HIV Raises Hepatitis C Liver Disease Risk in Women More Than Men

Women with HIV and HCV face higher odds of cirrhosis and liver decompensation but not liver cancer.

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Women living with both HIV and hepatitis C virus (HCV) may be at especially high risk for severe liver disease, according to a large Canadian study. In findings published in the journal AIDS, researchers report that HIV and sex together influence the risk for HCV-related cirrhosis and liver decompensation, though not for liver cancer.

Over time, chronic HCV infection can lead to liver fibrosis, cirrhosis, hepatocellular carcinoma (the most common type of liver cancer) and liver failure (hepatic decompensation). People with HIV and HCV coinfection can experience worse liver disease progression, but the impact of an individual's sex is less clear, as women have historically been underrepresented in research cohorts.

William McFarlane, PhD, of Queen's University in Ontario, and colleagues looked at the effects of HIV status and sex on cirrhosis, liver cancer and liver decompensation due to hepatitis C. The cohort included 65,151 people with hepatitis who were followed from 1999 to 2018. The researchers measured the relative excess risk due to interaction (RERI) of HIV status in women and men.

In this study cohort, 21,998 women and 41,015 men remained HIV negative throughout the follow-up period, while 460 women and 1,678 men tested positive for HIV. Cirrhosis was most prevalent in men without HIV, with 3,711 cases per 100,000 person-years. Liver decompensation was most common among women with HIV, with 1,575 cases per 100,000 person-years. Liver cancer was most prevalent among HIV-positive men, with 1,883 cases per 100,000 person-years.

The researchers found significant negative interaction effects for cirrhosis (RERI = -0.52) and liver decompensation (RERI = -1.50), suggesting that the impact of HIV on these outcomes differed by sex. In contrast, there was no significant interaction for liver cancer (RERI = 0.44), suggesting that HIV's effect on hepatocellular carcinoma risk did not meaningfully differ between women and men.

Women and men with hepatitis had different clinical outcomes according to HIV coinfection status. Women living with both HIV and HCV had a 44% greater risk of developing cirrhosis and were

more than two and a half times as likely to experience liver decompensation as women with HCV alone.

In keeping with earlier research, men with HCV but not HIV had a higher risk for cirrhosis, decompensation and liver cancer than women with hepatitis C alone. This lower risk in women is thought to reflect a protective effect of estrogen and a greater likelihood of HCV viral clearance either spontaneously or with antiviral treatment.

But concurrent HIV infection changed how liver disease risk differed by sex, with significant interaction effects for cirrhosis and decompensation, though not for liver cancer. These findings suggest that HIV may increase the risk of severe HCV-related liver disease in women more than men.

“The finding that HIV infection had a more deleterious effect on risk of HCV-associated cirrhosis and decompensation in females compared to males could be due to both biological factors relating to female sex, and social factors relating to female gender,” wrote the researchers.

“Biological females living with HIV have a higher risk of hepatotoxicity and metabolic dysregulation due to combination antiretroviral therapy, which could contribute to liver disease risk directly and through interruptions in HIV treatment,” they added. “HIV-positive individuals that identify as female also experience greater barriers to HIV care compared to HIV-positive individuals that identify as male; these barriers include discrimination and stigma from healthcare providers, childcare responsibilities and transportation barriers.”

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