Epidemiology of Hepatitis C Virus and HBV/HCV Coinfection: Trends in Disease Burden and Genotypic Diversity, a *Scoping Review*.

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https://doi.org/10.51867/scimundi.6.2.25

ABSTRACT

Hepatitis C virus (HCV) infection is a significant public health problem, with an estimated 50 million infected people worldwide, of which an estimated 1 million people are newly infected each year and more than 240,000 HCV-related deaths occur annually, mostly from cirrhosis and hepatocellular carcinoma (HCC). Hepatitis B virus (HBV)/HCV coinfection is less prevalent than mono-infection, but may be associated with more rapid progression of liver disease, more liver decompensation, hepatic cirrhosis, HCC, and hepatic mortality. This review aims to summarize recent available scientific literature and the most recent reports from the Centers for Disease Control and Prevention (CDC), the European Association for the Study of the Liver (EASL), World Health Organization (WHO), and other international organizations to assess the epidemiology, genotypic diversity, clinical implications, and public health concerns of HCV infection and HBV/HCV coinfection. Existing data suggest there is significant geographic diversity among the prevalence of HCV, with the highest prevalence found in regions of Africa, the Middle East, and Asia. There are eight major HCV genotypes (1-8); genotype 1 is responsible for about 46% of all HCV infections in the world, genotype 3 for 30%, genotype 2 for 13%, and genotype 4 for 8% of infections, and ten HBV genotypes (A-J), with varying geographic distributions and clinical implications. New serological assays, real-time polymerase chain reaction, next-generation sequencing and molecular epidemiology have greatly advanced the detection, characterization, monitoring and treatment of viruses. Global elimination of HCV has been revolutionized by universal use of direct-acting antivirals against pan-genotypes, which have improved to achieve more than 95% SVR rates, and expanded screening has improved global prevention of HBV. Although these have advanced, there are still significant challenges, such as in sub-Saharan Africa and other resource-limited areas where epidemiological data, genotype surveillance, molecular diagnostic capacity and access to antiviral therapy are still limited. The efforts to reach the WHO target of viral hepatitis elimination as a public health threat by 2030 will require strengthening of HBV/HCV surveillance systems, expanding molecular epidemiological research, improving access to diagnostics and treatment, and investments in public health infrastructure, in addition to current initiatives.

Keywords: Hepatitis C Virus; Hepatitis B Virus; HBV/HCV Coinfection; Genotype Diversity; Molecular Epidemiology; Viral Hepatitis Elimination.

I. INTRODUCTION

Viral hepatitis remains a major global cause of liver-related morbidity and mortality. Of the five hepatotropic viruses (HAV, HBV, HCV, HDV, and HEV), HBV and HCV account for most hepatitis-related deaths because of their propensity to establish chronic infection (Asandem et al., 2024; Quirino et al., 2024; WHO, 2024, 2025). In 2022, an estimated 254 million people were living with chronic HBV infection and 50 million with chronic HCV infection, causing over 1.3 million deaths annually, mainly from cirrhosis and hepatocellular carcinoma (HCC) (Quirino et al., 2024; WHO, 2024). The burden remains greatest in low- and middle-income countries because of limited access to screening, diagnosis, vaccination, and antiviral therapy (Jaquet et al., 2021).

HCV is a blood-borne positive-sense RNA virus, with 55–85% of infections progressing to chronic disease and increasing the risks of fibrosis, cirrhosis, end-stage liver disease, and HCC (Sallam & Khalil, 2024; Stasi et al., 2020). Although direct-acting antivirals (DAAs) achieve cure rates exceeding 95%, undiagnosed infections and pronounced regional disparities, particularly in Africa, Eastern Europe, Central Asia, and the Middle East, continue to sustain transmission (Bai et al., 2025; Farooq & Foster, 2025). Its extensive genotype diversity further influences transmission, disease progression, treatment response, and molecular epidemiology (Z. Li et al., 2026).

HBV/HCV coinfection, common among people who inject drugs (PWID), patients on hemodialysis, recipients of multiple blood transfusions, and people living with HIV, is associated with accelerated fibrosis, cirrhosis, HCC, increased liver-related mortality, and HBV reactivation following DAA therapy (Berumen et al., 2021; Maqsood et al.,

2023; Naderi et al., 2025; Nevola et al., 2023; Shahriar et al., 2022). Despite the WHO target of reducing new infections by 90% and hepatitis-related deaths by 65% by 2030, progress remains slow in many African and Asian countries because of inadequate surveillance and limited access to diagnostics and treatment (Jagunmolu et al., 2026; Venkatesh et al., 2024; WHO, 2024, 2025).

This narrative scoping review synthesizes literature published between 2020 and 2026 from PubMed/MEDLINE, Scopus, Web of Science, Google Scholar, and reports from the WHO, the European Association for the Study of the Liver (EASL), and the Centers for Disease Control and Prevention (CDC). It summarizes the epidemiology, genotype diversity, molecular epidemiology, diagnosis, prevention, and management of HCV infection and HBV/HCV coinfection in the context of the WHO 2030 viral hepatitis elimination agenda.

1.1 Statement of the Problem

Despite major advances in prevention, diagnosis, and treatment, HCV and HBV/HCV coinfection remain important causes of chronic liver disease, cirrhosis, HCC and mortality worldwide. In 2024, approximately 47 million people were living with HCV, with 0.9 million new infections and about 240,000 HCV-related deaths (WHO, 2025). HBV/HCV coinfection further accelerates liver disease progression, yet its burden remains inadequately characterized, particularly in low- and middle-income countries.

Sub-Saharan Africa remains especially underrepresented in epidemiological and molecular studies despite substantial viral hepatitis endemicity. Considerable HBV and HCV genetic diversity further complicates transmission surveillance, disease prognostication, and monitoring of emerging variants. Limited molecular diagnostics, genotype surveillance, treatment access, and fragmented HBV/HCV surveillance systems continue to constrain elimination efforts. This review therefore synthesizes current epidemiological, clinical, and molecular evidence to identify surveillance and research priorities required to accelerate progress toward the WHO 2030 viral hepatitis elimination targets (WHO, 2025).

1.2 Research Objectives

1. To assess the global and regional burden of HCV and HBV/HCV coinfection.
2. To characterize HBV and HCV genotype diversity and geographic distribution.
3. To examine the clinical impact and treatment outcomes of HBV/HCV coinfection.
4. To evaluate advances and gaps in diagnosis, prevention, treatment, surveillance, and viral hepatitis elimination.

