

“Hepatitis Awareness, Innovation and Elimination: Advances in Prevention, Diagnosis and Treatment Strategies”

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Abstract

Hepatitis comprises a group of inflammatory liver disorders that continue to impose a substantial burden on global health. The disease may result from viral infections, autoimmune conditions, excessive alcohol consumption, metabolic abnormalities, or exposure to hepatotoxic substances. Among these causes, infections with hepatitis A, B, C, D, and E viruses remain the leading contributors to acute and chronic liver disease. Persistent hepatitis B and C infections are particularly associated with progressive liver damage, including fibrosis, cirrhosis, liver failure, and hepatocellular carcinoma. Although considerable progress has been achieved in diagnostic techniques and antiviral therapies, the burden of hepatitis persists due to inadequate awareness, delayed diagnosis, limited access to healthcare services, and unequal implementation of preventive measures.⁽¹⁾

This review summarizes the current evidence regarding the epidemiology, pathogenesis, clinical manifestations, diagnosis, treatment, prevention, and public awareness of hepatitis. Recent therapeutic advances, including potent antiviral agents for chronic hepatitis B and direct-acting antivirals for hepatitis C, have markedly improved disease management and patient outcomes. Preventive strategies such as vaccination, safe injection practices, blood safety, infection control, improved sanitation, and routine screening of at-risk populations remain essential for limiting disease transmission. Furthermore, awareness and educational initiatives play a critical role in promoting early diagnosis, encouraging vaccination, reducing stigma, and improving treatment adherence.⁽²⁾ A coordinated approach involving healthcare professionals, policymakers, and communities is necessary to strengthen hepatitis control programs and support the World Health Organization's goal of eliminating viral hepatitis as a public health threat by 2030.⁽³⁾

Keywords

Hepatitis; Viral Hepatitis; Antiviral Therapy; Vaccination; Disease Prevention; Early Diagnosis; Public Awareness; Public Health; Liver Diseases; Health Promotion.

Introduction

Hepatitis is an inflammation of the liver that can range from a mild, self-limiting illness to severe chronic disease, including fibrosis, cirrhosis, liver cancer, and liver failure. It may result from viral infections, alcohol, certain medications, or autoimmune disorders, with viral hepatitis being the leading cause worldwide. The five major hepatitis viruses (A, B, C, D, and E) differ in their modes of transmission. Hepatitis A and E spread mainly through the faecal–oral route, while hepatitis B, C, and D are transmitted through infected blood and body fluids.⁽⁴⁾

Hepatitis is a condition characterized by inflammation and damage to the liver, leading to the destruction of liver cells. It is commonly identified by increased liver enzyme levels (ALT and AST), which indicate liver injury. Hepatitis may be acute (short-term) or chronic, with chronic hepatitis defined as persistent liver inflammation lasting for more than six months.⁽⁵⁾

Viral hepatitis continues to impose a significant global health burden. To support the WHO 2030 elimination target, many countries have implemented innovative national programs tailored to their healthcare systems. These initiatives emphasize data-driven planning, wider access to testing and treatment, stronger surveillance, and integration of hepatitis services into routine healthcare. The case studies show that sustained investment, effective policies, and collaboration across sectors can make hepatitis elimination achievable, even in resource-constrained settings. ⁽⁶⁾

The clinical manifestations of hepatitis vary widely, ranging from individuals with no apparent symptoms to those with significant liver dysfunction. When symptoms occur, they commonly include fatigue, fever, nausea, vomiting, abdominal discomfort, reduced appetite, dark-colored urine, pale or clay-colored stools, and jaundice. The diagnosis of hepatitis is established through a comprehensive assessment that includes clinical examination, liver function testing, serological investigations, and molecular diagnostic methods. These approaches help determine the underlying cause of the disease, confirm the specific type of hepatitis, and evaluate the extent of liver injury.

