

COVID-19 and the Liver: What Have We Learned So Far

David Bernstein, MD

Chief, Hepatology, Northwell Health

Professor of Medicine, Zucker School of Medicine at
Hofstra/Northwell



Liver Enzymes in COVID-19 Patients

- Elevated liver tests seen in 41-83% of patients upon presentation
- Elevations associated with poorer outcomes:
 - ICU admissions
 - Mechanical ventilation
 - Death

COVID-19 in Patients with Pre-existing Liver Disease

- Higher rate of mortality in patients with chronic liver disease
- Cirrhotics have higher mortality than non-cirrhotics
- NAFLD/NASH most common etiologies seen

Patients on Immunosuppressive Therapy and COVID-19

- Defined as population at risk for severe COVID-19
- Of 111 liver transplant patients admitted with COVID-19, 2 died of pneumonia¹
 - All 3 were male, > 65 years old, HTN, DM
- 29 liver transplant patients admitted with COVID, 9 died (23%)²

Factors Not Associated With Worse COVID-19 Outcomes

- Anti-viral therapy for HBV, HCV

COVID-19 Liver Findings

- 40-80% with abnormal liver tests
- Low albumin associated with severe COVID-19
- Liver histology is non-specific
- Autopsy findings suggest hepatic vascular involvement

Additional Recommendations: Abnormal Liver Tests and COVID-19

- Abnormal liver biochemistries should **not** be a contraindication to using investigational or off-label therapeutics for COVID-19 (e.g., remdesivir, tocilizumab, chloroquine, and hydroxychloroquine)
 - Although AST or ALT levels $>5\times$ ULN may exclude patients from consideration of some investigational agents
- Follow guidance in your clinical study protocol and/or by the U.S. Food and Drug Administration (FDA) for monitoring of liver biochemistries and discontinuation of study drug used to treat COVID-19

Considerations for Patients with Chronic Liver Disease

- Postpone visits to specialized centers
- Perform routine laboratory testing locally/off-site
- Use telemedicine/visits by phone wherever possible

Patients with Chronic Liver Disease: Special Considerations

Patients with viral hepatitis	Patients with NAFLD or NASH
<ul style="list-style-type: none">• No increased risk of a severe course of COVID-19• Send follow-up prescriptions for patients on antiviral therapy by mail	<ul style="list-style-type: none">• May suffer from DM, HTN and obesity, putting them at increased risk for a severe course of COVID-19
Patients with autoimmune liver disease	Patients with compensated cirrhosis
<ul style="list-style-type: none">• We currently advise against reducing immunosuppressive therapy.<ul style="list-style-type: none">• Reduction should only be considered under special circumstances after consultation with a specialist• Emphasize importance of vaccination for <i>Streptococcus pneumoniae</i> and influenza	<ul style="list-style-type: none">• Consider delaying HCC surveillance and screening for varices. Individualized and non-invasive risk assessment should be applied for stratification

Considerations for Patients with Decompensated Liver Disease (Including HCC)

- Maintain care according to guidelines
- Minimize exposure to medical staff by using telemedicine
- Restrict listing for transplantation to patients with poor short-term prognosis
- Reduce in-hospital liver transplant evaluation to the strictly necessary to shorten hospital stays
- Promote vaccination for *Streptococcus pneumoniae* and influenza
- Follow guidelines for prophylaxis of spontaneous bacterial peritonitis and hepatic encephalopathy
- Test for SARS-CoV-2 in patients with acute decompensation or acute-on-chronic liver failure

Considerations for People Actively Listed for Transplantation

- Perform SARS-CoV-2 routine testing before transplantation in both donors and recipients
 - Acknowledging that negative testing cannot completely rule out infection
- Consent for diagnostic and therapeutic procedures related to transplantation should include the potential risk for nosocomial COVID-19
- Living-donor transplantations should be considered on a case-by-case basis

Considerations for Patients with Hepatocellular Carcinoma

- Maintain care according to guidelines, including:
 - Continuing systemic treatments
 - Evaluation for liver transplantation
- Minimize exposure to medical staff by using telemedicine
- In case of COVID-19, early admission is recommended

Considerations for Patients After Liver Transplantation

- Maintain care according to guidelines, including:
 - Continuing systemic treatments
 - Evaluation for liver transplantation
- Minimize exposure to medical staff
- Emphasize importance of vaccination for *Streptococcus pneumoniae* and influenza
- Perform local lab testing (including drug levels) in stable patients
- We currently advise against reducing immunosuppressive therapy
 - Reduction should only be considered under special circumstances after consultation with a specialist

Summary

- COVID-19 commonly causes abnormal liver chemistries
- Higher rate of mortality in patients with chronic liver disease
- Cirrhotics have higher mortality than non-cirrhotics
- Best treatment is social distancing, masks, hand-washing
- Minimize testing and travel
- Admit when needed
- Vaccine development remains ongoing but is not on the horizon