II. LITERATURE REVIEW

2.1 Theoretical Review

2.1.1 Virological Characteristics of HBV and HCV

Hepatitis B Virus: HBV is a small enveloped DNA virus of the Hepadnaviridae family and a major cause of chronic liver disease worldwide (WHO, 2024). Its infectious Dane particle contains a lipid envelope with hepatitis B surface antigen (HBsAg) surrounding a nucleocapsid containing hepatitis B core antigen (HBcAg). The 3.2 kb partially double-stranded relaxed circular DNA genome comprises four overlapping open reading frames (S, C, P, and X), encoding HBsAg, HBcAg, HBeAg, viral polymerase, and the HBx regulatory protein (Boonstra & Sari, 2025; Zhu et al., 2025). HBV enters hepatocytes through the sodium taurocholate co-transporting polypeptide (NTCP) receptor. Relaxed circular DNA (rcDNA) is converted into covalently closed circular DNA (cccDNA), the template for viral transcription, while pregenomic RNA (pgRNA) is reverse transcribed to produce new virions and replenish cccDNA, ensuring viral persistence (L. Wang et al., 2024; Zhu et al., 2025).

HBV is classified into ten genotypes (A–J), differing by >7.5% across the complete genome. Genotype A predominates in Africa, Northern Europe, and North America; B and C in East and Southeast Asia; D in the Mediterranean, Middle East, and India; E in West Africa; F and H in Central and South America; whereas G, I, and J are uncommon (Kyaw et al., 2020). HBV genotype influences molecular epidemiology, disease progression, treatment response, and the risk of hepatocellular carcinoma (HCC).

Hepatitis C Virus: HCV is an enveloped, positive-sense single-stranded RNA virus of the Flaviviridae family (Hepacivirus genus) with a 9.6 kb genome encoding structural (core, E1, E2) and non-structural (p7, NS2–NS5B) proteins required for viral replication, assembly, and immune evasion (Martinez & Franco, 2020; Moustafa et al., 2019). HCV enters hepatocytes through receptors including CD81, scavenger receptor class B type I (SR-BI), claudin-1, and occludin. Following entry, viral RNA is translated into a polyprotein, processed by host and viral proteases, and replicated by the NS5B RNA-dependent RNA polymerase before new virions are assembled and released (Colpitts et al., 2020; Pierce et al., 2023). The error-prone NS5B polymerase generates extensive genetic diversity and quasispecies that promote immune escape and viral persistence. HCV comprises eight major genotypes and more than

90 subtypes with distinct geographic distributions, making genotype surveillance essential for understanding transmission, disease progression, antiviral susceptibility, and molecular epidemiology (Mbisa et al., 2024).

2.1.2 Biological Interactions During HBV/HCV Coinfection

Viral Interference: HBV/HCV coinfection is characterized by complex viral interactions that influence replication and clinical outcomes. Viral interference, whereby one virus suppresses the other, is common. HCV typically inhibits HBV replication through core and NS5A protein-mediated pathways and interferon-stimulated genes, whereas HBV may suppress HCV virion production through immune-mediated mechanisms and competition for intracellular resources (Liu et al., 2022).

Dominance Patterns: HBV/HCV coinfection may be HBV-dominant, HCV-dominant, or codominant. HCV-dominant infection is frequently associated with occult HBV infection and low HBV DNA levels, although viral dominance may shift during disease progression or antiviral therapy. Viral load, genotype, host immune responses, and treatment-related selective pressure are key determinants of viral dominance (Johnson et al., 2023). Immunological Interactions: Chronic HBV/HCV coinfection dysregulates host immunity through persistent activation of interferons, natural killer (NK) cells, and pro-inflammatory cytokines, promoting T-cell exhaustion, chronic inflammation, fibrosis, cirrhosis, and hepatocellular carcinoma (HCC) (Devi et al., 2021). Consequently, coinfected individuals have more severe liver disease and a higher risk of HCC than those with HBV or HCV mono-infection (Pocino et al., 2023; Wang et al., 2025). Viral interference, fluctuating viral dominance, and immune dysregulation underpin the adverse clinical outcomes and increased global burden associated with HBV/HCV coinfection.

2.2 Empirical Review

2.2.1 Global and Regional Burden of HCV and HBV/HCV Coinfection

Recent epidemiological evidence demonstrates substantial variation in the burden of HCV infection across geographical regions and populations. Global analyses have shown that HCV continues to contribute considerably to morbidity and mortality, with marked differences in disease burden between countries and over time (Yang et al., 2023; Bai et al., 2025). In sub-Saharan Africa, available evidence indicates considerable heterogeneity in the prevalence of viral hepatitis among the general population, with differences attributable to geographical setting, population characteristics and patterns of exposure (Sticher et al., 2025). Studies among populations at increased risk have also demonstrated considerable transmission of HCV. For example, a global systematic review and meta-analysis among people who inject drugs found substantial incidence of HCV infection and highlighted differences according to age and sex/gender (Artenie et al., 2023). These findings indicate that HCV transmission remains concentrated in particular populations even where overall population prevalence may be relatively low.

Evidence on HBV/HCV coinfection similarly demonstrates important geographical and population-level differences. A systematic review and meta-analysis among people living with HIV in Africa found that HBV and/or HCV infections remain important comorbidities in this population, although prevalence varied considerably between settings (Kenfack-Momo et al., 2022). Studies from individual African settings have also documented HBV/HCV coinfection, including among HIV-positive populations in southeastern Nigeria and northern Ethiopia (Nnakenyi et al., 2020; Teame et al., 2022). The available evidence further suggests that coinfection may contribute to more complicated clinical outcomes than mono-infection (Maqsood et al., 2023; Shahriar et al., 2022). However, substantial gaps remain in population-based and nationally representative data, particularly in sub-Saharan Africa, limiting accurate estimation of the overall burden and its geographical distribution (Jaquet et al., 2021).

2.2.2 HBV and HCV Genotype Diversity and Geographic Distribution

Global and regional studies have established distinct patterns of HCV genotype distribution, while recent evidence continues to identify variation within established genotypes and subtypes (Messina et al., 2015; Martinez & Franco, 2020). Studies from particular regions illustrate this geographical variation. For example, HCV genotype studies in Southeast Asia have identified regional differences in the distribution of genotypes, while research in Istanbul has documented the genotype profile of patients with chronic HCV infection (Wasitthankasem et al., 2015; Bulut et al., 2021). Evidence from South Africa has also demonstrated considerable variability within HCV genotype 5, emphasizing that genotype classification alone may not fully capture the underlying viral diversity (Maunye et al., 2023).

HBV likewise exhibits substantial genetic diversity, with genotypes showing distinct geographical patterns and associations with virological and clinical characteristics. A nationwide study in Myanmar, for example, demonstrated the distribution of HBV genotypes within the general population, while a longitudinal cohort study showed that HBV genotype can influence virological and biochemical measures over time (Kyaw et al., 2020; Keeshan et al., 2023). Recent African evidence has further emphasized the diversity and evolutionary history of HBV across the continent (Dujing et al., 2026). Importantly, emerging molecular evidence has identified novel HCV

subtypes and potentially new genotypes, demonstrating that viral diversity continues to evolve (Mbisa et al., 2024). These findings support the need for continued molecular and genomic surveillance, particularly in regions where genotype data remain limited.

