COVID-19 in Liver Disease
(When the Compensated Decompensate)

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Speakers Bureau: Gilead, Clinical Area- HCV
Speakers Bureau: Salix, Clinical Area- HE
Speakers Bureau: Abbvie, Clinical Area- HCV
Consultant (spouse): Bausch, Best Doctors, Biovie
Risk of Acquiring Infection

- Whether patients with liver disease are more susceptible is uncertain
- Chronic liver disease in the absence of immunosuppression is not known to increase risk of acquiring COVID-19
- BUT chronic liver disease = higher risk for severe disease from COVID-19

Liver Manifestations of COVID-19

- Liver susceptible to SARS-COV-2
  - Angiotensin Converting Enzyme 2 (ACE2) receptors in biliary and epithelial liver cells
  - SARS-COV-2 binds to ACE2 receptor to gain entry and damage the target organ

Liver-Related Clinical Features

• Transaminitis reported in hospitalized patients with COVID-19 is common
  – Ironic because more ACE2 receptors in cholangiocytes than hepatocytes
    • ACE2 may not fully explain the liver tropism
  – Usually mild (< 5x ULN)
  – AST > ALT, and this pattern associated with disease severity
  – Rare but severe acute hepatitis has been reported
Liver Histology Is Non-Specific

A. Steatosis & congestion but not much inflammation
B. Portal & lobular inflammation & congestion
C. Congestion & necrosis with apoptotic body
D. Portal-based inflammation

Lagana et al. 2020.
Additional Issues for Cirrhotic Patients

- Increased circulating ACE activity and angiotensin II levels
  - May facilitate entry of the virus into host cells
  - More vulnerable to direct virus-related cytotoxicity
- Reticulo-endothelial systems disruption affects immune surveillance activity → pancytopenia
- Hypoxic hepatitis exacerbated by portosystemic shunting, hypovolemic state
Risk of Severe COVID-19 & Mortality

- Pre-existing liver disease is associated with worse outcomes from COVID-19
- Higher rates of mortality NAFLD & NASH most common etiology
- Severity of liver disease associated with increased risk of mortality

Mortality: Cirrhosis & COVID-19

- Child-Pugh B and C independent predictors
- Mortality attributed to pulmonary disease in 79%
  - Altered pulmonary dynamics like hepatic hydrothorax, HPS, portopulmonary HTN may exacerbate
- Mortality liver-related in 12%

When to Test

• **Usual suspects**
  - Fever
  - Cough
  - Dyspnea
  - Myalgias
  - Aberrancy of taste/smell
  - (Fewer GI symptoms in cirrhosis!)

• **Chronic liver disease**
  - Transaminases at least threefold above baseline
  - Symptoms suggestive of disease flare
  - Decompensation
    - 25% of new decomps have no resp symptoms at diagnosis
## Clinical Characteristics of Cirrhotic Patients With COVID-19

<table>
<thead>
<tr>
<th>Ref</th>
<th>Patient #</th>
<th>Region</th>
<th>Etiology</th>
<th>Severity</th>
<th>ACLF</th>
<th>AD</th>
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</thead>
<tbody>
<tr>
<td>Moon et al.</td>
<td>103</td>
<td>International</td>
<td>HCV 10%, HBV 11%, ALD 20%, NAFLD 22%</td>
<td>CTP A 44%, CTP B 29%, CTPC 26%, MELD 10</td>
<td>N/A</td>
<td>AD 25% EVB 1% HE 17% Ascites 27% SBP 3%</td>
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<tr>
<td>Kimet et al.</td>
<td>227</td>
<td>US</td>
<td>N/A</td>
<td>Comp 59%, Decomp 41%</td>
<td>N/A</td>
<td>AD 30% EVB 3% HE 10% Ascites 5%</td>
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<tr>
<td>Marjot et al.</td>
<td>386</td>
<td>International</td>
<td>HCV 11%, HBV 21%, ALD 38%, NAFLD 26%</td>
<td>CTP A 52%, CTP B 30%, CTP C 17%, MELD 12</td>
<td>EASL 23%</td>
<td>AD 46% EVB 3% HE 27% SBP 3%</td>
</tr>
</tbody>
</table>
Prolonged Viral Shedding

• Liver transplant recipients & other immuno-compromised patients have a longer duration of viral shedding
• May have to modify isolation or clearance testing
Autoimmune Hepatitis & Liver Transplant

• Don’t adjust IS in patients without COVID-19 or in patients with mild symptoms
  – Risk of disease flare or rejection > Risk of COVID-19

• Reduce in severe COVID-19 or if ANC <1000
  – D/C antimetabolites

• Hospitalized – Steroids great for both COVID-19 and the liver in these cases
Viral Hepatitis

- No contraindication for continuing antivirals for HBV or HCV in COVID-19
- Reactivation of HBV observed with glucorticoids and tocilizumab
- Indirect epidemiologic evidence that HBV infection in SARS a risk factor for progression to ARDS

Remdesivir

- Elevated liver biochemistries not a contraindication
- Not recommended for patients with ALT > 5x upper limit of normal
- Discontinue with signs of liver injury
  - 15% of patients treated will have ALT elevation
- Handful of reports of use with Child Pugh C
  - EASL recommends to use with caution
Monoclonal Antibodies

• Specific hepatic metabolism
  – Broken down to amino acids in cells that take them up
  – No toxic intermediates

• Hepatotoxicity
  – No reports of ALT elevations
  – All 4 monoclonal anti-SARsCoV-2 antibodies: E (unlikely causes of clinically apparent liver injury)
  – Theoretically can generate an immune response that could lead to immune-mediated hepatic injury
Drugs Repurposed for COVID 19

- Chloroquine, hydroxychloroquine, azithromycin, ivermectin, fluvoxamine colchicine, interferon beta, lopinavir/ritonavir
  - Most of these agents have been implicated in rare causes of DILI but no specific instances have been convincingly shown in case reports and trials for COVID 19 treatment
- Data is sparse
Vaccination in Chronic Liver Disease

• DO IT!
• Efficacy unknown
  – Pfizer Phase 2/3 – 214 patients
  – Moderna Phase 3 – 196 patients
  – Jannsen Phase 3 – 206 patients
• Potential for severe COVID-19 outweighs uncertainty
Post-OLT

• Delay vaccine at least 1 month, 3 for induction
• Overall response lower than non-transplant
• Poor antibody response with antimetabolite therapy (MMF or AZA)
• 3rd dose of mRNA improved antibody response
  – Now recommended
How Can We Help Our Patients?

• Telemedicine
• Still masking
• 90-day scripts
• COVID 19 testing after new decomp
• And most importantly…………..
Thanks for Listening and…

THANKS FOR GETTING VACCINATED!