



Effects of COVID-19 on Liver and Digestive System

Dr Saeed Hamid

Prof of Medicine

Aga Khan University, Karachi

How does COVID-19 affect the liver and Digestive system?



- ACE 2 is the functional receptor of COV-19.
- This is present in the biliary (20 times higher) and liver epithelial cells.
- Elevated liver biochemistries may reflect a direct virus-induced cytopathic effect and/or immune damage from the provoked inflammatory response.
- Liver biopsies show moderate micro-vascular steatosis and mild lobular and portal activity, but do not show significant damage in hepatocytes or bile duct cells.

- ACE2 is also highly expressed in esophagus upper and stratified epithelial cells, and absorptive enterocytes from ileum and colon.
- Enteric symptoms like diarrhea may occur due to malabsorption by the invaded enterocytes.
- The virus is also present in reasonable quantities in the digestive system and is shed in the stool.
- It continues to be shed in the stool even after the naso-pharyngeal swabs become negative.

Mechanisms of liver damage from COVID-19 infection

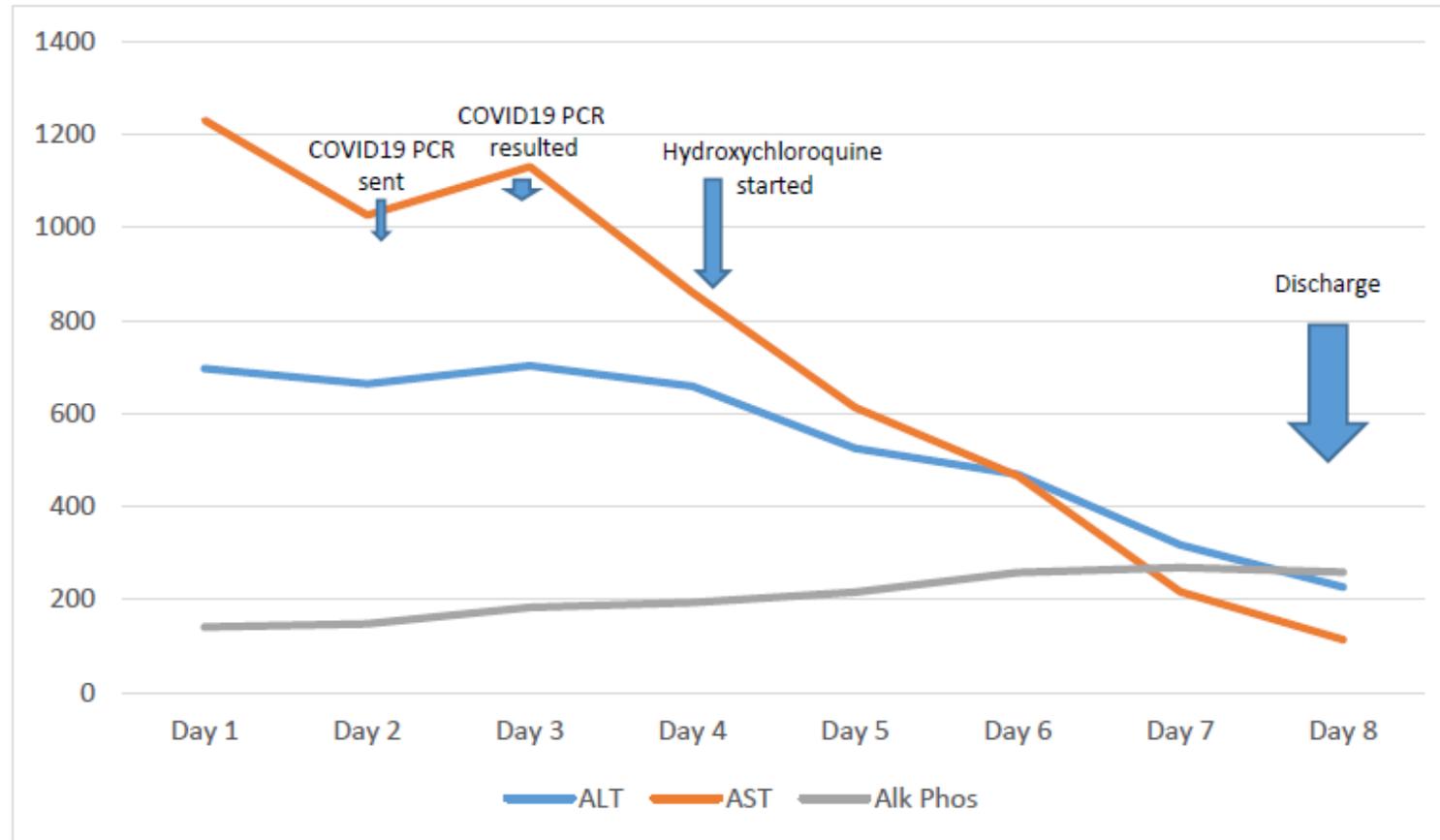


- Direct hepatocyte damage?
- Immune-mediated damage- “Bystander Hepatitis”
- As part of a multi-organ involvement- “Cytokine Storm”
- Drug toxicity