2.2.3 Clinical Outcomes and Treatment of HBV/HCV Coinfection

Empirical and clinical evidence indicates that HBV/HCV coinfection can have important consequences for liver disease progression. Studies of viral coinfection have reported complex interactions between HBV and HCV, including differences in viral dominance and host immune responses. Experimental and clinical evidence suggests that the presence of HCV may enhance immune responses associated with HBV clearance in some coinfected individuals, demonstrating that the interaction between the two viruses is not uniform (Liu et al., 2022). At the clinical level, HBV and HCV infection are important contributors to chronic liver disease, fibrosis, cirrhosis and hepatocellular carcinoma, with chronic inflammation and viral-host interactions contributing to disease progression (Berumen et al., 2021; Borgia et al., 2021; Goto et al., 2020). The clinical significance of genotype diversity is also increasingly recognized, with recent evidence indicating that particular HCV and HBV genotypes may influence disease progression and clinical outcomes (Badshah et al., 2025; Ran et al., 2025).

The introduction of direct-acting antivirals has substantially improved treatment outcomes for chronic HCV infection. Evidence from clinical practice demonstrates high treatment effectiveness, although outcomes may differ according to viral subtype and patient characteristics (Phillips et al., 2025). Recent studies also indicate that some patients may remain at risk of liver disease progression despite achieving sustained virological response, particularly where advanced liver disease or specific viral characteristics are present (Ran et al., 2025). In HBV/HCV coinfection, treatment requires particular attention to HBV status because antiviral treatment directed against HCV may alter the virological balance and create a risk of HBV reactivation. Consequently, current evidence supports HBV assessment and appropriate monitoring alongside HCV treatment (Maqsood et al., 2023; Cohen et al., 2024). These findings demonstrate that successful HCV treatment should be accompanied by appropriate assessment and management of HBV in coinfected patients.

2.2.4 Diagnosis, Prevention, Surveillance and Viral Hepatitis Elimination

Evidence from diagnostic studies demonstrates continuing improvements in the identification of HBV and HCV infection. Serological testing remains an important component of screening, while molecular assays are necessary for confirmation of active infection and assessment of viral characteristics. A multicentre laboratory evaluation demonstrated that rapid diagnostic tests can provide useful detection of HCV antibodies, including among individuals with HIV coinfection, although diagnostic performance varies between assays and settings (Vetter et al., 2020). Research on HCV antibody levels has also demonstrated their diagnostic relevance in identifying chronic infection (Kang et al., 2023). Increasing use of next-generation sequencing provides additional opportunities for characterizing viral diversity, transmission patterns and emerging variants (Satam et al., 2023). However, access to reliable diagnostics remains unequal, particularly in African and other resource-constrained settings, where infrastructure, affordability and availability of specialist services continue to present barriers (Jagunmolu et al., 2026).

Prevention and elimination evidence emphasizes the importance of vaccination, early diagnosis, treatment and integration of hepatitis services into health systems. Progress in HBV vaccination has substantially strengthened prevention, although coverage and implementation remain uneven across countries (Al-Busafi & Alwassief, 2024). For HCV, the availability of highly effective DAA therapy has created an important opportunity for elimination, but treatment access, diagnosis and linkage to care remain major challenges, particularly in low- and middle-income countries (Farooq & Foster, 2025; Venkatesh et al., 2024). Evidence from Africa similarly indicates that elimination efforts require stronger surveillance, improved access to diagnosis and treatment, and context-specific public-health strategies (Salomon et al., 2024). Consequently, achieving the WHO 2030 elimination targets will require integration of prevention, testing, treatment and surveillance rather than reliance on treatment expansion alone (Zhang & Cui, 2025; Toma et al., 2025).

III. METHODOLOGY

3.1 Research Design

This study adopted a scoping review design to systematically map and synthesize available evidence on the epidemiology of HCV and HBV/HCV coinfection, including disease burden, genotype diversity, clinical outcomes, diagnostic advances, and treatment and elimination strategies. A scoping review was considered appropriate because the literature encompasses diverse study designs, populations, geographical settings and methodological approaches. The review focused on identifying the breadth and characteristics of existing evidence and highlighting areas where evidence remains limited.

3.2 Search Strategy

A comprehensive literature search was conducted using major electronic databases, including PubMed/MEDLINE, Scopus, Web of Science and Google Scholar. Additional evidence was obtained from relevant reports and publications from authoritative organizations, including the World Health Organization (WHO), Centers for Disease Control and Prevention (CDC) and European Association for the Study of the Liver (EASL). Searches combined keywords and Boolean operators related to "HCV", "HBV", "coinfection", "epidemiology", "prevalence", "genotypes", "molecular epidemiology", "clinical outcomes", "diagnosis", "treatment and viral hepatitis elimination". The review primarily considered literature published between 2020 and 2026, while earlier seminal studies were considered where necessary to provide important scientific or epidemiological context.

3.3 Eligibility Criteria

Studies were considered eligible when they addressed HCV infection, HBV/HCV coinfection, epidemiological burden, genotype diversity, clinical outcomes, diagnosis, treatment, prevention or surveillance. Studies involving human populations and reporting relevant epidemiological, clinical or molecular findings were prioritized. Peer-reviewed articles, systematic reviews, relevant institutional reports and authoritative public-health publications were considered where they contributed directly to the objectives of the review.

Studies that were unrelated to the review objectives, duplicated publications, non-human studies and publications without sufficient information relevant to the research questions were excluded. Where multiple publications reported substantially overlapping findings from the same study population, the most relevant or comprehensive publication was prioritized.

3.4 Study Selection and Data Extraction

Retrieved records were screened by title and abstract for relevance, followed by assessment of potentially eligible full-text publications. Relevant information was extracted using a structured data-charting approach. Extracted information included author and publication year, country or geographical region, study design, study population, sample size, prevalence or epidemiological measures, viral genotypes, clinical outcomes, diagnostic or molecular methods, treatment outcomes and major conclusions.

The selected studies were subsequently organized according to the four study objectives. This approach enabled comparison of evidence relating to disease burden, genotype diversity, clinical and treatment outcomes, and diagnosis, prevention, surveillance and elimination.

3.5 Data Synthesis

Because of the expected heterogeneity in study designs, populations, outcomes and geographical settings, findings were synthesized narratively rather than through statistical meta-analysis. Evidence was grouped thematically and geographically to identify recurring patterns, similarities and differences across studies. Particular attention was given to differences between regions, especially between high-income settings and sub-Saharan Africa, and to areas where empirical evidence remains insufficient.

3.6 Quality and Reporting Considerations

The review followed established principles for conducting and reporting scoping reviews, with the search, screening, selection and synthesis processes documented systematically. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) framework was used to guide reporting and presentation of the review process. Where appropriate, the methodological characteristics and limitations of included studies were considered when interpreting the strength and consistency of the available evidence.

