testing followed by HCV RNA confirmation is standard. In pregnant women with acute hepatitis, HEV should be suspected, especially in endemic regions. For monitoring chronic hepatitis B and C, serial quantitative PCR is essential.

Discussion

The five hepatitis viruses, despite their common hepatotropism, represent a diverse group of pathogens with distinct biological behaviors. This diversity necessitates a nuanced, multi-layered approach to laboratory diagnosis. The advent of highly sensitive and specific serological assays (EIA/CLIA) and molecular techniques (real-time PCR, nested PCR) has



dramatically improved our ability to diagnose, differentiate, and manage viral hepatitis. For HBV, the interpretation of serological marker patterns (e.g., "window period," occult HBV infection) requires clinical expertise. For HCV, the inability of serology to distinguish active from resolved infection makes molecular confirmation indispensable. HDV remains underdiagnosed globally due to low awareness, despite its ability to accelerate liver disease in HBV-infected individuals. HEV is increasingly recognized as a cause of autochthonous (locally acquired) hepatitis in developed countries, not just a travel-associated pathogen.

Major challenges include access to molecular diagnostics in low-resource settings, the high cost of quantitative PCR and genotyping, and the need for point-of-care tests that can differentiate etiologies rapidly. Furthermore, the emergence of HBV escape mutants and HCV variants with resistance-associated substitutions requires continuous assay updates. Future directions include the integration of multiplex PCR platforms capable of detecting all five viruses simultaneously, the use of dried blood spots for sample collection to improve access, and the development of affordable point-of-care molecular tests for viral load monitoring.

Conclusion

Viral hepatitis caused by HAV, HBV, HCV, HDV, and HEV remains a significant global health burden. Accurate laboratory diagnosis is the cornerstone of effective clinical management and public health control. A combination of biochemical tests, serological marker profiling, and molecular nucleic acid amplification is required for definitive diagnosis, differentiation of acute versus chronic infection, assessment of viral replication, and monitoring of treatment response. While serology remains the first-line screening tool, molecular methods (PCR, qPCR) are essential for confirmation, quantification, and genotyping. Continued investment in accessible, affordable, and multiplex diagnostic platforms is critical to achieving the WHO's goal of eliminating viral hepatitis as a public health threat by 2030.

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