More expansive diagnosis and treatment are urgently needed to eliminate the global burden of HBV

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Worldwide, chronic hepatitis B virus (HBV) infection affected 257.5 million people in 2022, which contribute to adverse outcomes including cirrhosis, liver failure, and hepatocellular carcinoma.[1] In 2015, HBV-related diseases resulted in an estimated 0.86 million deaths, a number projected to rise to over 1.1 million in 2030 without effective intervention.[1,2] The World Health Organization (WHO) has recommended a strategy combining prevention and treatment to achieve HBV elimination by 2030. Targets include reducing mortality by 65% from the 2015 baseline, diagnosing 90% of patients, and treating 80% of eligible patients at least.[3]

However, significant gaps in testing and treatment remain. The Polaris Observatory Collaborators reported their modelling results of worldwide HBV prevalence in 2022, estimating that only about 14% of individuals with chronic hepatitis B have been diagnosed, and only 8% of those eligible for treatment have received it.[1] In the United States (US), a population-based study showed that only 15.2% of those who tested positive for hepatitis B surface antigen (HBsAg) were aware of having liver disease, with a treatment rate of merely 4.6%.[4] Moreover, a study using data from a large US private insurance database indicated that 81.4% of chronic hepatitis B individuals were undiagnosed.[5] The situation is much worse among the uninsured populations, and the lack of health insurance is a significant barrier to the diagnosis and treatment rates of hepatitis B. Additionally, significant sex and ethnic disparities also exist in chronic hepatitis B evaluation and treatment across the world.[6]

China bears a large part of the global burden of hepatitis B. Nationwide HBsAg prevalence decreased from around 10% before 1984 to 3% in 2021 in China, with approximately 43.3 million chronic hepatitis B individuals remaining in 2021.[7] Another study estimated that only 18.9% of HBV-infected individuals have been diagnosed, and 12.6% have received treatment over their lifetime.[8] The low rates of diagnosis, treatment and surveillance for chronic hepatitis B are attributed to the asymptomatic nature, stigma and discrimination, out-of-pocket expenses, and a lack of knowledge on HBV among patients and health-care providers.[3,9]

In the Lancet Regional Health-Americas, Makuza and colleagues reported the effect of anti-HBV treatment on all-cause and liver-related death among 4962 individuals with chronic hepatitis B and cirrhosis in a North America cohort, which showed that antiviral therapy was associated with a significant reduction in all-cause mortality (115.47 vs. 35.72 per 1000 person-years, adjusted hazard ratio (aHR) 0.74 [95% CI 0.65–0.84]) and liver- related mortality (49.86 vs. 11.39 per 1000 person-years, adjusted subdistribution hazard ratio (asHR) 0.72 [95% CI 0.58–0.89]) in patients with cirrhosis.[10] This study quantified the benefits of antiviral therapy in reducing mortality risk among patients with cirrhosis, and have significant clinical implications. However, several limitations should be considered. Mortality risk factors, such as severity of liver disease and complications of cirrhosis, were not fully assessed. The inclusion of individuals with hepatitis C virus or HIV co-infection and those who had undergone liver transplantation, rather than solely HBV-infected individuals, may potentially reduce the reliability of the results. Additionally, the fact that half of the individuals did not receive anti-HBV treatment may introduce confounding bias.

For patients with chronic hepatitis B, nucleos(t)ide analogues treatment is highly effective and well tolerated. It is associated with higher survival, less progression or even reversal of liver fibrosis, and decreased risk of hepatocellular carcinoma.[11] The WHO released new guidelines on prevention, diagnosis and treatment of chronic hepatitis B in 2024.[12] The new guidelines expanded and simplified treatment criteria for adults and adolescents. Tenofovir disoproxil fumarate and entecavir continue to be recommended as the preferred first-line treatment regimens. In elderly patients with chronic hepatitis B, treatment with tenofovir disoproxil fumarate is associated with increased risk of fracture compared to entecavir.[13]

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Discontinued anti-HBV treatment, which can be attributed to factors such as long-term drug exposure, unaffordable costs, and medication adherence, leads to severe hepatitis flares or hepatic decompensation in approximately 1–2% patients with chronic hepatitis B.[14] Further efforts are needed to improve awareness of timely antiviral therapy and the management of HBV reactivation among all health-care providers.

As 2030 approaches, low diagnosis rate, limited treatment coverage and insufficient public awareness hinder efforts to achieve the HBV elimination targets. Enhancing screening for high-risk groups or even universal screening to find undiagnosed patient, followed by providing timely and sustained antiviral therapy, is urgently needed. To achieve the HBV elimination target will require strengthened collaboration among all stakeholders to address the multiple barriers to hepatitis B screening, diagnosis and treatment at patients, health-care providers, and society levels, especially in resource-poor regions and vulnerable populations.

Contributors

All authors conceived the paper. YL and XY: wrote the first draft. FJ: writing-review and finalization. All authors approved the submitted version.

Declaration of interests

FJ has received speaker fees from Gilead Sciences, MSD, and Ascletis, in addition to consulting or advisory board fees from Gilead and MSD. All other authors report no potential conflicts.

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