Detectable HIV and Lower CD4 Count Raise Liver Cancer Risk

HIV-positive people with a higher viral load over a longer period appear more likely to develop hepatocellular carcinoma.

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People with HIV who spend more time with a detectable viral load and those with low CD4 T-cell levels are at higher risk of developing liver cancer without advanced fibrosis, according to research presented at the Conference on Retroviruses and Opportunistic Infections (CROI 2019) last week in Seattle.

As expected, having hepatitis B or C was associated with a higher likelihood of developing liver cancer regardless of the extent of liver fibrosis. But among those with less fibrosis, HIV viremia and worse immune suppression also played a role, reported Jessie Torgersen, MD, of the University of Pennsylvania Perelman School of Medicine in Philadelphia.

Since the advent of effective antiretroviral therapy, liver disease has become a leading cause of illness and death for people living with HIV. The incidence of liver cancer in this group has quadrupled since 1996, and HIV-positive people have about a fourfold higher risk of HCC compared with the HIV-negative population, Torgersen noted as background. However, the causes of this disparity remain unclear.

Over years or decades, chronic hepatitis B or C virus (HBV or HCV), heavy alcohol use and other causes of liver injury can lead to hepatocellular carcinoma (HCC), the most common type of primary liver cancer. These factors as well as metabolic abnormalities such as obesity, diabetes and fatty liver disease contribute to liver inflammation and the buildup of scar tissue, known as fibrosis. Over time, this can progress to advanced scarring, or cirrhosis, and the development of HCC as the liver tries to repair itself.

Torgersen's team aimed to learn more about the effect of higher viral load and duration of detectable virus, as well as lower CD4 cell count, on the risk of liver cancer and whether this varies according to cirrhosis status.

The researchers looked at electronic medical records from the Veterans Aging Cohort Study, an ongoing study of HIV-positive veterans across the United States. The analysis included data from 1999 through 2015 for people with available viral load and CD4 count measurements and at least

six months of follow-up. Those with existing HCC at the start of the study were excluded. As a measure of cirrhosis, the researchers used a noninvasive index called FIB-4 that incorporates age, platelet count and ALT and AST liver enzyme levels; a score over 3.25 suggests advanced fibrosis or cirrhosis.

The analysis included 2,497 people—about 8 percent—with advanced fibrosis or cirrhosis and 29,836 people with absent, mild or moderate fibrosis. In both groups, almost all were men and about half were African American.

Those with advanced liver disease had a higher median age (50 versus 46) and were more likely to have hepatitis B (10 percent versus 5 percent), hepatitis C (59 percent versus 30 percent) or an alcohol-related diagnosis (47 percent versus 29 percent). In addition, they were more likely to have an HIV viral load above 500 copies per milliliter (63 percent versus 56 percent) and a CD4 count below 200, indicating substantial immune suppression (39 percent versus 26 percent).

During follow-up, 278 people were diagnosed with hepatocellular carcinoma. While liver cancer usually develops after cirrhosis—only about 13 percent develop HCC without cirrhosis in the general population—in this HIV-positive cohort, 43 percent of those with HCC did not have advanced fibrosis or cirrhosis according to FIB-4 scores.

People with hepatitis C were over six times more likely to develop HCC regardless of fibrosis status. Among those with advanced fibrosis or cirrhosis, people with hepatitis B were over twice as likely to develop liver cancer, while among those without advanced fibrosis, HBV was associated with a nearly fivefold higher risk.

HIV viral load and CD4 count had no significant effect on liver cancer risk among people with advanced fibrosis or cirrhosis. But among those without advanced fibrosis, having a higher viral load was associated with a 24 percent greater HCC risk. Having an HIV RNA level of at least 500 copies/ml for a year or more conferred a 57 percent greater risk of liver cancer. And having a CD4 count below 200 was associated with a 58 to 78 percent higher risk.

These findings indicate that risk factors for HCC in HIV-positive people vary according to fibrosis stage, Torgersen said. While HBV and HCV increased liver cancer risk in both FIB-4 groups, HIV-related factors were also important in those without advanced fibrosis or cirrhosis.

This study provides the “strongest evidence to date that HIV viremia [and] low CD4 cell count contribute to risk of HCC,” the researchers concluded.

As a limitation of the study, Torgersen noted that these findings may not apply to women, as this cohort of veterans included only a small proportion (867 women, or about 2 percent). In addition, the potential confounding effect of fatty liver disease could not be determined given the available medical record data.

Click here to read the study abstract.

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