A case of acute hepatitis due to COV-19?

complaint: Dark Urine

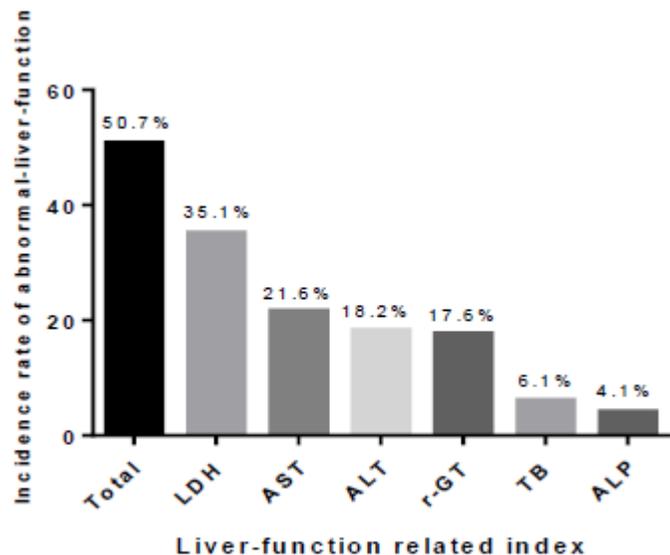
All viral and other acute markers negative





Liver Biochemical tests in COVID-19

- Elevated liver enzymes reported from China in 14-53% of admitted patients.
- Proportion of infected men ranged from 58-73%
- In most cases ALT and AST are raised 1-2 times the ULN at presentation:



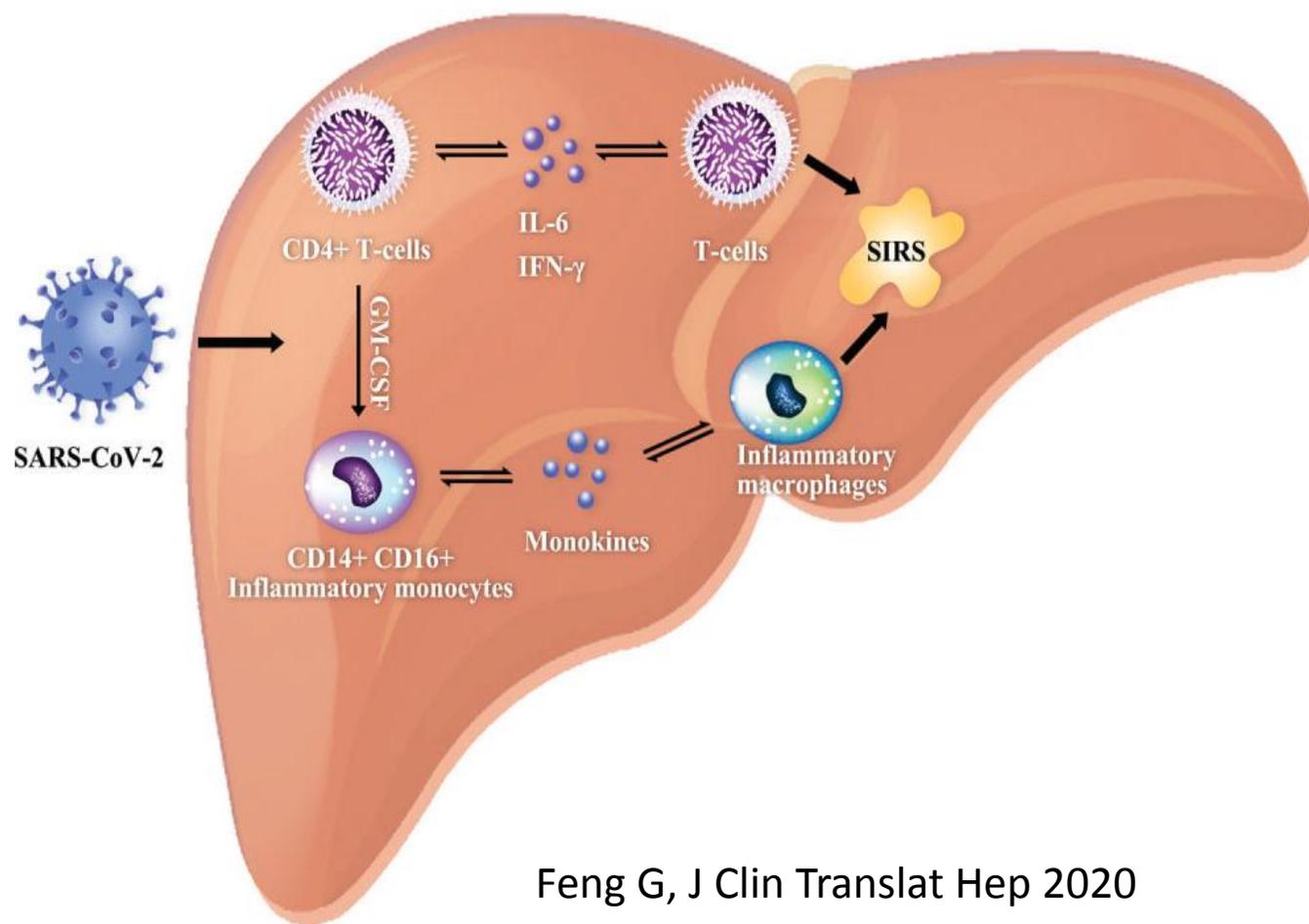
	AST	ALT	Required ICU
> ULN	33%	21%	9.5%
> 2x ULN	10%	5.8%	28%
> 5x ULN	2.4%	1.6%	39%*