IV. FINDINGS & DISCUSSION

4.1 Global Burden of HCV Infection

4.1.1 Global Prevalence

Current estimates indicate that 50 million people were living with chronic HCV infection in 2022, with approximately 1 million new infections annually and a global prevalence of 0.6%, although marked regional variation exists (Fosu et al., 2025; Stroffolini & Stroffolini, 2024; WHO, 2024, 2025). Anti-HCV seroprevalence exceeds HCV viremia because many infected individuals achieve spontaneous viral clearance or cure following antiviral therapy (Kang et al., 2023). Improved blood safety, safer injection practices, harm-reduction programs, and direct-acting antivirals (DAAs), which achieve sustained virological response rates exceeding 95%, have substantially reduced HCV transmission and chronic infection (Aydin et al., 2025; Toma et al., 2025; Torre et al., 2024). However, underdiagnosis, limited access to testing and treatment, ongoing transmission among high-risk populations, and

healthcare disparities, particularly in low- and middle-income countries, continue to impede HCV elimination (Phelan et al., 2022).

4.1.2 Regional Distribution

HCV prevalence varies markedly across regions. Africa has an estimated prevalence of 1–3%, with the highest burden in North, Central, and West Africa, where limited diagnostics and access to DAAs continue to impede control (Boukaira et al., 2025; WHO, 2024). The Asia-Pacific region bears the largest absolute burden, largely driven by China, India, and Pakistan (Yang et al., 2023). In Europe, prevalence remains highest in Eastern Europe and Central Asia, while North America has experienced rising incidence among people who inject drugs (PWID), largely associated with the opioid epidemic (Artenie et al., 2023; Ekushov et al., 2026). HCV prevalence is generally moderate in Latin America and remains a significant public health concern in the Middle East and North Africa (MENA), despite notable progress in countries such as Egypt (WHO, 2024). These regional disparities are largely driven by socioeconomic conditions, healthcare infrastructure, blood safety, public health policies, and injection drug use.

4.1.3 Morbidity and Mortality

Chronic HCV infection develops in 55–85% of infected individuals and is a leading cause of fibrosis, cirrhosis, portal hypertension, hepatic decompensation, liver failure, and hepatocellular carcinoma (HCC). Disease progression is influenced by host factors, HIV coinfection, and viral genotype (Huang et al., 2023; Goto et al., 2020; Toma et al., 2025). Viral hepatitis causes approximately 1.3 million deaths annually, with HCV accounting for nearly one-quarter of these deaths (WHO, 2024). Although direct-acting antivirals (DAAs) have markedly reduced liver-related complications and mortality, disparities in diagnosis, treatment access, and healthcare infrastructure continue to hinder achievement of the WHO 2030 viral hepatitis elimination targets.

4.2 Epidemiology of HBV/HCV Coinfection

Global Prevalence: BV/HCV coinfection occurs when both viruses infect the same individual and is most common in endemic regions and populations with shared transmission risks. Compared with mono-infection, coinfection accelerates progression to cirrhosis, hepatocellular carcinoma (HCC), and liver-related mortality (Marin et al., 2025). Although affecting <1% of the general population, coinfection remains a substantial public health burden. Meta-analyses estimate that 2–10% of patients with chronic HCV are HBsAg-positive, while 1–15% of those with chronic HBV are coinfected with HCV, with markedly higher prevalence among people who inject drugs (PWID), patients on hemodialysis, recipients of multiple blood transfusions, and people living with HIV (PLHIV) (Teame et al., 2022; WHO, 2024). The true burden is underestimated because of underdiagnosis, inconsistent surveillance, limited molecular diagnostics, and geographic variation. Nevertheless, HBV vaccination, improved blood safety, and expanded access to direct-acting antivirals (DAAs) have reduced transmission, although HBV/HCV coinfection remains a significant challenge, particularly in resource-limited settings (Al-Busafi & Alwassief, 2024).

4.2.1 Regional Distribution of Coinfection

Africa bears a substantial HBV/HCV coinfection burden because of high HBV endemicity and ongoing HCV transmission. Coinfection prevalence ranges from 1–8%, with the highest rates reported in West and Central Africa (Kenfack-Momo et al., 2022). Limited diagnostics, inadequate screening, and restricted access to antiviral therapy contribute to underdiagnosis and poor outcomes, while historical HCV epidemics have further increased the burden in North Africa, particularly Egypt. Asia accounts for a large proportion of the global HBV/HCV coinfection burden because of the high endemicity of both viruses. Countries such as China, India, Pakistan, and Mongolia contribute substantially to this burden (Chen et al., 2025). Although expanded HBV vaccination and HCV elimination programs have reduced transmission, coinfection remains a major contributor to chronic liver disease and HCC, particularly in East and Southeast Asia. Europe exhibits marked regional variation in HBV/HCV coinfection, with the highest prevalence in Eastern Europe and marginalized populations. Injection drug use and migration from endemic regions remain major drivers of transmission, while improved surveillance and widespread antiviral therapy have strengthened disease control and elimination efforts (Assoumou et al., 2025).

HBV/HCV coinfection is less common in the Americas than in Africa and Asia but remains concentrated among people who inject drugs (PWID), incarcerated populations, and people living with HIV (PLHIV) in North America, while disparities in healthcare access and screening continue to influence disease distribution in Latin America (CDC, 2026; Kenfack-Momo et al., 2022). Regional differences largely reflect HBV/HCV endemicity, socioeconomic conditions, healthcare infrastructure, and high-risk behaviors.

4.2.3 Risk Factors for Coinfection

Injection drug use remains the leading risk factor for HBV/HCV coinfection because sharing contaminated needles facilitates transmission (CDC, 2026). Although improved blood screening has reduced transfusion-associated infections, unsafe transfusions remain a concern where blood safety is inadequate. Patients on hemodialysis and people living with HIV (PLHIV), particularly those with HIV/HBV/HCV triple infection, are also at increased risk of accelerated liver disease progression (Nnakenyi et al., 2020). Healthcare-associated exposures, including unsafe injections, inadequate sterilization, surgical procedures, and occupational exposure, continue to contribute to transmission, especially in resource-limited settings. Despite advances in HBV vaccination, diagnostics, and direct-acting antivirals (DAAs), HBV/HCV coinfection remains a major public health challenge. Understanding its epidemiology and risk factors is essential for targeted prevention, improved case detection, and achievement of viral hepatitis elimination goals.

