International Registries Shed More Light on Liver Disease and COVID-19

People with advanced liver cirrhosis are at greater risk for severe COVID-19 illness and death.

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People with advanced liver disease are at greater risk for developing and dying of severe COVID-19, according to research presented at the recent Digital International Liver Congress. Liver transplant recipients, however, do not appear to have higher COVID-19 mortality.

It is now well established that people with coexisting conditions and those with advanced immune suppression are at greater risk for serious complications related to COVID-19. People with liver disease may be at risk for more severe COVID-19 in part because they have higher rates of comorbidities. Those with non-alcoholic fatty liver disease (NAFLD) or its more severe form, nonalcoholic steatohepatitis (NASH), for example, often have obesity and diabetes.

Prior studies have shown that people with liver cirrhosis have more COVID-19 complications and higher mortality. However, the impact of liver disease has not been as well studied as other conditions.

COVID-19 and Cirrhosis Severity

Thomas Marjot, MRCP, of the University of Oxford, presented the latest findings from the international SECURE-Cirrhosis (COVIDCirrhosis.org) and COVID-HEP (COVID-Hep.net) registries.

The registries were established in March to track the health outcomes of people with chronic liver disease and COVID-19. SECURE-Cirrhosis includes data from North and South America and parts of Asia, while COVID-HEP includes reports from the rest of the world. As of August 14, the registries had collected reports of 1,097 cases from 35 countries.

A previous analysis published in the Journal of Hepatology looked at data collected from March 25 through April 20. Marjot presented an updated analysis of reports through July 8.

This analysis included 745 people with chronic liver disease and COVID-19, of whom 386 had cirrhosis and 359 did not. People who had received liver transplants were excluded. Most reports involved hospitalized patients, and Marjot noted that the data don't shed much light on nonhospitalized people with liver disease who have milder cases of COVID-19.

The majority of reports came from the United States and the United Kingdom (each contributing about 25% of cases) and China (16%). NAFLD was the most common cause of liver disease (38%), followed by alcoholic liver disease (18%), hepatitis B (10%) and hepatitis C (9%).

The analysis compared people without cirrhosis and those with three levels of cirrhosis severity: Child-Turcotte-Pugh (CPT) Class A, B and C, with C being most severe. The researchers found that for each level of liver disease severity, the risk of adverse COVID-19 outcomes—including intensive care unit (ICU) admission, mechanical ventilation and death—increased in a stepwise manner.

Most people without cirrhosis survived, with mortality rates of 8% for those who were hospitalized and 21% for those put on ventilators. But mortality rose steeply with worsening liver disease. Among those with CTP Class A, mortality rates were 22% once hospitalized and 52% once put on a ventilator; the corresponding rates were 39% and 74% for CTP Class B patients. Among those with CTP Class C, a majority of hospitalized patients (54%), and most of those put on ventilators (90%) died.

The most common cause of death for people with cirrhosis was respiratory disease (71%), far exceeding liver-related deaths (19%) and cardiac deaths (5%). Nearly half of people with cirrhosis (46%) progressed to decompensated liver disease, in which the organ can no longer carry out its vital functions. But even among those with decompensation, lung disease remained a more frequent cause of death than liver-related complications (64% versus 24%).

Mortality rates were much higher for people with cirrhosis compared to people without cirrhosis in all age groups except those age 80 or older, who had high mortality regardless of cirrhosis status. In addition to age and cirrhosis severity, alcoholic liver disease was also an independent risk factor for death. NAFLD and viral hepatitis were not linked to elevated mortality after controlling for other risk factors.

Comparing these results against a U.K. cohort of COVID-19 patients without liver disease, the people in the registry who had chronic liver disease but had not yet developed cirrhosis appeared to have a similar rate of death after adjusting for sex, age and other comorbidities.

“There are diminishing chances of survival as chronic liver disease patients require increasing levels of medical support and diminishing chances with more severe baseline liver disease,” the researchers concluded.

Liver Transplantation

In another presentation, Marina Berenguer Haym, MD, of the University of Valencia in Spain, described an analysis of outcomes among liver transplant recipients with COVID-19 in the same two registries. The findings were also published in The Lancet Gastroenterology and Hepatology.

Early in the pandemic, transplant recipients were singled out as being at particularly high risk for contracting the coronavirus because the drugs they take to prevent organ rejection suppress the immune system. But data about what happens if they do get COVID-19 is lacking. Many of the

complications of advanced COVID-19 are related to an overactive immune response to the virus, and immunosuppressive therapies, such as dexamethasone, can actually help some patients.

This analysis included 181 liver transplant recipients in 18 countries. Nearly 70% were men, and the median age was 60. They were compared against 627 COVID-19 patients who had not received transplants (median age 73).

Transplant recipients and non-transplant patients with COVID-19 were hospitalized at similar rates (82% versus 76%, respectively), but the transplant patients were more likely to be admitted to an ICU (28% versus 8%) and to be put on ventilators (20% versus 5%). However, the transplant group had a lower mortality rate than those who did not undergo transplants (19% versus 27%).

“We should be reassured that clinicians and health policy makers should be aware liver transplantation does not confer major additional susceptibility to adverse outcomes,” Thomas Berg, MD, of the University of Leipzig in Germany, said at a press briefing in advance of the conference. “This should be considered when assessing the relative risk and benefits of delivering clinical follow-up and monitoring of liver transplant patients.”

A bigger worry, he suggested, is that necessary transplants could be deferred due to reductions in services and concern about patients contracting the coronavirus. He also noted that fear of the virus could lead people with liver disease to avoid important medical care, such as liver cancer screenings, which could result in subsequent waves of advanced liver disease.

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Click here to view the liver transplant presentation.

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