The Causes of Liver Cancer Are Changing

Liver cancer is now less likely to be caused by hepatitis B or C, but more likely to be caused by fatty liver disease or alcohol.

July 21, 2022 By Liz Highleyman

The main drivers of liver cancer are changing worldwide, with fewer cases caused by viral hepatitis but more related to non-alcoholic steatohepatitis (NASH) or heavy alcohol consumption, according to a new report in Cell Metabolism.

“Urgent measures are required at a global level to tackle underlying metabolic risk factors and slow the growing burden of NASH-associated liver cancer, especially in the Americas,” conclude senior study author Rohit Loomba, MD, of the University of California San Diego School of Medicine, and colleagues.

Over years or decades, chronic hepatitis B or hepatitis C, fatty liver disease (NASH and its less severe form, non-alcoholic fatty liver disease, or NAFLD), heavy alcohol use and other causes of liver injury can lead to serious complications, including cirrhosis and hepatocellular carcinoma, the most common type of liver cancer.

Liver cancer is often diagnosed late, and it is difficult to treat, making it one of the leading causes of cancer-related mortality worldwide and among the fastest-rising causes of cancer death in the United States. In 2020, more than 830,000 people worldwide and 30,000 people in the U.S. died from liver cancer.

Loomba’s team estimated global and regional trends in liver cancer burden and mortality as well as the contribution of various causes of liver disease using data from the Global Burden of Disease study.

In 2019, there were an estimated 534,000 new cases of liver cancer and 485,000 deaths due to liver cancer worldwide. This represents a 27% increase in liver cancer incidence and a 25% increase in mortality since 2010. After adjusting for age, worldwide incidence and death rates did not change significantly—except for a substantial rise in the Americas.

The Western Pacific region (where hepatitis B is common) accounted for more than half of global liver cancer deaths in 2019, but mortality remained stable compared with 2010. Age-adjusted liver

cancer deaths declined in all other regions except one: Mortality “rose sharply” in the Americas.

Global liver cancer deaths related to hepatitis B and C declined overall, thanks to widespread hepatitis B virus (HBV) vaccination and treatment and the advent of effective direct-acting antiviral therapy that can cure hepatitis C virus (HCV).

But in contrast with all other regions, HBV-associated liver cancer deaths rose in the Americas, “possibly due to underdiagnosis and a lack of disease awareness,” the study authors suggested. This was also the only region that did not see a decline in mortality from HCV-associated liver cancer, perhaps due to “major gaps in diagnosis and linkage to care.”

Between 2010 and 2019, fatty liver disease and alcohol use accounted for a growing share of liver cancer mortality. In fact, NASH became the fastest growing cause of age-adjusted liver cancer death worldwide—especially in the Americas—which the authors attribute to “rapidly rising obesity rates.” Another recent study found that NAFLD is the leading cause of liver cancer for older Americans covered by Medicare.

NAFLD and NASH are often accompanied by abdominal obesity, hypertension, elevated blood sugar and abnormal blood fat levels, collectively known as metabolic syndrome. With no effective approved medical therapies, disease management depends on lifestyle changes, such as weight loss and exercise.

Loomba and colleagues projected that NASH-associated liver cancer would continue to increase over the next decade in the United States, Europe and Asia. “Urgent measures are required at a global level to tackle the underlying metabolic risk factors and slow the growing burden of NASH-related liver cancer,” they wrote.

Alcohol use was the second fastest rising cause of liver cancer, again increasing most in the Americas. The authors noted that global alcohol consumption is projected to climb further, especially in the Western Pacific and Southeast Asia, which could result in more liver cancer cases in the future.

“Implementing policies such as an increased price and taxation for alcohol may be considered at a national level to reduce the burden of alcohol-associated liver cancer in countries with a high alcohol-per-capita consumption,” they suggested.

Click here to read the study in Cell Metabolism.

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