4.3 Genotypic Diversity of HCV

4.3.1 Classification of HCV Genotypes

HCV exhibits remarkable genetic diversity because of the error-prone NS5B RNA-dependent RNA polymerase, which generates quasispecies that promote viral persistence and adaptation (Martinez & Franco, 2020; Topi et al., 2024). HCV comprises eight major genotypes (1–8) and over 90 subtypes, differing by approximately 30–35% and 15–25% at the nucleotide level, respectively (Martinez & Franco, 2020). Although pan-genotypic direct-acting antivirals (DAAs) have reduced the need for routine genotyping in treatment selection, genotype determination remains important for molecular epidemiology, transmission tracking, outbreak investigation, and surveillance (Phillips et al., 2025).

4.3.2 Geographic Distribution

Genotype 1 is the most prevalent HCV genotype globally, accounting for approximately 46–49% of infections. Subtype 1a predominates in North America and Northern Europe, whereas 1b is more common in Southern Europe, Japan, China, and Latin America. Historically, its widespread distribution has been driven by blood transfusions and healthcare-associated transmission (Bulut et al., 2021). Genotype 2 accounts for approximately 9–13% of global HCV infections and is believed to have originated in West Africa. It is also found in Europe, the Caribbean, and East Asia, with its wider distribution largely attributed to historical population movements, including the transatlantic slave trade.

Genotype 3 accounts for approximately 18–22% of global HCV infections and predominates in South Asia, particularly India, Pakistan, Bangladesh, and Nepal. It is also common among people who inject drugs (PWID) in Europe, Australia, and North America and is associated with hepatic steatosis and more rapid disease progression (Salomon et al., 2024). Genotype 4 accounts for approximately 8–13% of global HCV infections and predominates in North Africa and the Middle East. Its high prevalence in Egypt is largely attributed to historical unsafe injections during mass anti-schistosomal treatment campaigns (Messina et al., 2015).

Genotype 5 is a relatively rare genotype, being responsible for less than 1% of infections worldwide. It primarily occurs in Southern Africa and South Africa, and in its low turnaround is still an important disease in the country (Maunye *et al*., 2023). The genotype 6 is very variable and is mainly distributed in Vietnam, Thailand, Myanmar, Laos, Cambodia and Southern China. The high genetic variability observed in this region indicates a long history of evolution within this area and is important for understanding HCV evolution and transmission dynamics (Wasitthankasem *et al*., 2015). Genotype 7 is the rarest and was first detected in people from Central Africa. The epidemiology is still poorly known because there are few reported cases, but more widespread migration throughout the world could help spread the disease (Dujing *et al*., 2026).

Genotype 8, the most recently recognized HCV genotype, has been identified mainly in Central Africa. Its detection highlights ongoing HCV evolution and the need for molecular surveillance in underrepresented regions (Mbisa et al., 2024). Migration, globalization, healthcare-associated transmission, blood transfusion, injection drug use, and population movement have increasingly spread HCV genotypes beyond their traditional endemic regions.

4.4 Clinical Significance of HCV Genotypes

4.4.1 Disease Progression

HCV genotypes impact disease outcomes and disease progression. Infection with genotype 3 is a consistent risk factor for greater hepatic steatosis, faster fibrosis progression and increased risk for HCC when compared to a number of other genotypes (Ran *et al*., 2025). Other factors like host age, sex, alcohol use, metabolic syndrome, HIV coinfection, and immune status also play a role in determining disease severity.

4.4.2 Response to Antiviral Therapy

Historically, HCV genotyping was essential for interferon-based therapy because treatment duration and sustained virological response (SVR) varied considerably by genotype, with genotypes 1 and 4 responding less favorably than genotypes 2 and 3 (Chen & Yu, 2010; Younossi et al., 2014). Although pan-genotypic DAAs now achieve cure rates exceeding 95% across most genotypes, genotype-specific differences in treatment response, resistance-associated substitutions, and retreatment strategies remain clinically relevant.

4.4.3 Implications for Elimination Programs

Continued HCV genotype surveillance is essential for viral hepatitis elimination, supporting molecular epidemiology, transmission tracking, antiviral resistance monitoring, and detection of emerging variants and recombinant strains (WHO, 2024). Genotype data inform screening, resource allocation, and public health interventions, making sustained surveillance critical for achieving the WHO 2030 elimination targets (Zhang & Cui, 2025).

4.5 HBV Genotypes and Their Relevance in Coinfection

HBV is classified into 10 genotypes (A–J) that differ by >7.5% across the complete genome and exhibit distinct geographic and clinical characteristics (Bello et al., 2023; Locarnini et al., 2021). Genotype A predominates in Africa, Northern Europe, and North America; B and C in East and Southeast Asia; D in the Mediterranean, Middle East, Europe, and South Asia; E in West Africa; F and H in Central and South America; whereas G, I, and J are uncommon (Kyaw et al., 2020; WHO, 2024). Migration and globalization have increasingly reshaped these distribution patterns.

HBV genotype influences viral replication, HBeAg seroconversion, disease progression, and treatment response. Genotype C is associated with higher viral loads and greater risks of cirrhosis and hepatocellular carcinoma (HCC), genotype D with more severe liver disease, and genotype A with better responses to interferon therapy (Keeshan et al., 2023; Sant'Anna & Araujo, 2023). In HBV/HCV coinfection, HBV genotype may influence viral interference, dominance, and disease severity, although evidence remains limited. Coinfection involving HBV genotype C and HCV genotype 3 may increase the risk of fibrosis progression and HCC (Badshah et al., 2025; Jose-Abrego et al., 2023). Integrated HBV/HCV genotyping therefore remains important for molecular epidemiology, surveillance, and viral hepatitis elimination strategies (Locarnini et al., 2021).

4.6 Clinical Impact of HBV/HCV Coinfection

4.6.1 Natural History

Chronic Infection: HBV/HCV coinfection is characterized by complex viral interactions and accelerated liver disease progression. HBV persists through maintenance of covalently closed circular DNA (cccDNA), whereas HCV establishes chronic infection through rapid genetic evolution and quasispecies-mediated immune escape (Naidu & Margeridon, 2025; Quirino et al., 2024). Viral interference is common, with HCV typically suppressing HBV replication, although HBV dominance and codominance also occur (Maqsood et al., 2023). Compared with HBV or HCV mono-infection, coinfection is associated with persistent immune activation, impaired virus-specific T-cell responses, chronic hepatic inflammation, and cumulative hepatocyte injury, resulting in faster progression to advanced liver disease, hepatocellular carcinoma (HCC), and increased liver-related mortality (Borgia et al., 2021).

Fibrosis Progression: Liver fibrosis is a major determinant of clinical outcomes in HBV/HCV coinfection. Persistent viral replication, chronic inflammation, oxidative stress, hepatocyte apoptosis, and hepatic stellate cell activation accelerate fibrosis progression (Somnay et al., 2024). Coinfected individuals have a 1.5–2-fold higher risk of advanced fibrosis than those with mono-infection, with progression further influenced by age, sex, alcohol use, metabolic syndrome, HIV coinfection, and viral variants (Shahriar et al., 2022). Advanced fibrosis substantially increases the risks of cirrhosis, portal hypertension, hepatic decompensation, hepatocellular carcinoma (HCC), and liver-related mortality.

