ADVANCES IN HEPATOLOGY

Current Developments in the Treatment of Hepatitis and Hepatobiliary Disease

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Screening for Hepatitis B Virus and Tuberculosis

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G&H Currently, how common is coinfection of hepatitis B virus and tuberculosis (active or latent) in the United States?

AC It is challenging to assess estimates of burden of chronic hepatitis B virus (HBV) and tuberculosis (TB) because active TB disease surveillance systems in the United States do not routinely collect data on chronic HBV. In addition, chronic HBV surveillance systems have incomplete reporting, and there is no surveillance system for latent TB infection (LTBI). LTBI is defined as evidence of *Mycobacterium tuberculosis* infection with no signs or symptoms of TB disease (ie, positive tuberculin skin test or interferon-gamma release assay, no symptoms or clinical examination findings concerning for TB disease, and a negative chest radiograph [CXR]). Individuals with LTBI are at risk for developing TB disease, and at least 85% of active TB cases reported in the United States are owing to reactivation of LTBI.

As a result, there are limited published data on coinfections of chronic HBV and TB. According to an analysis of New York City TB surveillance data from 2000 to 2010, 3.7% of persons with active TB were coinfected with chronic HBV. My colleagues and I conducted a systematic review and meta-analysis of studies around the world and noted a chronic HBV prevalence of 2.2% among individuals with TB in North America.

There are also limited data in the literature regarding LTBI and chronic HBV. A study from 2002 of a community clinic in Iowa found an LTBI prevalence of 55% among Vietnamese immigrants with chronic HBV. However, the prevalence of LTBI is lower when looking at broader populations. My colleagues and I reviewed the majority of studies from North America assessing prevalence of LTBI among persons with chronic HBV in a systematic review and meta-analysis, and detected an LTBI prevalence of 34% among chronic HBV patients.

In addition, LTBI is likely more prevalent in chronic HBV patients than in the general population (5.0% LTBI prevalence in the general US population in the National Health and Nutrition Examination Survey [NHANES] and 15.9% in non–US-born persons). Similarly, chronic HBV prevalence is likely higher in TB patients than in the general population (0.35% chronic HBV prevalence in the general US population in NHANES and as high as 3% in an updated analysis of non–US-born persons). However, additional studies are needed. Dr Robert Wong and I, along with other colleagues, are currently working on analyses looking at chronic HBV and LTBI in a large national laboratory database, an integrated health care system, claims data, and statewide surveillance data.

G&H What are the similarities between HBV and TB?

AC Chronic HBV and TB are common chronic infections that can be prevented with vaccination or treatment of latent infection, respectively. In addition, if either infection develops, it can be treated with effective medications that can reduce the risk of morbidity and mortality (10% mortality for both infections; 7 years-per-life-lost for TB and 14 years-per-life-lost for chronic HBV). The infections also have similar epidemiologic and demographic risk factors. In the United States, both infections

disproportionately affect non–US-born persons, who have a 15-fold higher incidence of TB as well as a 6- and 8-fold higher prevalence of LTBI and chronic HBV, respectively. In particular, all of these infections disproportionately affect non–US-born Asians.

G&H Does the presence of one of these infections necessarily increase the severity of the other?

AC The presence of one infection does not increase the severity of the other, although coinfection poses challenges in clinical management. For example, persons with active TB and chronic HBV have nearly a 2-fold higher risk of drug-induced liver injury. Likewise, individuals with LTBI and chronic HBV also have a higher risk of drug-induced liver injury, and there may be certain drug-drug interactions that may have to be factored in between chronic HBV medications and the LTBI regimen that is selected.

Chronic HBV should not affect the progression of LTBI to active TB disease. However, newer treatments and regimens being evaluated in clinical trials for chronic HBV utilize immunosuppressants such as programmed death ligand 1 inhibitors, which may increase the risk of progression from LTBI to active TB disease.

G&H What is the clinical meaning of screening?

