Causes of liver cancer are changing around the world: Some up, some down

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The primary causes of liver cancer are well known: viral (hepatitis B and C), alcohol and non-alcoholic steatohepatitis (NASH), a condition in which fat builds up in the liver, resulting in chronic inflammation and damage.

But in a paper published June 3, 2022 in *Cell Metabolism*, an international team of scientists, led by researchers at University of California San Diego School of Medicine, say the etiologies of liver cancer are changing—and the prognosis is mixed.

On the plus side, advances in hepatitis B (HBV) vaccinations and greater availability of antiviral therapies have reduced HBV-associated liver cancer. On the negative, *alcohol consumption* and the prevalence of obesity (another risk factor) are rising dramatically.

"The impact of these changes on global liver cancer burden is not yet clear," said senior author Rohit Loomba, MD, director of hepatology at UC San Diego Health and professor of medicine in the UC San Diego School of Medicine.

One thing that hasn't changed: Liver cancer continues to kill. It is the third leading cause of cancer death worldwide. In 2020, more than 830,000 persons around the world died from the disease, with approximately 30,000 deaths in the United States alone.

Loomba and colleagues used methodology from the Global Burden of Disease Study, an ongoing research collaboration involving more than 3,600 researchers in 145 countries, to survey worldwide incidence of liver cancer, and more specifically, global and regional changes in the causes of liver cancer.

Between 2010 and 2019, the authors found, there was a 27 percent increase in liver cancer cases across the 204 countries surveyed, a 25 percent increase in liver cancer deaths and a 21 percent increase in disability-adjusted life years (DALY), a statistical measure that accounts for the adverse effects of disease apart from death. One DALY is the equivalent loss of one year of full health. In 2019 alone, there were an estimated 12.5 million DALYs due to liver cancer.

Liver cancer prevalence is uneven around the world. In 2019, for example, liver cancer death rates were highest in Asia (including countries like China, Japan, Thailand and Mongolia) and lowest in most of Africa.

The causes of liver cancer varied measurably around the world. Age-standardized death rates (ASDR) due to HBV-associated liver cancer decreased between 2010 and 2019, most likely due...
to successful vaccination campaigns, antiviral therapies and programs to reduce aflatoxins, a family of fungi-generated toxins found on agricultural crops, such as corn, peanuts and cottonseed.

The only region where the ASDR rose was in the Americas, possibly due to underdiagnoses of liver cancer cases and lack of disease awareness, wrote the authors. HCV-associated cases also declined due to the availability of highly effective oral antiviral therapy, except in the Americas.

NASH was the fastest growing cause of liver cancer deaths globally, especially in the Americas, driven by rapidly rising obesity rates. The prevalence of obesity in the U.S. in 2017 was 42.4 percent, according to the Centers for Disease Control, up from 30.5 percent in 2000. Researchers said the incidence of liver cancer due to NASH is projected to increase further in the U.S., Europe and Asia over the next 10 years, tracking with rising rates of obesity.

Alcohol was the second fastest rising cause of liver cancer, again with the highest increase in the Americas. Global alcohol-per-capital consumption was projected to rise further, especially in Western Pacific and Southeast Asia countries.

"In California and particularly in San Diego, cirrhosis due to both NAFLD and alcohol-associated liver disease are rising and are important cause of liver cancer," said Loomba, director of the NAFLD Research Center in the UC San Diego School of Medicine. NAFLD is the acronym for nonalcoholic fatty liver disease, an umbrella term for a range of liver conditions affecting people who drink little to no alcohol. Like NASH, it increases the risk of liver cancer.

"We are developing better ways to treat both of these conditions earlier to reduce the burden of disease and trying to better screen those who are at a higher risk of developing liver cancer by offering better and more personalized screening strategies. Early recognition and prompt treatment is needed to improve outcomes."

More information: Daniel Q. Huang et al,