4.6.2 Liver Disease Outcomes

Cirrhosis is a major complication of HBV/HCV coinfection. Persistent inflammation and fibrogenesis accelerate progression to end-stage liver disease (ESLD), with coinfected individuals experiencing a higher cirrhosis burden and earlier disease onset than those with HBV or HCV mono-infection (Kmentt et al., 2025). Consequently, coinfection increases hospitalization, liver transplantation, and healthcare utilization. Cirrhosis predisposes patients to hepatic decompensation, including portal hypertension, ascites, variceal bleeding, hepatic encephalopathy, spontaneous bacterial peritonitis, and jaundice (Huang et al., 2020). Compared with mono-infection, HBV/HCV coinfection is associated with earlier and more severe decompensation, particularly in the presence of delayed antiviral therapy, advanced fibrosis, alcohol use, metabolic comorbidities, and uncontrolled viral replication. Hepatic

decompensation carries a poor prognosis and often necessitates liver transplantation. HBV/HCV coinfection is a major viral risk factor for hepatocellular carcinoma (HCC). HBV promotes carcinogenesis through HBx protein expression, viral DNA integration, and genomic instability, whereas HCV contributes through chronic inflammation, oxidative stress, and repeated hepatocyte injury (WHO, 2024). Coinfected individuals have a 2–6-fold higher risk of HCC than those with HBV or HCV mono-infection, particularly in endemic regions such as East Asia and sub-Saharan Africa (Maqsood et al., 2023).

4.7 Impact on Treatment Outcomes

HBV/HCV coinfection poses unique therapeutic challenges because treatment must account for viral dominance and the risk of HBV reactivation. Direct-acting antivirals (DAAs) achieve sustained virological response rates exceeding 95% in coinfected patients, comparable to HCV mono-infection (Morsica et al., 2022). However, HCV clearance may trigger HBV reactivation; therefore, the WHO, European Association for the Study of the Liver (EASL), and the American Association for the Study of Liver Diseases (AASLD) recommend HBsAg screening, HBV DNA monitoring, and nucleos(t)ide analogue prophylaxis (e.g., tenofovir or entecavir) for at-risk patients (Cohen et al., 2024; Cornberg et al., 2025). Limited access to diagnostics, HBV DNA testing, fibrosis assessment, and antiviral therapy continues to impede optimal care in many low- and middle-income countries. Consequently, integrated screening, surveillance, and antiviral management remain essential to reduce fibrosis, cirrhosis, hepatic decompensation, hepatocellular carcinoma (HCC), and liver-related mortality.

4.8 Advances in Diagnosis and Molecular Epidemiology

4.8.1 Serological Diagnosis

Serological testing remains the cornerstone of HBV and HCV screening, diagnosis, and surveillance. HBV diagnosis uses HBsAg, anti-HBs, anti-HBc, HBeAg, and anti-HBe, while HCV screening relies on anti-HCV detection by enzyme-linked immunosorbent assay (ELISA), chemiluminescent immunoassay (CLIA), or rapid diagnostic tests (RDTs), with ELISA and CLIA demonstrating >99% sensitivity and specificity (Song & Kim, 2016; Vetter et al., 2020; WHO, 2024).

However, serology cannot distinguish active from resolved HCV infection and requires confirmatory nucleic acid testing. Occult HBV infection, window periods, immunosuppression, and assay limitations may also affect accuracy. Nevertheless, serological assays remain indispensable for blood donor screening, epidemiological surveillance, and monitoring viral hepatitis elimination efforts (Song & Kim, 2016; Vetter et al., 2020; WHO, 2024).

4.8.2 Molecular Detection Methods

Polymerase Chain Reaction (PCR): Molecular diagnostics have transformed HBV and HCV detection and management. Conventional polymerase chain reaction (PCR) enables sensitive detection of HBV DNA and HCV RNA, facilitating confirmation of active infection, identification of occult HBV infection, and viral genotyping for research and molecular epidemiology (WHO, 2024, 2025). Although highly sensitive, conventional PCR is qualitative, labor-intensive, and more susceptible to contamination than newer molecular techniques. Real-Time PCR: Real-time polymerase chain reaction (qPCR) is the reference standard for quantifying HBV DNA and HCV RNA, providing accurate viral load measurements for disease monitoring, treatment response, infectivity assessment, and hepatocellular carcinoma (HCC) risk prediction (P. Li et al., 2026). In HBV/HCV coinfection, serial qPCR helps determine viral dominance, detect HBV reactivation during HCV therapy, and monitor treatment efficacy. Widely used platforms include Roche COBAS®, Abbott RealTime®, and GeneXpert®, all offering high sensitivity and reproducibility.

Sequencing Technologies: Sequencing technologies have greatly advanced understanding of HBV and HCV genetic diversity, evolution, and transmission. Sanger sequencing remains widely used for genotype determination and mutation analysis, while next-generation sequencing (NGS) platforms, including Illumina, Ion Torrent, and Oxford Nanopore, enable high-throughput whole-genome and deep sequencing for detecting quasispecies, resistance-associated variants, mixed infections, and recombinant strains (Satam et al., 2023). These technologies are increasingly important for precision medicine, outbreak investigations, antiviral resistance monitoring, and molecular surveillance. However, their widespread implementation remains limited in many low- and middle-income countries because of high costs and the need for specialized technical and bioinformatics expertise.

4.8.3 Molecular Epidemiology and Phylogenetics

Transmission Networks: Molecular epidemiology combines genomic and epidemiological data to explain the ways in which viruses are transmitted. Phylogenetic analysis can help identify transmission clusters, track the source of an outbreak and differentiate between healthcare associated infections (HAIs) and community-acquired infections (CAIs) (WHO, 2025). These strategies have been especially effective with people who inject drugs, men who have sex

with men, incarcerated people and people with HIV, among other populations in which ongoing viral transmission is often fuelled by transmission networks.

Evolutionary Dynamics: HBV and HCV are constantly mutating, recombining, genetically drifting and being subjected to selection pressure by host immunity and anti-viral drugs. In addition to its error-prone NS5B RNA polymerase, HCV is highly evolvable and has a large diversity of quasispecies. HBV evolution is caused by reverse transcription-mediated mutation, recombination events (Rothhaar *et al*., 2025). Such evolutionary processes enable immune escape, antiviral resistance and adaptation to various host populations, thus influencing the distribution and dynamics of global genotypes.