Epidemiology of Viral Hepatitis

Viral hepatitis continues to be a significant public health concern worldwide. Hepatitis B virus (HBV) has affected billions of people globally, with hundreds of millions developing chronic infection. The disease burden is unevenly distributed, with the highest prevalence reported in sub-Saharan Africa, parts of Asia, the Middle East, and selected regions of Eastern Europe and Latin America. Long-term HBV infection can progress to severe liver diseases such as cirrhosis, liver cancer, and liver failure.⁽⁷⁾

Among patients undergoing hemodialysis, HBV infection remains an important concern, although its prevalence differs considerably between countries because of variations in screening practices and infection-control measures. While new HBV infections have declined in many countries due to vaccination and preventive strategies, hepatitis C virus (HCV) continues to pose a major challenge⁽⁸⁾. A large number of HCV infections remain undiagnosed because many individuals have no symptoms. Chronic HCV infection is a leading cause of liver-related illness and death and is particularly common in patients with end-stage renal disease receiving dialysis, owing to repeated blood exposure and other healthcare-related risk factors.⁽⁹⁾

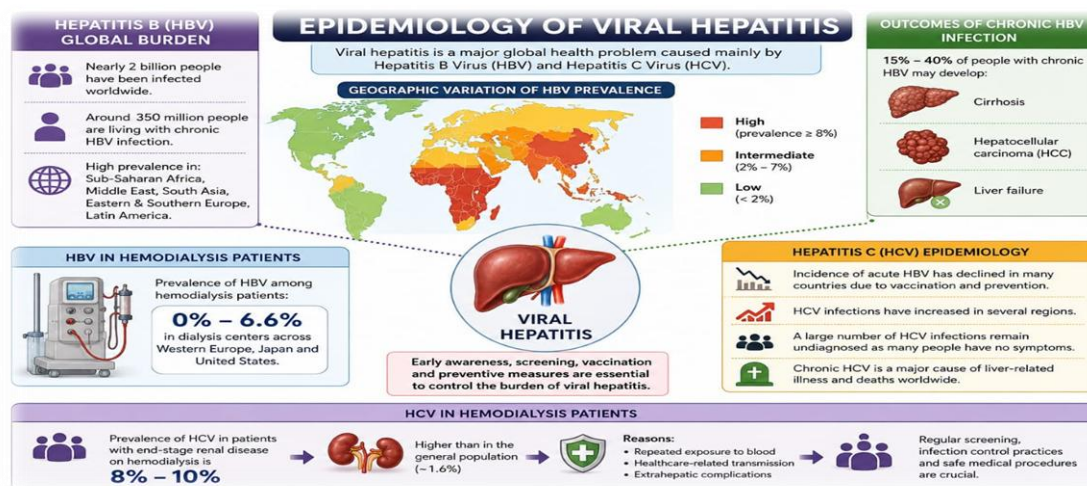


Figure 1: Epidemiology of Viral Hepatitis

Categorization of Hepatitis :

1.Categorization Based on Etiology (Cause)

a) Viral Hepatitis

Viral hepatitis is the most prevalent form of liver inflammation and is caused by a group of hepatotropic viruses that selectively infect hepatic tissue. The principal viruses responsible for this condition are Hepatitis A (HAV), Hepatitis B (HBV), Hepatitis C (HCV), Hepatitis D (HDV), and Hepatitis E (HEV). Although all five viruses target the liver, they differ considerably in their viral characteristics, mechanisms of transmission, clinical manifestations, and long-term outcomes. Infections caused by HAV and HEV are generally acute and self-limiting, with complete recovery in most individuals. In contrast, HBV, HCV, and HDV have the potential to establish persistent infections, which may progress to chronic hepatitis, liver fibrosis, cirrhosis, and hepatocellular carcinoma if left untreated.⁽¹⁰⁾

b) Alcoholic Hepatitis

Alcoholic hepatitis is an inflammatory liver disorder resulting from prolonged and excessive alcohol intake. Chronic alcohol consumption leads to the formation of toxic metabolites, particularly acetaldehyde, which promotes oxidative stress, inflammatory responses, and damage to liver cells. The condition commonly presents with clinical features such as jaundice, fever, right upper abdominal pain, hepatomegaly, and elevated liver

enzymes. In severe cases, progressive hepatic injury may culminate in acute liver failure and other life-threatening complications.

c) Drug-Induced Hepatitis

Drug-induced hepatitis refers to liver inflammation that develops as an adverse reaction to medications, herbal preparations, dietary supplements, or chemical agents. Hepatic injury may occur through predictable dose-related toxicity or unpredictable idiosyncratic reactions. Frequently implicated agents include paracetamol (acetaminophen), isoniazid, methotrexate, amoxicillin-clavulanate, and several herbal remedies. Clinical manifestations range from asymptomatic elevations of liver enzymes to severe hepatic necrosis and acute liver failure.⁽¹¹⁾

