COVID-19 (the disease) has become a global threat to human health

- In December 2019, an outbreak of a novel coronavirus (SARS-CoV-2)(The VIRUS), started in Wuhan, China\(^1\)
- > 2,600,000 confirmed cases of COVID-19 have now been reported worldwide\(^2\)
- SARS-CoV-2 shares 82% genome sequence similarity to SARS-CoV and 50% genome homology to MERS-CoV\(^1\)
- SARS-CoV-2 binds to target cells through angiotensin-converting enzyme 2 (ACE2) (as does SARS-CoV). ACE2 occurs abundantly on liver and biliary epithelial cells, and the liver is a potential target for infection\(^3\)
- Liver test abnormalities and in some, liver impairment, has previously been reported in up to 60% of patients with SARS and has also been reported in patients with MERS-CoV\(^1\)
- At least seven relatively large-scale case studies in China have reported the clinical features of patients with COVID-19\(^1\)
- 2–11% of patients with COVID-19 had liver comorbidities and 14–53% of cases reported abnormal levels of ALT and AST (dominates) during disease progression\(^1\)
- Higher rates of liver test elevation and possible liver dysfunction appear to be associated with patients with severe COVID-19 disease\(^1\)

3. AASLD: Clinical insights for hepatology and liver transplant providers during the COVID-19 pandemic

Recent Data on studies showing comorbidity with liver disease and liver test change in patients with COVID-19

<table>
<thead>
<tr>
<th></th>
<th>Patients with COVID-19</th>
<th>Patients with pre-existing liver conditions</th>
<th>Patients with abnormal liver tests during disease progression</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guan, et al&lt;sup&gt;1&lt;/sup&gt;</td>
<td>1099</td>
<td>23 (2.3%)</td>
<td>AST abnormal (22.2%) ALT abnormal (21.3%)</td>
<td>Elevated levels of AST were observed in 112 (18.2%) of 615 patients with non-severe disease and 56 (39.4%) of 142 patients with severe disease. Elevated levels of ALT were observed in 120 (19.8%) of patients with non-severe disease and 38 (28.1%) of 135 patients with severe disease</td>
</tr>
<tr>
<td>Huang et al&lt;sup&gt;2&lt;/sup&gt;</td>
<td>41</td>
<td>1 (2.0%)</td>
<td>15 (31.0%)</td>
<td>Patients with severe disease had increased incidence of abnormal liver tests. Elevation of AST level was observed in eight (62%) of 13 patients in the ICU compared with seven (25%) 25 patients who did not require care in the ICU</td>
</tr>
<tr>
<td>Chen, et al&lt;sup&gt;3&lt;/sup&gt;</td>
<td>99</td>
<td>NA</td>
<td>43 (43.0%)</td>
<td>One patient with severe liver function /damage</td>
</tr>
<tr>
<td>Wang, et al&lt;sup&gt;4&lt;/sup&gt;</td>
<td>138</td>
<td>4 (2.9%)</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Shi, et al&lt;sup&gt;5&lt;/sup&gt;</td>
<td>81</td>
<td>7 (.6%)</td>
<td>43 (53.1%)</td>
<td>Patients who had a diagnosis of COVID-19 confirmed by CT scan while in the subclinical phase had significantly lower incidence of AST abnormality than did patients diagnosed after the onset of symptoms</td>
</tr>
<tr>
<td>Xu, et al&lt;sup&gt;6&lt;/sup&gt;</td>
<td>62</td>
<td>7 (11.0%)</td>
<td>10 (16.1%)</td>
<td></td>
</tr>
<tr>
<td>Yang, et al&lt;sup&gt;7&lt;/sup&gt;</td>
<td>52</td>
<td>NA</td>
<td>15 (28.6%)</td>
<td>No difference for the incidences of abnormal liver tests between survivors (30%) and non-survivors (28%)</td>
</tr>
<tr>
<td>Zhang, et al (unpublished)</td>
<td>56</td>
<td>2 (3.6%)</td>
<td>16 (28.6%)</td>
<td>One fatal case, with elevated liver tests and liver injury</td>
</tr>
</tbody>
</table>

Table from Zhang C, et al. Lancet Gastroenterol Hepatol 2020
Surveillance of COVID-19 patients with pre-existing liver conditions is required

Chronic HBV or HCV¹

Patients with chronic liver disease, especially viral hepatitis B and/or C, may be more susceptible to liver damage from SARS-CoV-2, as was the case with SARS-CoV, but supporting data are lacking.

