EDITORIAL

Simplifying the Diagnosis and Treatment of Hepatitis B Infection: One Step for Addressing Deficits in the Care Cascade, One Leap for Elimination

Hepatitis B virus (HBV) infection affects an estimated 1.25–2.49 million persons in the United States and 257–291 million persons globally, and represents the leading cause of hepatocellular carcinoma and liver-related death worldwide.[1–5] The World Health Organization and US Department of Health and Human Services have developed formal plans to achieve hepatitis elimination by 2030, including a reduction of incident HBV infections by 90% and decrease in HBV-associated mortality by 65%.[1] Multiple deficits persist in the HBV care cascade, including screening, diagnosis, linkage to care, and treatment.[6] Furthermore, although global HBV immunization efforts have been estimated to prevent 210 million new chronic HBV infections as of 2015, ongoing limitations in global access and implementation of HBV immunization are estimated to contribute to 63 million new cases of chronic HBV and 17 million HBV-related deaths between 2015 and 2030.[7] In fact, available evidence suggests that perhaps the most important drivers to achieving hepatitis elimination remain adequate scale up of coverage for birth-dose vaccination (80% of neonates), infant vaccination (90% of infants), use of peripartum antivirals (80% of hepatitis B e antigen positive mothers), as well as population-wide testing and treatment (80% of eligible people), which in turn may avert 7.3 million deaths and 1.5 million cancer deaths between 2015 and 2030.[7] As such, a multimodal approach to HBV prevention, identification, and treatment will be essential to achieving HBV elimination in the United States and worldwide.

In this issue of *Gastro Hep Advances*, Dieterich et al. present a consensus proposal to simplify guidelines for HBV screening, diagnosis, and management to achieve "health equity" and "achieve HBV elimination".[8] Although many of the key recommendations of this group largely overlap with guidance of the American Association for the Study of Liver Diseases (AASLD), European Association for the Study of the Liver (EASL), and Asian Pacific Association for the Study of the Liver, and are generally good clinical practice, the authors do advocate for several consequential changes that go beyond what is widely accepted, for which we will focus on 3.

First, the expert panel recommends universal, one-time testing for HBV in all adults and pregnant women with each pregnancy with a combination of hepatitis B surface antigen, hepatitis B core antibody, and hepatitis B surface antibody. Although this conflicts with current risk-based screening guidance of the EASL,[3] AASLD,[4] US Centers for Disease Control and Prevention, and US Preventive Services Task Force (USPSTF),[9] this mirrors draft recommendations of the Centers for Disease Control and Prevention which announced a proposal in April 2022 to update its guidance to universal HBV screening and is awaiting final approval.[10] This is a necessary policy change given the flawed and failed approach of risk-based screening,[11] and is likely to be cost-effective,[12] but does not have the same regulatory and payor effect of USPSTF recommendations, and therefore will require significant multistakeholder investment to translate these recommendations to clinical practice, including addressing such barriers as guideline awareness, access to lab testing, payor coverage, and implementation across a complex spectrum of clinical settings. Second, the expert panel recommends broad testing for coinfections including hepatitis C virus, human immunodeficiency virus, and hepatitis delta virus (HDV). The former 2 are currently included in universal screening policies among US adults by the USPSTF, but the latter is not presently supported by any US organization including the AASLD, which recommends HDV testing among human immunodeficiency virus-infected persons, persons who inject drugs, men who have sex with men, high-risk individuals for sexually transmitted diseases, and elevated liver tests.[4] Although a transition from risk-based to standard HDV testing in the United States may be justified given a growing body of literature that has confirmed that a HDV prevalence of 4%–5% among hepatitis B surface antigen-positive individuals[13] and significant underdiagnosis of HDV coinfection, the inclusion of universal testing in context of a proposed simplification of HBV management is bold and would require non-negligible and potentially prohibitive cost and laboratory resources for implementation in resource-limited settings. Third, the expert panel recommendations for treatment represent a major departure from current society guidance[3–5] of AASLD, EASL, and Asian Pacific Association for the Study of the Liver which prioritizes antiviral therapy for patients within the immunoactive phase of chronic HBV. In contrast, the panel recommends a more proactive and simplified paradigm which identifies 3 primary groups for treatment: 1) all patients with cirrhosis and detectable HBV DNA; 2) all patients age $\geq$ 30 years with HBV DNA $>$2000 IU/mL; 3) patients under age 30 years with HBV DNA $>$2000 IU/mL and elevated serum alanine aminotransferase. This series of recommendations more closely mirror those of the 2015 World Health Organization treatment guidelines[14] and represents a bold and important expansion of treatment eligibility. Growing evidence confirms the presence of ongoing significant risk for hepatocellular carcinoma and

other liver events among patients with chronic HBV in the indeterminate and immunotolerant phases,[15,16] and the highly complex and nuanced guidance of the liver societies may be associated with undertreatment in both primary care and specialty settings.[17] On this basis, application of simplified antiviral guidelines may meaningfully increase overall treatment of chronic HBV, as suggested by studies which estimate an increase from 6.7% of patients with chronic HBV per AASLD criteria to 14.1%–33.5% of patients using simplified criteria.[18]

Real-world application of simplified guidelines may be challenging but necessary—one small step toward addressing major deficits in the HBV care cascade, but potentially one important leap toward elimination. Of course, one size guidelines do not fit all global contexts, and therefore these recommendations should be applied in a pragmatic manner in context of regional HBV prevalence, local access to virologic lab testing and imaging, availability of specialty care, patient preference and engagement, and access to antiviral medications.[19] Future investigation and validation of this and other simplified treatment algorithms across clinical settings will be necessary to strengthen evidence to support broader implementation in the United States and worldwide.

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