d) Autoimmune Hepatitis

Autoimmune hepatitis is a chronic immune-mediated liver disease in which the body's immune system mistakenly attacks hepatocytes, resulting in persistent hepatic inflammation. The disease is characterized by the presence of specific autoantibodies, elevated serum immunoglobulin G (IgG) concentrations, and characteristic histopathological findings. Without appropriate treatment, ongoing inflammation may lead to progressive fibrosis, cirrhosis, and hepatic insufficiency. Standard therapy consists of corticosteroids, either alone or in combination with immunosuppressive medications.⁽¹²⁾

e) Metabolic Hepatitis

Metabolic hepatitis develops as a consequence of metabolic abnormalities that promote excessive fat accumulation within liver cells, leading to inflammation and hepatocellular injury. The most common form is metabolic dysfunction-associated steatohepatitis (MASH), formerly known as non-alcoholic steatohepatitis (NASH). Major risk factors include obesity, insulin resistance, type 2 diabetes mellitus, dyslipidemia, and metabolic syndrome. Persistent disease may progress to fibrosis, cirrhosis, and hepatocellular carcinoma.

g) Ischemic Hepatitis: Ischemic hepatitis, commonly referred to as shock liver, occurs when there is a sudden reduction in hepatic blood flow and oxygen delivery. This condition is most often associated with severe hypotension, heart failure, septic shock, or respiratory failure. It is characterized by a rapid and marked elevation of serum aminotransferase levels due to widespread hepatocellular injury. Restoration of adequate

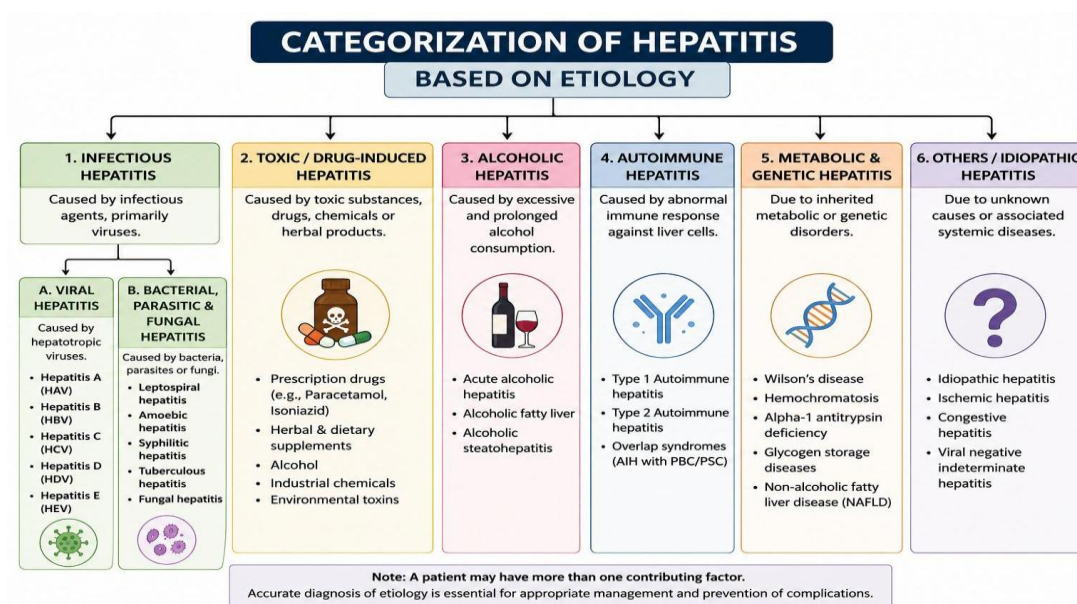


Figure 2: Categorization of Hepatitis

Table 1: Categorization of Viral Hepatitis

Feature	Hepatitis A (HAV)	Hepatitis B (HBV)	Hepatitis C (HCV)	Hepatitis E (HEV)
Virus	Positive-sense single-stranded RNA virus belonging to Hepatovirus (Picornaviridae). Six genotypes; I–III infect humans.	Partially double-stranded DNA virus belonging to Hepadnaviridae. Replicates through reverse transcription.	Enveloped positive-sense single-stranded RNA virus of the Flaviviridae family. Eight genotypes (1–8).	Positive-sense single-stranded RNA virus of the Orthohepevirus genus. Eight genotypes. HEV-1 & 2 infect humans; HEV-3 & 4 are zoonotic.

