

# ADVANCES IN HEPATOLOGY

Current Developments in the Treatment of Hepatitis and Hepatobiliary Disease

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## Liver Transplantation During the COVID-19 Pandemic



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**G&H** Are patients awaiting liver transplantation at greater risk of becoming infected with coronavirus disease 2019?

**KRR** Patients with advanced liver disease are cited by the Centers for Disease Control and Prevention as a population potentially at risk for severe coronavirus disease 2019 (COVID-19), which is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Although there likely is reason to believe that this population is at greater risk, we do not have convincing data showing that this is true. Research has focused on the number of patients who have been infected, but there are many people in the country who have advanced liver disease and/or are awaiting liver transplantation, and we do not know how many have been infected and have any consequences. The rate of infection and the severity of COVID-19 might be similar to the general population.

**G&H** What are the effects of COVID-19 specifically on the liver?

**KRR** Many papers have suggested that hepatic biochemical tests can be variably abnormal in infected patients. Some papers have suggested that hepatic involvement is associated independently with poor outcomes, but it might just be a factor in overall multiorgan failure. There is no evidence that there is a direct infection of the liver by SARS-CoV-2 that leads to unique manifestations in the liver.

**G&H** How has COVID-19 affected the evaluation of patients for liver transplantation?

**KRR** The evaluation process has been evolving. When there was a lockdown, my center in Pennsylvania suspended living donor liver transplantation, and evaluations were restricted largely to telemedicine. Over time, we are programmatically opening up face-to-face or in-person evaluation for certain categories of patients while still performing telemedicine. Thus, in essence, a hybrid model is currently being used. There may have been a relatively slow evaluation process and the number of patients coming in for evaluation, as well as the number of referrals, likely decreased, but now these numbers are starting to increase as areas with low rates of COVID-19 are opening up and moving forward.

**G&H** How has organ donation and procurement been affected?

**KRR** During the initial period of the pandemic, there was quite a decrease in terms of organ donation as well as procurement. The latter was because surgeons who procure livers did not want to go to a COVID-19 epicenter such as New York. Similarly, it was not considered ideal for teams from a COVID-19 epicenter to go to non-COVID-19 epicenters to harvest organs.

**G&H** Have there been any effects on the liver transplant waiting list?

**KRR** Liver transplantation was designated by the Centers for Medicare and Medicaid Services as a procedure that was not to be impacted by COVID-19 restrictions. Thus,

We found that hospitalized patients with cirrhosis who did not have COVID-19 had the same mortality as patients with cirrhosis who were infected with COVID-19.

sick patients have been undergoing liver transplantation during the pandemic. My center, for example, has noted transplant volumes similar to those in the pre-COVID-19 era. The main impact has been the suspension of living donor liver transplantation, which is starting to resume now in areas where COVID-19 rates are low.

**G&H** Are transplant candidates who are infected with COVID-19 still being considered for the procedure?

**KRR** No, that has been an area where transplantation has been restricted. Even in very sick patients, there have been contentious discussions as to whether the patients should be transplanted if they have COVID-19. At least 2, possibly 3, weeks after COVID-19 positivity, a variable number of negative COVID-19 tests are required by most transplant programs to consider such patients for transplantation. There may be exceptions, but, generally, most programs have refrained from transplanting a COVID-19 patient. Likewise, donors with COVID-19 have not been used.

**G&H** What have been the main challenges of performing liver transplantation during the COVID-19 pandemic?

**KRR** Apart from a decrease in organ donation and procurement, there has been a long learning period about the risks of performing liver transplantation, and there have been many discussions on what precautionary measures should be adopted. There have been challenges in terms of hospitalizing patients. In addition, there have been restrictions on allowing families to visit patients. Some

patients were offered a transplant but refused to undergo the procedure because they wanted a family member or caregiver to be there. As previously mentioned, organ donation and procurement have decreased but are starting to slowly return to baseline. There was also a shortage of blood supply, so some of the complex cases may not have been performed.

**G&H** How has posttransplant care changed during the COVID-19 pandemic?

**KRR** There are general precautions, such as avoiding crowds and maintaining social distancing, as well as limiting the number of people in an examination room unless absolutely necessary. These are the types of measures that apply to any patients. The American Association for the Study of Liver Diseases recently released best practice advice for liver transplant providers from an expert panel, which can be found online at <https://www.aasld.org/sites/default/files/2020-06/AASLD-COVID19-ExpertPanelConsensusStatement-June252020-v2-FINAL.pdf>. This consensus statement provides guidance to the community on how to manage liver transplant candidates and recipients as well as transplantation in general.

**G&H** Are liver transplant recipients at greater risk of acquiring COVID-19, particularly severe cases?

**KRR** This is an important question, but the answer is still not clear. A website from the University of Washington in Seattle collected data on transplant recipients. During the initial period of the pandemic in New York, a fair number of transplant recipients developed severe COVID-19. However, this research lacked contemporaneous non-transplant or transplant recipient cohorts to assess for any differences in their clinical features and outcomes, particularly the impact of COVID-19. My center has had fewer than 10 cases of COVID-19 in liver transplant recipients, and those were mostly only mild or moderate cases. My colleagues and I recently published a study in *Gut* on patients with cirrhosis who were hospitalized. We found that hospitalized patients with cirrhosis who did not have COVID-19 had the same mortality as patients with cirrhosis who were infected with COVID-19. What was interesting was that patients with cirrhosis and without COVID-19 were dying of cirrhosis complications and patients with both cirrhosis and COVID-19 were dying of COVID-19 complications. Overall, however, mortality in the patients with cirrhosis in both groups combined was higher than in COVID-19 cases alone. That is the type of study needed to address the question of adverse impact of COVID-19 on liver transplant recipients.

Although quite a few studies have reported on patients who underwent transplantation and had severe COVID-19, it is not known whether this occurs at a rate higher than in the general population.

### **G&H** Should immunosuppression be reduced in liver transplant recipients during the COVID-19 pandemic?

**KRR** No, the reduction of immunosuppression is not being recommended. There are some individuals in whom there has been discussion about perhaps reducing or stopping an antimetabolite, but the risk-benefit ratio needs to

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be considered carefully. A priori reduction in immunosuppression may put the patient at risk for graft rejection. A similar philosophy is followed in autoimmune hepatitis.

### **G&H** Do patients with immunosuppression have a higher risk of acquiring COVID-19?

**KRR** At this stage, we do not have good enough reason to believe that altering immunosuppression would in any way lead to favorable outcomes. Although immunosuppressed patients are at risk, we do not have convincing data to suggest that they are at any overwhelming risk for COVID-19 relative to the general population. Outcomes

in liver transplant recipients with COVID-19 have been described to be severe, but individuals in the general population also have had severe outcomes. It is also unclear whether outcomes are likely worse in liver transplant recipients than in individuals in the general population who have comorbid conditions such as chronic kidney disease, obesity, diabetes, and chronic obstructive pulmonary disease.

### **G&H** What further research is needed in the management of these patients?

**KRR** It would be useful to know if a liver transplant recipient with COVID-19 would be a candidate for any of the investigational drugs to treat COVID-19. It would also be helpful to collect information from across the country on the outcomes of patients who underwent liver transplantation while they had ongoing COVID-19, particularly because there are some very sick candidates for transplantation who cannot wait until COVID-19 has resolved.

#### **Disclosures**

*Dr Reddy has no relevant conflicts of interest to disclose.*

#### **Suggested Reading**

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