Fatty Liver Disease Linked to Cardiovascular Risk in People with HIV

NAFLD is associated with risk factors such as obesity and inflammatory biomarkers and with events including heart attacks and strokes.

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Fatty liver disease is common among people living with HIV and is associated with metabolic problems and inflammation that raise the risk for cardiovascular disease, according to new results from the REPRIEVE study published in the journal AIDS.

Another study found that HIV-positive people with non-alcoholic fatty liver disease (NAFLD) are more likely to experience heart attacks, strokes and other cardiovascular events.

As people with HIV live longer thanks to effective antiretroviral treatment, cardiovascular disease (CVD) has become a leading cause of illness and death. Research shows that HIV-positive people are at greater risk for CVD than their HIV-negative peers, and they tend to develop heart and blood vessel problems at a younger age.

Cardiovascular Risk Factors

Jordan Lake, MD, of the University of Texas Health Science Center in Houston, and colleagues analyzed the prevalence of hepatic steatosis, or buildup of fat in the liver, and its association with cardiovascular and metabolic characteristics among participants in the large REPRIEVE trial, which tested a statin medication for people with HIV.

This international Phase III study enrolled nearly 7,800 HIV-positive people ages 40 to 75 who were mostly on stable antiretroviral therapy (ART) with an undetectable viral load. They had demographics, comorbidities and laboratory values reflecting low to moderate cardiovascular risk. This group would not ordinarily be prescribed statins, but CVD scoring systems developed for the general population can underestimate the risk for people with HIV.

As reported at this summer's International AIDS Society Conference on HIV Science, participants who were randomly assigned to receive daily pitavastatin had a 35% lower risk for heart attacks, strokes and other major cardiovascular events compared with those who received a placebo.

In addition to this primary endpoint analysis, REPRIEVE also included a variety of sub-studies and smaller cohorts established to shed more light on CVD manifestations and progression among

people living with HIV.

The new analysis focused on liver steatosis, including NAFLD. Some prior studies have seen a high prevalence of fatty liver disease among people with HIV. Often associated with obesity and diabetes, fatty liver disease is increasingly recognized as a component of metabolic syndrome, a cluster of CVD risk factors that includes high blood pressure, excess abdominal fat, elevated blood sugar and triglyceride levels and low HDL (good) cholesterol. Over time, the buildup of fat in the liver can lead to serious complications, including cirrhosis, liver cancer and liver failure.

A subset of 687 REPRIEVE participants underwent computed tomography (CT) scans to assess the presence of hepatic steatosis and NAFLD, defined as liver fat buildup in the absence of heavy alcohol use or viral hepatitis. In this sub-group, the median age was 51 years, and about 80% were men. Nearly 40% were white, 34% were Black and 24% were Latino. The median body mass index (BMI) was 27, in the middle of the overweight range. Almost all had viral suppression, and the median CD4 count exceeded 600.

More than one in five participants had hepatic steatosis, and a similar proportion had NAFLD, for a baseline prevalence of 22% and 21%, respectively. Even among lean people, NAFLD prevalence reached 8%. These conditions were more common among men, older individuals and white people compared with Black people.

Fatty liver disease was linked to metabolic syndrome, larger waist circumference, higher BMI (especially obesity), higher levels of a marker of vascular inflammation know as lipoprotein-associated phospholipase A_2 (Lp-PLA_2), another inflammatory biomarker called high-sensitivity C-reactive protein (hs-CRP), insulin resistance (HOMA-IR), lower HDL cholesterol and higher atherosclerotic CVD risk scores.

However, hepatic steatosis and NAFLD were not associated with viral load, CD4 count or type of antiretroviral treatment. In fact, the only HIV-related factor linked to fatty liver disease was a history of AIDS-defining illnesses.

This is reassuring because older nucleoside/nucleotide reverse transcriptase inhibitors were associated with lactic acidosis and severe hepatomegaly (liver enlargement) with steatosis; this is still listed as a warning in the prescribing information for widely used modern drugs in this class. What's more, tenofovir alafenamide and certain integrase inhibitors have been linked to weight gain, which can raise the risk for fatty liver disease.

"Hepatic steatosis and NAFLD are common in middle-aged and older adults with treated HIV, even in the setting of low-to-moderate cardiovascular risk and preserved renal function," the study authors concluded. "Additional work is needed to determine optimal screening and treatment for hepatic steatosis in this population, with the ultimate goal of reducing cardiometabolic disease and improving overall health."

They noted that because REPRIEVE included mostly middle-aged people with well-controlled HIV and low to moderate CVD risk, the prevalence of fatty liver disease might well be higher among older and less healthy people with HIV. They also cautioned that CT scans are most reliable for detecting moderate to severe steatosis, so people with milder fatty liver disease might have been missed.

Cardiovascular Events

Another recent study, also published in AIDS, looked more directly at the link between NAFLD and major cardiovascular events in people living with HIV. Arunkumar Krishnan, MBBS, of West Virginia University School of Medicine, and colleagues conducted a retrospective cohort study using data from 151,868 HIV-positive people in the TriNetX electronic medical records database who received care at U.S. health centers between January 2008 and December 2020. Those with alcohol-related liver disease or liver cancer were excluded.

The researchers identified 4,969 participants with NAFLD. In this group, the mean age was 42 years, 60% were men, 55% were white, 23% were Black and the mean BMI was 29, near the top of the overweight range. A sub-group of 4,463 participants with NAFLD were matched with people without NAFLD according to age, race, comorbidities, BMI, CD4 count and use of antiretroviral therapy.

People with NAFLD were a bit older (median 42.9 versus 40.8 years), more likely to be Latino, more often current or former smokers, more likely to have elevated blood lipids and certain comorbidities and more likely to be taking medications to manage cardiovascular risk.

After an average follow-up period of about five years, people with NAFLD had a higher risk for all adverse cardiovascular events relative to the control group without fatty liver disease. These included myocardial infarction, new-onset heart failure, unstable angina (chest pains), stroke, transient ischemic attack and procedures to treat or manage these conditions.

“The results indicate the need for targeted efforts to improve awareness of risk factors associated with adverse cardiovascular event risk in people with HIV with NAFLD,” the researchers concluded.

At this time, there are no approved medications to treat NAFLD, so management relies on lifestyle changes such as diet, exercise and weight loss. However, there are numerous candidates in the pipeline, and some research suggests that drugs used to treat diabetes and weight loss, such as semaglutide (Ozempic and Wegovy), may improve fatty liver disease as well.

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