Transmission	Fecal–oral route through contaminated food, water, or close contact.	Blood transfusion, contaminated needles, sexual contact, and mother-to-child transmission.	Mainly blood-borne; IV drug use, contaminated blood products, needle-stick injury.	Fecal–oral route (contaminated water) and consumption of undercooked pork, wild game, or camel products.
Incubation	2–8 weeks (average 2–4 weeks)	45–180 days (average 90 days).	2–26 weeks (average 6–7 weeks).	2–8 weeks (average 5–6 weeks).
Natural History	Acute or chronic; may progress to cirrhosis and HCC	Acute, self-limiting; no chronic infection	80% become chronic; may progress to cirrhosis and HCC	Usually acute; chronic infection in immunocompromised patients
Clinical Features	Fever, jaundice, dark urine, clay-colored stool	Often asymptomatic initially; chronic liver disease, cirrhosis	Often asymptomatic; chronic hepatitis, cirrhosis	Acute hepatitis; severe in pregnancy; neurological and extrahepatic manifestations
Diagnosis	Anti-HAV IgM (acute), Anti-HAV IgG (past), HAV RNA	HBsAg, HBeAg, Anti-HBe, HBV DNA (PCR), ELISA	Anti-HCV antibody, HCV RNA (PCR)	HEV RNA (gold standard), Anti-HEV IgM, Anti-HEV IgG
Complications	Rare fulminant hepatic failure	Chronic hepatitis, cirrhosis, hepatocellular carcinoma	Chronic hepatitis, cirrhosis, hepatocellular carcinoma	Fulminant hepatic failure (especially pregnancy), chronic hepatitis in immunocompromised
Treatment	Supportive care;	Interferon- α ,	Direct-acting	Usually supportive;

	liver transplant for FHF	nucleos(t)ide analogues (viral suppression), liver transplantation if needed	antivirals (current standard); previously pegylated interferon + ribavirin	ribavirin for chronic infection; pegylated interferon in selected cases
Prevention	Inactivated/live vaccines, sanitation, hygiene HBV vaccine, safe blood, safe sex, screening	HBV vaccine, safe blood, safe sex, screening	No vaccine; safe injections, blood screening ⁽¹⁴⁾	Sanitation, safe food (avoid undercooked meat); Hecolin vaccine available in China
Chronic Infection	No	Yes	Yes	Only in immunocompromised patients
Vaccine Available	Yes	Yes	No	Yes (Hecolin, limited availability)

Polyherbal Therapy for treatment

Hepatitis management primarily relies on antiviral therapy to suppress viral replication, prevent disease progression, and reduce the risk of cirrhosis and hepatocellular carcinoma. In addition to standard antiviral agents, silymarin (*Silybum marianum*) has been investigated as an adjunctive hepatoprotective therapy because of its antioxidant, anti-inflammatory, and membrane-stabilizing properties. A meta-analysis of 55 randomized clinical trials demonstrated that silymarin significantly reduced serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels, indicating improvement in hepatocellular injury, particularly in patients with viral hepatitis.

The hepatoprotective activity of silymarin is associated with attenuation of oxidative stress, inhibition of inflammatory signaling pathways, stabilization of hepatocyte membranes, and promotion of liver cell regeneration. It has also demonstrated antiviral effects by interfering with viral replication and modulating host immune responses. Current evidence supports the use of silymarin as an adjunct to conventional antiviral therapy rather than a replacement, with greater clinical benefits observed in viral hepatitis than in advanced alcoholic or drug-induced liver disease. ⁽¹⁴⁾

Recent innovation (In Treatment)

There are different therapies to diagnose and cure the hepatitis as follows,

A)CRISPR-Cas13b as a Novel Therapeutic Strategy for Hepatitis B

CRISPR-Cas13b is an emerging RNA-targeting gene-editing platform with potential applications in the treatment of chronic hepatitis B virus (HBV) infection. This technology selectively degrades HBV RNA, thereby suppressing viral replication and reducing the production of viral proteins. Experimental studies have reported reductions of up to 96% in HBV-associated viral markers, highlighting its strong antiviral potential.