Emerging Variants: The rapid development of genomic surveillance has allowed the identification of new HBV and HCV variants, new HBV and HCV recombinant strains, and new genotypes that were not previously identified. New variants could impact disease course, diagnostic testing, treatment and vaccine efficacy. Novel HCV genotypes 7 and 8 and recombinant HBV strains have provided a glimpse of the continuous evolution of viral hepatitis pathogens, and the need for ongoing surveillance (Satam *et al*., 2023). Genomic monitoring has become increasingly important to viral hepatitis control programs as a tool for early detection of epidemiologically significant variants and provision of public health response. In recent years, serological tests, molecular diagnostic assays, sequencing technologies and phylogenetic analysis have revolutionized the diagnosis and epidemiological investigation of both HBV and HCV infections. These tools have had been useful in clinical management, understanding the dynamics of viral hepatitis transmission, conducting surveillance of emerging variants, and advancing the goals of viral hepatitis elimination globally.

4.9 Prevention, Treatment and Elimination Strategies

4.9.1 HBV Vaccination

HBV vaccination remains the most effective strategy for preventing HBV infection and reducing the burden of HBV/HCV coinfection. Recombinant HBV vaccines induce protective antibodies against hepatitis B surface antigen (HBsAg), providing immunity in over 95% of vaccinated individuals (WHO, 2024). The WHO recommends universal infant vaccination, including a birth dose within 24 hours, which has substantially reduced chronic HBV infection and mother-to-child transmission worldwide. Catch-up vaccination is also recommended for unvaccinated adolescents, adults, and high-risk groups, including people who inject drugs, healthcare workers, household contacts of infected individuals, and immunocompromised persons (WHO, 2025). Although more than 80% of children completed the three-dose HBV vaccine series in 2022, birth-dose coverage remains suboptimal in many low- and middle-income countries, particularly in sub-Saharan Africa (WHO, 2024). Despite marked reductions in chronic HBV infection, HCC, and liver-related mortality, inequitable vaccine access, weak health systems, and low awareness continue to limit global vaccine coverage.

4.9.2 HCV Direct-Acting Antivirals

DAAs have transformed HCV treatment, replacing interferon-based regimens that were limited by modest cure rates, prolonged therapy, and significant adverse effects. DAAs target key viral proteins, including NS3/4A protease, NS5A, and NS5B polymerase (WHO, 2024). Pan-genotypic regimens such as sofosbuvir/velpatasvir and glecaprevir/pibrentasvir achieve SVR rates exceeding 95%, markedly reducing the risks of cirrhosis, HCC, hepatic decompensation, and liver-related mortality, including among individuals with HBV/HCV coinfection (Satam et al., 2023). However, HCV clearance may trigger HBV reactivation, necessitating HBV screening before DAA initiation and appropriate monitoring or prophylactic antiviral therapy for at-risk patients (WHO, 2025). Despite their effectiveness, high costs, limited diagnostic capacity, and poor access to healthcare continue to restrict DAA uptake in many resource-limited settings.

4.9.3 Screening and Linkage to Care

Early diagnosis is essential for reducing viral hepatitis transmission and improving treatment outcomes. The World Health Organization (WHO) recommends population- and risk-based screening, particularly for pregnant women, blood donors, healthcare workers, people who inject drugs, incarcerated individuals, and people living with HIV (WHO, 2024). Rapid diagnostic tests (RDTs) and point-of-care assays have expanded access to screening, especially in resource-limited settings, while positive serological results require confirmatory nucleic acid testing. Despite these advances, major gaps remain in the hepatitis care cascade because of underdiagnosis, poor linkage to care, stigma, limited healthcare access, and financial barriers. Integrating viral hepatitis services into primary healthcare, expanding community-based screening, decentralizing testing, and streamlining treatment pathways have improved diagnosis and treatment coverage.

4.9. 4 WHO Elimination Strategy

The World Health Organization Global Health Sector Strategy on Viral Hepatitis aims to eliminate HBV and HCV as public health threats by 2030 through a 90% reduction in new infections and a 65% reduction in hepatitis-related deaths (WHO, 2024). Key interventions include universal HBV vaccination, expanded screening and diagnosis, equitable access to antiviral therapy, improved blood safety, and harm-reduction programs for people who inject drugs (PWID). Although several high-income countries have made substantial progress, many low- and middle-income countries, particularly in Africa and Asia, remain off track because of limited diagnostic capacity, restricted treatment access, weak surveillance systems, and inadequate healthcare financing. Achieving elimination will require sustained political commitment, strengthened surveillance, investment in health systems, and international collaboration. An integrated strategy combining vaccination, widespread screening, early diagnosis, access to effective antiviral therapy, and robust surveillance is essential to reduce the burden of HBV/HCV coinfection and achieve the WHO 2030 viral hepatitis elimination targets (WHO, 2024).

4.10 Knowledge Gaps and Future Directions

Although considerable progress has been made in prevention, diagnosis and treatment of viral hepatitis, there remain large gaps in knowledge that are impeding progress towards the WHO 2030 target of eliminating viral hepatitis as a public health threat. In many LMICs, the understanding of the epidemiology, genotypic diversity and transmission dynamics of HBV, HCV and HBV/HCV coinfection is limited (WHO, 2024). This will involve a coordinated investment in surveillance, molecular epidemiology, lab infrastructure, and international cooperation to address these limitations.

4.10.1 Underrepresentation of African Data

The epidemiology and molecular diversity of HBV and HCV remain poorly characterized in Africa because of limited population-based studies, weak surveillance systems, and inadequate molecular diagnostic capacity (Sticher et al., 2025). Most available data are derived from high-risk groups, blood donors, or hospital-based studies, limiting accurate estimation of community disease burden. These gaps hinder evidence-based policymaking and hepatitis control efforts. Strengthening population-based surveillance, multicountry cohort studies, molecular diagnostic capacity, and collaborative research networks across Africa is therefore essential to generate representative epidemiological data and support viral hepatitis elimination (Sticher et al., 2025).

4.10.2 Limited Genotype Surveillance

Despite the importance of HBV and HCV genotyping in molecular epidemiology, genotype surveillance remains highly uneven globally. Recent genomic analyses show that available HBV and HCV sequences are disproportionately derived from a small number of countries, particularly China and the United States, while many high-burden countries in Africa and the Western Pacific remain markedly underrepresented. HBV genotype E and HCV genotypes 5 and 8 are particularly undersampled despite their epidemiological relevance in Africa.

This gap is especially evident in Africa. A recent systematic review of HBV genetic epidemiology identified genotypes A, D, and E as major circulating lineages, with genotype E predominating in several regions, but found relatively few genotype studies and limited linkage between genotype and clinical outcomes (Bello et al., 2026). More broadly, genomic surveillance capacity remains concentrated in relatively few African countries, while limitations in sequencing infrastructure, trained personnel, bioinformatics capacity, data storage, and sustainable financing restrict routine molecular surveillance.