AC Screening refers to the testing of asymptomatic individuals to detect a clinical condition. The goal is to identify infection or disease in individuals when it is asymptomatic so that appropriate treatment can be provided to reduce morbidity and mortality. This is routinely done in clinical practice for diabetes, cancer, and heart disease.

For chronic HBV and TB, individuals who have risk factors should be screened and tested. An individual who tests negative for HBV should be vaccinated. However, an individual who tests positive should undergo additional tests and should be evaluated to determine whether he or she is eligible for treatment for chronic HBV. An individual who tests positive for TB, is asymptomatic, and has a negative CXR should be offered treatment for LTBI to prevent the occurrence of TB disease.

G&H What are the current screening guidelines for HBV, and is screening for this disease cost-effective?

AC Chronic HBV screening guidelines from the American Association for the Study of Liver Diseases (AASLD) recommend screening for persons who have a risk factor, which includes persons born in countries with a high prevalence of hepatitis B surface antigen, US-born persons who were not vaccinated or whose parents were born in HBV-endemic regions with a prevalence of 8% or higher, pregnant women, persons who will receive immunosuppressive therapy, or other persons at risk of infection. However, these guidelines are challenging because it is difficult for busy clinicians to operationalize the guidelines in a clinic setting and not all patients divulge their risk factors.

Recently published cost-effectiveness analyses have noted that universal 1-time hepatitis B surface antigen testing of adults 18 to 69 years of age, compared with the current practice, would prevent an additional 7 cases of compensated cirrhosis, 3 cases of decompensated cirrhosis, 5 cases of hepatocellular carcinoma, 2 liver transplants, and 10 HBV-related deaths, and would result in a saving of $263,000 per 100,000 adults screened. However, although universal 1-time hepatitis B surface antigen testing may be effective at identifying cases of chronic HBV, it is also important, from a clinical perspective, to order tests for antibody to hepatitis B surface antigen as well as immunoglobulin G antibody to hepatitis B core antigen. Ordering these additional tests will appropriately identify individuals who may benefit from receiving the hepatitis B vaccine, require additional testing to determine whether they are infected, or need education regarding potential risk for HBV reactivation in the future. This strategy has been advocated by primary care and HBV experts.

I anticipate that the current AASLD guidelines may change based on updated cost-effectiveness analyses and because the Centers for Disease Control and Prevention/Advisory Committee on Immunization Practices (CDC/ACIP) recently revised their own guidance on hepatitis B vaccination. The CDC/ACIP now recommend that all individuals 19 to 59 years of age receive the hepatitis B vaccine; however, a risk factor–based approach to hepatitis B vaccine was retained among those 60 years of age and older because universal vaccination in this age group would not lead to substantial reductions in preventing acute HBV cases and be cost-effective.

G&H Has there been any research on the cost-effectiveness of screening for HBV in patients with TB, or vice versa?

AC There are no cost-effectiveness data on screening for HBV in TB or LTBI patients, or vice versa. However, based on overlapping epidemiologic and demographic risk factors and high burden, it would be appropriate to routinely screen for these infections in individuals with risk factors.

G&H How are these patients linked to care after screening?

AC Nearly all patients who have risk factors should be screened by primary care providers. Some patients are screened in public health TB clinics (ie, active TB cases or contacts to active TB cases who are being followed by public health clinics).

Nevertheless, an important point about both infections is that there are substantial gaps in the cascade of care. Not everyone who should be screened receives the appropriate screening, and those who test positive do not always receive the appropriate follow-up or treatment. In particular, only 40% of patients with LTBI and 20% of patients with chronic HBV are diagnosed, and only 20% of each of those diagnosed groups receive treatment. As a result, reducing the burdens of chronic HBV and TB will require interventions from multiple levels: health care providers, the health care system, public health, and policies.

G&H What are the priorities of research in terms of HBV and TB screening?

AC There are several priorities, including a better understanding of the disease burdens and determining whether chronic HBV patients can tolerate certain LTBI regimens, such as isoniazid and rifapentine. It is also important to identify interventions that would improve the cascade of care of both infections.