Unlike DNA-editing systems, CRISPR-Cas13b specifically targets viral RNA, reducing the likelihood of permanent alterations to the host genome. Although this approach remains in the preclinical stage, it represents a promising therapeutic strategy that could complement or replace long-term antiviral therapy and contribute to the development of a functional cure for chronic hepatitis B. Further preclinical and clinical studies are required to establish its safety, efficacy, and long-term therapeutic value.^(15,16,17)

B)AI-Assisted Diagnosis

Artificial intelligence (AI) is increasingly used to support the diagnosis of liver diseases through the analysis of medical images, including ultrasound and CT scans, enabling reliable detection of liver fibrosis, cirrhosis, and hepatocellular carcinoma (HCC). In addition, AI-based analysis of digital pathology and multi-omics datasets facilitates personalized treatment planning by predicting therapeutic outcomes and guiding antiviral treatment decisions. ⁽¹⁸⁾

C)RNA-Targeting Antiviral Therapy

Antisense Oligonucleotides, ASOs :

Antisense oligonucleotides, such as bepirovirsen, selectively bind to HBV messenger RNA (mRNA), suppress viral protein synthesis, promote degradation of viral RNA, and enhance host immune-mediated viral clearance.

Capsid Assembly Modulators (CAMs) :

Second-generation capsid assembly modulators interfere with HBV nucleocapsid formation by inducing aberrant capsid assembly or destabilizing preformed capsids, thereby inhibiting viral replication.⁽¹⁹⁾

D)Combination Hepatitis Vaccines

Combination hepatitis vaccines have been developed to provide simultaneous protection against multiple infectious diseases while minimizing the number of vaccine doses and improving immunization compliance. Currently available formulations include the combined hepatitis A and B vaccines (Twinrix and Ambirix), hepatitis A–typhoid vaccines (Viatim/Vivaxim and Hepatyrix), and the hexavalent vaccine (Hexaxim; DTaP-IPV-HB-Hib), which also confers immunity against diphtheria, tetanus, pertussis, poliomyelitis, hepatitis B, and Haemophilus influenzae type b.

These multivalent vaccines enhance vaccination coverage, simplify immunization schedules, and improve cost-effectiveness without compromising safety or immunogenicity. The hepatitis A–B vaccine is routinely administered in a three-dose schedule (0, 1, and 6 months), producing durable protective antibody responses. Hepatitis A–typhoid vaccines are primarily indicated for travelers to endemic regions, offering convenient single-dose protection. Hexaxim is incorporated into routine infant immunization programs and has demonstrated a favorable safety profile, robust immune responses, and sustained clinical effectiveness, supporting its widespread global implementation.

The combination therapy is best option to treat the patients and there are different types of therapeutic vaccines which are used in combination. These three types of therapeutic vaccines are given as follows,

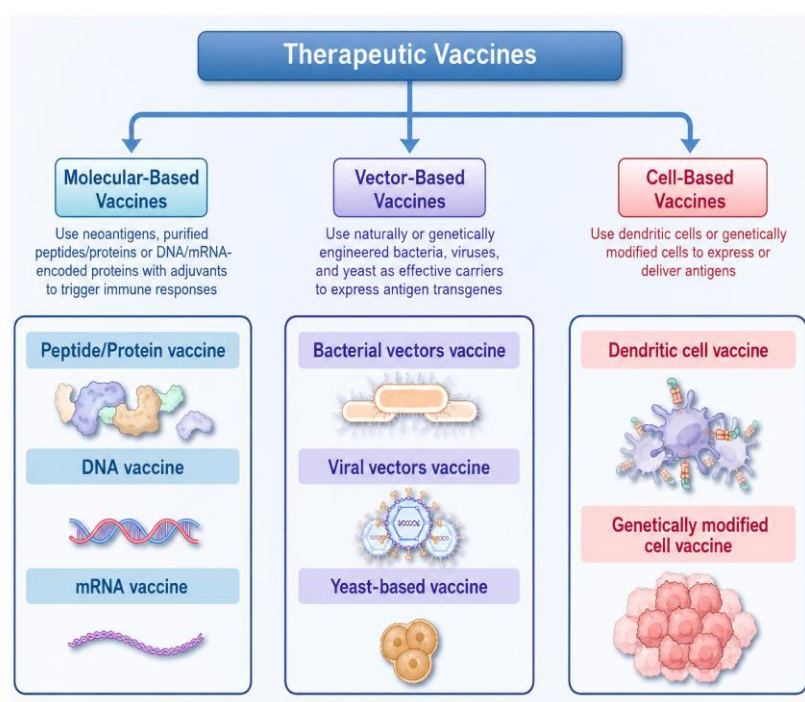


Figure.3: Therapeutic Vaccines

E)Combination Human Monoclonal Antibody Therapy:

