# Abnormal Liver Tests Linked to Worse COVID-19 Outcomes

The prevalence of abnormal liver tests in people hospitalized with COVID-19 is higher than previously found.

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Most people hospitalized with COVID-19 have abnormal liver biomarker tests, and those with worse tests results also had poorer outcomes, according to findings published in Hepatology.

“Abnormal liver tests are very common in hospitalized patients with COVID-19 and possibly more common in U.S. patients than previously reported in China,” wrote the researchers.

The novel coronavirus that causes COVID-19 has resulted in over 7,000,000 cases of infections and 200,000 deaths in the United States. To date, the effect of the coronavirus, known as SARS-CoV-2, on the liver is poorly understood.

Previous research from China has shown that some 15% of people hospitalized with COVID-19 have abnormal liver tests. Moreover, such test results have been associated with longer hospital stays and a higher likelihood of developing severe COVID-19 and death. But little is known about such associations in hospitalized people with COVID-19 in the United States.

To that end, Joseph Lim, MD, of the Yale School of Medicine in New Haven, Connecticut, and colleagues set out to understand abnormal liver tests and their links with clinical outcomes in people hospitalized due to COVID-19.

The research team conducted a retrospective cohort study of 1,827 people who tested positive for SARS-CoV-2 and were hospitalized at five hospitals in the Yale New Haven Health System between March 14, 2020 and April 23, 2020. The average age of the group was 65 years; 43% had obesity, and 39% had diabetes—two risk factors for more severe COVID-19. The researchers did not report how many had hepatitis B or C, which can lead to abnormal liver tests. Some of the participants were treated with hydroxychloroquine, remdesivir, tocilizumab or a combination of lopinavir and ritonavir (Kaletra).

The researchers noted clinical symptoms and liver test information at three different stages—at baseline prior to infection, at admission and at peak hospitalization—as well as the participants’ outcomes such as severe COVID-19, intensive care unit (ICU) admission, mechanical ventilation

and death.

They included five tests looking for abnormal levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), total bilirubin, and albumin. Higher than normal levels of these liver biomarkers would indicate liver dysfunction and inflammation in liver cells and bile ducts.

The researchers commonly observed abnormal liver test results, with the proportions generally rising over time. Among those with available data prior to SARS-CoV-2 infection and hospitalization, 20% had abnormal AST, 19% had abnormal ALT, 13% had abnormal ALP, 4% had elevated bilirubin and 27% had abnormal albumin.

At the time of hospital admission, 67% had abnormal AST, 42% had abnormal ALT, 14% had abnormal ALP 4% had elevated bilirubin, and 57% had abnormal albumin. Most patients with abnormal liver tests at admission had minimal elevations—one to two times the upper limit of the normal range—but some had very high AST and ALT levels. At peak hospitalization, the corresponding proportions were 83%, 62%, 23%, 16% and 87%.

Predictors of abnormal liver tests at admission included older age, male sex, higher body mass index and diabetes. These same factors predicted abnormal levels at peak hospitalization, along with use of medications for COVID-19.

These levels are much higher than those seen in studies in China. One possible explanation for this is the higher prevalence of fatty liver disease in the U.S. population. “We can speculate that U.S. patients may have an increased rate of other risk factors, such as alcoholic or non-alcoholic fatty liver disease,” Lim said in a press release. “In the U.S., close to one third of people have fatty liver disease, and several million people have chronic hepatitis B or C,” added Michael Nathanson, MD, PhD, the director of the Yale Liver Center.

The team found strong links between abnormal liver tests and poorer outcomes in people with COVID-19, such as ICU admission, mechanical ventilation and death.

Also, the researchers found that drugs used to treat COVID-19, especially tocilizumab, were linked to abnormally high levels of liver enzymes indicative of liver damage. But it was difficult to tell whether abnormal liver tests occurred because of the disease or due to liver injury caused by the drugs.

“Rather than the liver itself driving poorer outcomes in COVID-19 patients, the organ is more likely ’a bystander’ affected by the hyperinflammation associated with COVID-19 and by the side effects of related treatments,” Nathanson suggested.

Click here to read the study in Hepatology.
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