Primary Biliary Cirrhosis or Primary Sclerosing Cholangitis¹

It is unknown whether SARS-CoV-2 infection exacerbates cholestasis in those with underlying cholestatic liver disease such as PBC or PSC or with underlying cirrhosis.

Liver Transplant Recipient or Autoimmune Hepatitis¹

In liver transplant recipients or patients with autoimmune hepatitis on immunosuppressive therapy, acute cellular rejection or disease flare, respectively, should not be presumed in the face of active COVID-19.

 Decompensated Cirrhosis or those awaiting Liver Transplantation¹

There are currently no clear data on the effects of SARS-CoV-2 infection in patients with decompensated cirrhosis or those awaiting liver transplantation.

Additional considerations²

- Liver inflammation in mild cases of COVID-19 is often transient and may return to normal without any special treatment. Liver protective drugs have usually been administered in Chinese patients when severe liver damage occurs.
- Immune-mediated inflammation, such as cytokine storm and pneumonia-associated hypoxia, may also contribute to liver injury or develop into liver failure in critically ill COVID-19 patients.
- Concomitant drug therapies may also result in hepatotoxicties, which may explain some of the variation across cohorts.

¹ AASLD: Clinical insights for hepatology and liver transplant providers during the COVID-19 pandemic
Available at: https://www.thelancet.com/pdfs/journals/langas/PIIS2468-1253(20)30057-1.pdf (Accessed March 2020)

GGT: gamma-glutamyl transferase; HCC: hepatocellular carcinoma; NAs: nucleos(t)ide analogues
Flow chart for the prioritization of patient care in patients with chronic liver disease.

The individual management of these patients strongly depends on the local COVID-19 burden and officially implemented rules and regulations. In some countries and areas, maintenance of standard care might not be able and transplantation activities might be reduced. COVID-19, coronavirus disease 2019; HCC, hepatocellular carcinoma; NAFLD, non-alcoholic fatty liver disease; NASH, non-alcoholic steatohepatitis; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.
AASLD: COVID and the Liver

Major Updates to COVID-19 Clinical Insights Document

4/16/2020

- Emerging data suggest that patients with NAFLD may be at higher risk for COVID-19
- Patients with chronic liver disease and transplant recipients are potentially at increased risk for severe COVID-19 until further data become available
- Consider etiologies unrelated to COVID-19, including other viruses such as hepatitis A, B, and C when assessing patients with COVID-19 and elevated liver biochemistries
  - Updated Figure 1
- Proceed with treatment of hepatitis B and C in patients without COVID-19 as clinically warranted
- Initiating treatment of hepatitis B in a patient with COVID-19 is not routinely warranted but should be considered if there is clinical suspicion of a hepatitis B flare or when initiating immunosuppressive therapy
- Initiating treatment of hepatitis C in a patient with COVID-19 is not routinely warranted
- Consider the following issues in hospitals with a high prevalence of COVID-19:
  - The risk of nosocomial transmission during the transplant admission
  - Difficulty obtaining procedures or other resources when complications arise
  - Limitations on family/caregiver visitation for a postoperative period that often relies on the engagement of caregivers
- Due to cancelations of elective/non-urgent endoscopy:
  - Consider, in the interim, primary prophylaxis with beta blocker therapy for patients with clinically significant portal hypertension or high risk of decompensation
- Data suggest that a surgical mask worn by infected individuals may reduce the risk of transmission (source control)
  - All healthcare workers should wear a surgical mask in patient care settings