Combined human monoclonal antibodies targeting the preS2 and hepatitis B surface antigen (HBsAg) effectively neutralize hepatitis B virus (HBV) particles, resulting in a marked reduction in viral load in preclinical animal models and demonstrating potential as a novel immunotherapeutic strategy.⁽²⁰⁾

Hepatatis elimination Program

Viral hepatitis causes approximately 1.1 million deaths annually worldwide. Although acute infections are often self-limiting, persistent infection can progress to chronic hepatitis, cirrhosis, hepatocellular carcinoma, and liver

failure. In 2015, viral hepatitis elimination was incorporated into the Sustainable Development Goals (SDGs), prompting the World Health Organization (WHO) to implement the Global Health Sector Strategy on Viral Hepatitis (2016–2021), which has since been updated. In alignment with these global initiatives, India launched the National Viral Hepatitis Control Program (NVHCP) in 2018, targeting elimination of viral hepatitis as a public health threat by 2030. Recent evidence-based recommendations emphasize expanded vaccination, prevention of mother-to-child transmission, improved screening through point-of-care and self-testing, simplified treatment protocols, and optimized healthcare delivery to accelerate progress toward the 2030 elimination goal.⁽²¹⁾

Challenges

Viral hepatitis remains a major global health challenge, affecting millions of individuals and placing a substantial burden on healthcare systems. The ability of hepatitis viruses to establish persistent infection, evade host immune responses, and promote progressive liver disease limits the effectiveness of current antiviral therapies, which rarely achieve complete viral eradication. Consequently, the development of innovative therapeutic strategies aimed at achieving a functional cure, characterized by sustained viral suppression, reduced disease progression, and prevention of transmission, has become a key research priority. Emerging approaches, including RNA-based therapeutics, viral entry inhibitors, nucleic acid polymers, immunomodulatory agents, and therapeutic vaccines, offer promising avenues for improving long-term clinical outcomes.⁽²²⁾

Future prospective

❖ Improved Early Diagnosis:

Establish standardized diagnostic criteria for acute HCV infection to enable timely detection of primary infection, reinfection, and superinfection.

❖ Enhanced Risk-Based Screening:

Strengthen surveillance in individuals with elevated alanine aminotransferase (ALT) levels and those at high risk of HCV exposure to facilitate early diagnosis.

❖ Optimization of DAA Therapy:

Conduct further clinical studies to validate and expand the use of direct-acting antivirals (DAAs) for the treatment of acute HCV infection.

❖ Universal Access to Treatment:

Improve affordability, licensing, and healthcare policies to ensure equitable global access to DAA therapy.

❖ Strengthened Public Health Measures:

Reinforce infection-control strategies, including universal precautions, harm-reduction programs, safe sexual practices, and post-treatment viral surveillance to reduce HCV transmission.

❖ **Development of Prophylactic Vaccines:**

Prioritize the design of safe and effective preventive vaccines, particularly for populations with high HCV prevalence and ongoing transmission risk.

❖ **Broadly Neutralizing Vaccine Strategies:**

Develop vaccines capable of inducing cross-genotype neutralizing antibodies to provide broad protection against diverse HCV strains.

❖ **Enhanced Cellular Immunity:**

Focus on vaccine platforms that stimulate durable CD4⁺ and CD8⁺ T-cell responses to improve long-term immune protection.

❖ **Evaluation of Next-Generation Vaccines:**

Advance promising multivalent and pangenotypic vaccine candidates through preclinical and clinical studies to assess their safety and efficacy.

❖ **Translational and Clinical Research:**

Promote large-scale clinical trials and translational research to accelerate the development of effective preventive and therapeutic strategies for HCV elimination.

Conclusion

Hepatitis continues to be a significant global health concern, affecting millions of people and contributing to substantial morbidity and mortality. Although considerable progress has been made in the prevention and treatment of viral hepatitis, challenges such as delayed diagnosis, limited healthcare access, and inadequate public awareness remain barriers to disease control. Vaccination, safe healthcare practices, improved sanitation, routine screening, and timely antiviral therapy are the cornerstones of effective hepatitis prevention and management.

Increasing public awareness through education and community-based initiatives is essential to promote early detection, reduce transmission, and encourage treatment adherence. Collaborative efforts among healthcare providers, researchers, governments, and public health organizations are necessary to expand access to preventive and therapeutic services. A comprehensive strategy that combines prevention, early diagnosis, effective treatment, and sustained awareness is vital for reducing the burden of hepatitis and supporting the World Health Organization's goal of eliminating viral hepatitis as a public health threat by 2030.⁽²³⁾

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