

Strong link found between abnormal liver tests and poor COVID-19 outcomes

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Researchers at the Yale Liver Center found that patients with COVID-19 presented with abnormal liver tests at much higher rates than suggested by earlier studies. They also discovered that higher levels of



liver enzymes—proteins released when the liver is damaged—were associated with poorer outcomes for these patients, including ICU admission, mechanical ventilation, and death.

The study appeared online on July 29 in *Hepatology*.

Previous studies in China found that approximately 15% of patients with COVID-19 had abnormal liver tests. The Yale study, which looked retrospectively at 1,827 COVID-19 patients who were hospitalized in the Yale New Haven Health system between March and April, found that the incidence of abnormal liver tests was much higher—between 41.6% and 83.4% of patients, depending on the specific test.

In all, the Yale researchers examined five liver tests, looking at factors such as elevations in aspartate aminotransferase (AST) and alanine transaminase (ALT), which indicate liver cell inflammation; an increase in bilirubin, which indicates liver dysfunction; and increased levels of alkaline phosphatase (ALP), which may indicate inflammation of bile ducts.

Although the researchers do not know why the incidence of abnormal liver tests was so much higher than in previous studies from China, senior author Dr. Joseph Lim, professor of medicine and director of the Yale Viral Hepatitis Program, said other health differences between the Chinese and U.S. populations could account for it.

"We can speculate that U.S. patients may have an increased rate of other risk factors such as alcoholic or <u>non-alcoholic fatty liver disease</u>," he said.

Liver disease is widespread in the U.S. population. Dr. Michael Nathanson, the Gladys Phillips Crofoot Professor of Medicine (digestive diseases), professor of cell biology, director of the Yale Liver Center,



and a co-author of the study, said: "In the U.S., close to one-third of people have fatty liver disease, and several million people have chronic hepatitis B or C."

Because the Yale researchers had access to patients' health records, they were also able to look at their liver tests prior to being diagnosed with COVID-19. Approximately one-quarter of patients in the study had abnormal liver tests prior to being admitted for the virus. But regardless of whether patients came to the hospital with existing liver problems or developed them during their COVID-19-related hospitalization, a strong association was observed between abnormal liver tests and the severity of the COVID-19 cases, the researchers said.

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 said.

The study noted a relationship between drugs used to treat severe COVID-19 and liver damage, most significantly the drug tocilizumab.

"We observed a strong association between the use of COVID-19 medications and abnormal liver tests," said Lim, but added that they could not confidently tease out that the abnormal tests were due to "druginduced liver injury" as opposed to the disease.

The researchers have additional clinical and lab-based studies underway to further understand COVID-19's impact on liver pathology. Nathanson noted that as one of only four National Institutes of Health-sponsored liver centers in the country, the Yale Liver Center is uniquely positioned to advance this research.

More information: Melanie A. Hundt et al. Abnormal Liver Tests in



COVID-19: A Retrospective Observational Cohort Study of 1827 Patients in a Major U.S. Hospital Network, *Hepatology* (2020). DOI: 10.1002/hep.31487

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