These limitations have important epidemiological consequences. Inadequate sequencing reduces the ability to characterize genotype and subgenotype distributions, identify recombinant or emerging strains, reconstruct transmission networks, and monitor antiviral resistance. Recent evidence indicates a substantial mismatch between hepatitis disease burden and genomic sampling, meaning that regions with considerable HBV and HCV burden may have some of the poorest genomic representation. Consequently, current global genotype distributions may partly reflect where sequencing has been performed rather than the full extent of circulating viral diversity.

Strengthening genotype surveillance therefore requires expansion of sequencing and bioinformatics capacity, standardized collection of genomic and epidemiological data, and integration of molecular surveillance into national hepatitis programs. Linking genotype data with clinical and epidemiological information would improve transmission tracking, resistance monitoring, identification of emerging variants, and evaluation of elimination interventions. Such investment is particularly important in sub-Saharan Africa and other underserved regions if genomic surveillance is to contribute meaningfully to the WHO 2030 viral hepatitis elimination agenda.

4.10.3 Emerging Genotypes and Recombinant Strains

HBV and HCV continuously evolve through mutation, selection, and, particularly for HBV, recombination, generating novel variants with potential epidemiological and clinical significance. HBV recombination occurs across genotypes and contributes substantially to viral diversity, with recombinant A/E and E/A forms documented in low- and middle-income countries (Revill et al., 2020; Asamoah et al., 2026).

HCV diversity is similarly expanding as whole genome and deep sequencing identify previously unrecognized lineages and subtypes. Recent sequencing, for example, has identified genetically distinct genotype 5 variants, including a putative subtype 5b, illustrating that diversity within supposedly restricted genotypes may be greater than previously recognized (Murphy et al., 2025). Mixed infections and recombinant forms further complicate genotype classification and may influence transmission patterns, antiviral resistance, and treatment response.

These emerging variants also have implications for molecular diagnostics and surveillance because assays developed against well characterized lineages may perform less reliably against highly divergent strains. For HBV, genomic variation can additionally generate immune escape and drug resistance associated mutations, although currently available HBV vaccines remain broadly protective against recognized genotypes (Revill et al., 2020).

Consequently, expanded whole genome sequencing and genomic surveillance are required to identify emerging genotypes, subtypes, recombinant strains, minority variants, and transmission clusters. Recent studies demonstrate that both portable sequencing platforms and alternative specimens such as dried blood spots can facilitate HBV and HCV genomic surveillance, potentially improving implementation in resource constrained settings (Tshiabuila et al., 2024; Tully et al., 2024). Such surveillance is particularly important in underrepresented regions, where uncharacterized viral diversity may remain undetected and its implications for diagnosis, treatment, and disease progression remain poorly defined.

4.10.4 Need for Integrated HBV/HCV Surveillance

Integrated HBV/HCV surveillance is increasingly important because conventional systems often separate epidemiological, laboratory, clinical, and molecular data, limiting comprehensive assessment of transmission and disease burden. WHO recommends strengthening national hepatitis information systems by linking prevention, diagnosis, treatment, and outcome indicators to support evidence based programmatic decisions (WHO, 2024). The 2026 WHO consolidated guidance further emphasizes integrated, person centred monitoring across the HBV and HCV continuum of care as countries progress toward elimination.

Integration of genomic surveillance is particularly important. Combining sequencing data with demographic, clinical, behavioral, and epidemiological information can identify transmission clusters, characterize circulating genotypes and recombinant strains, and monitor antiviral resistance. This approach is already reflected in CDC surveillance programs that integrate HCV genomic and epidemiological data to identify transmission networks and strengthen outbreak responses. Next generation sequencing and bioinformatics could further enhance surveillance by allowing detailed characterization of viral diversity and transmission patterns.

However, substantial geographic inequalities remain. A recent analysis integrating 10,996 HBV and 3,533 HCV whole genome sequences with disease burden estimates demonstrated marked global disparities in genomic surveillance, with genomic representation poorly aligned with disease burden in many settings. These gaps are particularly relevant to low- and middle-income countries, where laboratory infrastructure, sequencing capacity, bioinformatics expertise, and sustainable financing remain limited. WHO similarly identifies major inequalities in access to hepatitis diagnostics and treatment across high burden countries.

Future surveillance should therefore integrate serological and molecular diagnostics, genotype and genomic data, clinical outcomes, treatment information, and epidemiological risk factors within interoperable national and regional databases. Strengthening laboratory capacity, standardized data collection, digital reporting, and international data sharing would improve burden estimation and enable earlier detection of emerging variants and transmission networks. For sub-Saharan Africa and other underserved regions, expanding population-based surveillance and genomic sequencing is particularly important. Such integrated systems would provide more representative evidence for targeting interventions, evaluating elimination programs, and accelerating progress toward the WHO 2030 viral hepatitis elimination goals.

V. CONCLUSION & RECOMMENDATIONS

5.1 Conclusion

Despite major advances in prevention, diagnosis, and treatment, HCV infection and HBV/HCV coinfection remain important global public health challenges. HCV continues to affect millions worldwide, with marked regional disparities, while HBV/HCV coinfection, although less common than mono-infection, is associated with accelerated fibrosis, cirrhosis, hepatic decompensation, HCC and increased liver-related mortality. The substantial genetic

diversity of both viruses further influences transmission dynamics, disease progression, treatment response, and molecular epidemiology. Recent advances in serological testing, molecular diagnostics, sequencing technologies, and highly effective DAAs have transformed HCV diagnosis, surveillance, and management. Nevertheless, sustained HBV and HCV transmission, together with persistent inequalities in access to vaccination, diagnostics, antiviral therapy, and healthcare services, continue to impede progress toward the World Health Organization (WHO) 2030 viral hepatitis elimination targets.

Significant knowledge gaps remain, particularly in low- and middle-income countries and sub-Saharan Africa, where epidemiological data, genotype surveillance, and molecular diagnostic capacity are limited. Strengthening population-based surveillance, expanding genomic monitoring, improving equitable access to diagnostics and treatment, and fostering international research collaboration are essential to better define disease burden and guide evidence-based interventions. Ultimately, integrated prevention, surveillance, vaccination, and antiviral treatment strategies, supported by sustained investment in research and public health infrastructure, will be critical to reducing the global burden of HCV infection and HBV/HCV coinfection and achieving viral hepatitis elimination as a public health threat.

5.2 Recommendations

There is a need to strengthen integrated HBV and HCV surveillance through routine testing, improved access to affordable diagnostics and antiviral treatment, and expanded molecular and genomic monitoring to detect genotype diversity and emerging variants. Health systems, particularly in low- and middle-income countries, should prioritize high-risk and underserved populations, strengthen prevention measures including HBV vaccination and harm-reduction services, and improve linkage to care and treatment. Greater investment in research, data sharing, regional collaboration, and capacity building is also recommended to address evidence gaps, particularly in sub-Saharan Africa, and support progress toward the WHO 2030 viral hepatitis elimination targets.

Declaration of Interest

The authors declare that they do not have any known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Funding Declaration

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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