Chronic Hep B Doubles Risk of AIDS Illnesses and Death in People Living With HIV

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Chronic hepatitis B virus (HBV) infection almost doubles the risk of AIDS or death in people diagnosed with HIV infection, compared with those only living with HIV, according to a new paper published ahead of print in The Journal of Infectious Diseases (JID). These important findings, the authors write, "may have implications for many aspects of HBV coinfection, including early diagnosis and, foremost, prevention of hepatitis B."

Much like in people coinfected with HIV and hepatitis C virus (HCV), there is no shortage of evidence suggesting that HIV infection negatively affects HBV-related liver disease progression, including increased risks of end-stage liver disease and liver cancer. And while it is generally believed that chronic HCV infection doesn't directly affect HIV disease progression—thought it can mean complex drug interactions between hepatitis C and HIV meds and hasten liver toxicity while using ARVs—it hasn't been clear whether chronic HBV infection is an independent risk factor for HIV disease progression or death.

Unfortunately, the JID study results authored by Helen Chun, MD, of the National Naval Medical Center in Bethesda and her colleagues confirm earlier suggestions that HBV does negatively impact HIV outcomes.

The results come from the U.S. Military HIV Natural History Study, which has the advantage of including people who test positive for HIV while receiving care through a variety of Army- and Navy-based medical facilities throughout the country. This allowed Chun and her colleagues to focus specifically on 2,352 individuals whose date of HIV infection could be estimated within three years—thereby allowing the researchers to circumvent a common problem in disease progression studies, notably accounting for significant variations in patient duration of HIV infection—and whose HBV infection status was known or determined with two years of becoming infected with HIV.

Each patient's HBV status was classified as being chronic (active infection), resolved (earlier infection followed by clearance and immunity), or no evidence of past or current infection.

Of the 2,352 recent HIV seroconverters in the study, 20 percent had resolved HBV infection and 3 percent had chronic HBV infection. Roughly 74 percent had no evidence of HBV infection. An additional 3 percent tested positive for hepatitis B "core" antibodies (HBcAb) alone, in the absence

of other antibodies, which comes with a number of possible interpretations and generally requires more extensive testing.

HIV-positive study subjects classified as having chronic HBV were twice as likely to die or develop an AIDS-defining illness, compared with those who were HBV negative. Even participants with resolved HBV infection or isolated HBcAb faced elevated risks of HIV disease progression or death, compared with HBV-negative individuals. Among those with resolved HBV infection, the relative risk was increased 35 percent. Among those with isolated HBcAb, the relative risk was increased 54 percent.

When Chun and her colleagues adjusted the data for confounding factors—for example, the date of HIV infection, given that nearly half of those included in the study were infected with HIV before 1996 when AIDS-related illnesses and death were much more common—the relative risk of developing an AIDS-related illness or dying among those with chronic HIV/HBV coinfection was still 80 percent higher compared with HIV-positive, HBV-negative individuals in the study. Increases in the relative risks of AIDS-related illness or death were also documented in those with resolved HBV infection and isolated HBcAB in the adjusted analysis, but these increases were not statistically significant; they could have been due to chance.

Of note, HCV infection was also associated with an increased risk of developing an AIDS-related illness or death in the study. However, resolved or chronic HCV infection was uncommon in the cohort—only 1.7 percent were positive for HCV antibodies—and, thus, no firm conclusions could be drawn from this finding.

The reasons for the higher risks of AIDS-related illnesses and deaths were not apparent to Chun's team. Chronic HBV infection did not appear to increase average viral load levels, in the absence of ARV treatment, nor did it appear to be associated with lower CD4 cell counts. In turn, the authors note, it is still necessary to determine "whether hepatitis B is a surrogate of poorer outcome or whether it has a direct harmful impact on HIV disease progression."

While key questions remain, there are important lessons to be learned from this study, according to an accompanying editorial written by Philip Peters, MD, and Barbara Marston, MD, of the U.S. Centers for Disease Control and Prevention. "The analysis of [Chun's group] moves us further toward an understanding of the increased mortality among persons with HIV/HBV coinfection. Although we remain with questions about whether HIV disease is indeed progressing more rapidly in these patients, there is no need to wait for answers before we amplify our response." Examples listed by Peters and Marston include stepped-up HBV vaccination efforts and the careful use of medications active against both HIV and HBV—such as Epivir (lamivudine), Emtriva (emtricitabine), Viread (tenofovir) or Truvada (tenofovir/emtricitabine)—in ARV drug regimens.

"There are undeniable barriers to achieving high rates of HBV vaccination and optimal treatment of HIV/HBV coinfection, both in the United States and internationally," the CDC commentators note. "However, effective interventions exist and can be integrated into public health practice and clinical care."