G&H Is there any ongoing or upcoming research in this area that you would like to highlight?

AC Dr Wong, I, and colleagues recently analyzed data from a large national laboratory system to provide estimates of LTBI and chronic HBV prevalence as well as testing patterns for both infections. This paper will be published in the *Journal of Public Health Management and Practice* soon. We found that 11% of chronic HBV patients were tested for LTBI, among whom the prevalence of coinfection was approximately 20%, which was twice the LTBI prevalence seen in patients who did not have chronic HBV. In addition, 32% of LTBI patients were tested for chronic HBV, among whom the prevalence of coinfection was 1.5%. This was 3 times the chronic HBV prevalence in persons who did not have LTBI. We also found that Asians had the highest prevalence of coinfection and that certain geographic regions in the United States had the highest prevalence of coinfection.

Disclosures

Dr Chitnis has no relevant conflicts of interest to disclose.

Suggested Reading

Bushnell G, Stennis NL, Drobnik AM, et al. Characteristics and TB treatment outcomes in TB patients with viral hepatitis, New York City, 2000-2010. *Epidemiol Infect*. 2015;143(9):1972-1981.

Chen J, Hubbard A, Bagley L, Shiau R, Wong RJ, Chitnis AS. Prevalence of latent tuberculosis infection among persons with chronic hepatitis B virus infection: a systematic review and meta-analysis [published online May 30, 2021]. *Dig Dis Sci*. doi:10.1007/s10620-021-07056-5.

Chitnis AS, Cheung R, Gish RG, Wong RJ. Epidemiology and prevention of tuberculosis and chronic hepatitis B virus infection in the United States. *J Immigr Minor Health*. 2021;23(6):1267-1279.

Chitnis AS, Jaganath D, Gish RG, Wong RJ. Diagnosis and treatment of latent tuberculosis infection. *Am J Gastroenterol*. 2021;116(11):2155-2158.

Drobnik A, Pinchoff J, Bushnell G, et al. Matching HIV, tuberculosis, viral hepatitis, and sexually transmitted diseases surveillance data, 2000-2010: identification of infectious disease syndemics in New York City. *J Public Health Manag Pract*. 2014;20(5):506-512.

Lim JK, Nguyen MH, Kim WR, Gish R, Perumalswami P, Jacobson IM. Prevalence of chronic hepatitis B virus infection in the United States. *Am J Gastroenterol*. 2020;115(9):1429-1438.

Miramontes R, Hill AN, Yelk Woodruff RS, et al. Tuberculosis infection in the United States: prevalence estimates from the National Health and Nutrition Examination Survey, 2011-2012. *PLoS One*. 2015;10(11):e0140881.

Terrault NA, Lok ASF, McMahon BJ, et al. Update on prevention, diagnosis, and treatment of chronic hepatitis B: AASLD 2018 hepatitis B guidance. *Hepatology*. 2018;67(4):1560-1599.

Toy M, Hutton D, Harris AM, Nelson N, Salomon JA, So S. Cost-effectiveness of 1-time universal screening for chronic hepatitis B infection in adults in the United States. *Clin Infect Dis*. 2022;74(2):210-217.

Weng MK, Doshani M, Khan MA, et al. Universal hepatitis B vaccination in adults aged 19-59 years: updated recommendations of the Advisory Committee on Immunization Practices - United States, 2022. *MMWR Morb Mortal Wkly Rep*. 2022;71(13):477-483.

Wong RJ, Brosgart CL, Welch S, et al. An updated assessment of chronic hepatitis B prevalence among foreign-born persons living in the United States. *Hepatology*. 2021;74(2):607-626.

Wong RJ, Hubbard A, Bagley L, Shiau R, Chitnis AS. Estimating prevalence of hepatitis B virus coinfection among adults with tuberculosis: a systematic review with meta-analysis [published online April 9, 2021]. *J Clin Gastroenterol*. doi:10.1097/MCG.0000000000001533.