HIV/HBV/HDV Triple Infection Linked to Liver-Related Death

Hepatitis D superinfection worsens clinical outcomes for people with HIV and hepatitis B, even with access to antiviral treatment.

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Among people with HIV and hepatitis B virus (HBV) coinfection, “superinfection” with hepatitis D virus (HDV) is a serious risk factor for liver-related death despite antiviral treatment, according to study findings published in Clinical Infectious Diseases.

HIV and hepatitis B have overlapping transmission routes, and around 10% of people living with HIV worldwide also have HBV. What’s more, people with HIV/HBV coinfection may also acquire hepatitis D, or delta, a defective virus that can only replicate when HBV is present. Over time, chronic hepatitis B can lead to liver cirrhosis and hepatocellular carcinoma—the most common types of liver cancer—and those who also have HDV are at higher risk.

Tenofovir disoproxil fumarate (sold alone as Viread and a component of some antiretroviral single-tablet regimens) is active against both HIV and HBV, and people coinfected with both viruses are advised to use regimens with dual activity. Studies have shown that tenofovir-containing antiretroviral therapy improves survival in people with HIV/HBV coinfection. An antiviral for hepatitis D, bulevirtide (Hepcludex), is authorized in Europe, but the Food and Drug Administration has not yet approved it in the United States.

Yu-Shan Huang, MD, of the National Taiwan University Hospital and College of Medicine, and colleagues assessed the occurrence and outcomes of HDV superinfection among people with HIV/HBV coinfection.

This retrospective study included 534 people ages 20 or older with HIV/HBV coinfection who were registered at the National Taiwan University Hospital when they presented for HIV care between 2011 and 2022. They were followed through December 2023.

At the start of the study, 36 participants (6.7%) tested positive for HDV. Over nearly 4,000 person-years of follow-up, 50 of the 498 people (10.0%) who initially tested negative for HDV seroconverted, for an overall incidence rate of 12.54 cases per 1,000 person-years. Notably, 88% of those who seroconverted (44 out of 50) were men who have sex with men.

After a median follow-up of 10.2 years, during most of which tenofovir-containing antiretroviral therapy was available, the all-cause mortality rate was 4.7%. However, those with HDV had much higher rates of liver-related death (3.5% versus 0.4%), cirrhosis (11.3% versus 3.6%) and hepatitis flares (28.2% versus 14.2%) compared to those without HDV. The significant increase in liver-related mortality among people with triple infection occurred despite similar rates of hepatocellular carcinoma in people with and without HDV.

“HBV-coinfected people with HIV remain at risk for HDV superinfection, and HDV infection is associated with liver-related death in the era of tenofovir-containing antiretroviral therapy,” the researchers concluded. They suggested that people with HIV and HBV should be regularly monitored for HDV status.

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