Data on 1076 presenting to CMC, NY

* No difference in age, ethnicity and BMI

- ALP and GGT levels might increase disproportionately to ALT/AST levels in some cases.
- Low Albumin predictor of severe disease

The systemic inflammatory response syndrome induced by COVID-19- The Cytokine Storm



Feng G, J Clin Translat Hep 2020

In 52 critically ill patients with multiple organ damage:

- 35 (67%) had ARDS
- 15 (29%) had acute kidney injury
- 15 (29%) had liver injury
- 12 (23%) had cardiac injury

Liver failure not listed as a cause of death for any patient so far.

Yang X, Lancet Respir Med 2020

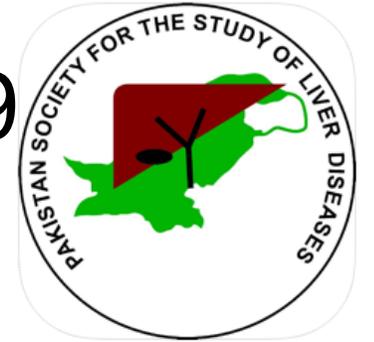
Impact of COVID-19 in patients with chronic liver disease



- No evidence so far suggests that patients with controlled chronic hepatitis B or C virus infection are at increased risk of COVID-19 infection.
- CDC Data: 0.6% (N=41) of 7162 COVID-19 cases underlying chronic liver disease.
- Chinese Data: 2-11% of patients had comorbid chronic liver disease.
- Infection with COVID-19 may impact existing chronic liver disease in three ways:
 - Lead to hepatic decompensation in patients with compromised hepatic reserves.
 - Lead to viral reactivation in patients with chronic viral hepatitis.
 - Drugs used for treatment of COVID-19 may produce hepatotoxicity.

Include testing for SARS-CoV-2 in patients with acute decompensation or ACLF.

Impact of Chronic liver Disease on COVID-19 Infection



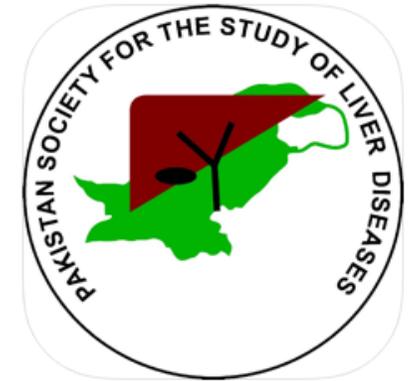
- Pre-existing liver disease is not yet specifically listed in the comorbid conditions leading to poor prognosis. IT SHOULD BE.
- Elevated ALT levels, reduced platelet counts and reduced albumin levels at admission have been associated with higher mortality.
- Quite likely, patients with liver cirrhosis-associated immune dysfunction, liver transplant and autoimmune diseases patients who are on immuno-suppression remain at increased risk for COVID-19.
- Chronic hepatitis B virus infection does not seem to affect COVID-19 outcomes.
- Patients NAFLD may have comorbidities such as diabetes, hypertension and obesity putting them at increased risk of a severe course of COVID-19.

Potential Liver Toxicity due to COVID-19 therapies under study



- Remdesivir:
 - 23% patients in the compassionate use study developed liver enzyme elevations.
 - Two patients discontinued due to significantly elevated liver enzymes.
- Hydroxychloroquine:
 - Clinically apparent liver injury is rare.
- Chloroquine:
 - Has rarely been linked to serum aminotransferase elevations or to clinically apparent acute liver injury.

Recommendations for assessing liver function in patients with COVID -19



ILCA:

- Baseline liver tests (ALT, AST, ALP, GGT, albumin, total bilirubin, and PT/INR) are strongly recommended.
- All patients with COVID-19 should be regularly monitored with LFTs, particularly severe cases.
- In patients who have jaundice or hyperbilirubinemia, the need for imaging and other procedures should be carefully considered to minimize unnecessary exposure.

AASLD:

- Test for hepatitis B and C in patients with COVID-19 and elevated liver tests.
- Ultrasound or other advanced imaging should be avoided, if possible.
- The presence of abnormal liver tests should not be a contraindication to using investigational or off-label therapeutics for COVID-19.
- Regular monitoring of liver tests.

COVID-19 and Elevated Liver Enzymes



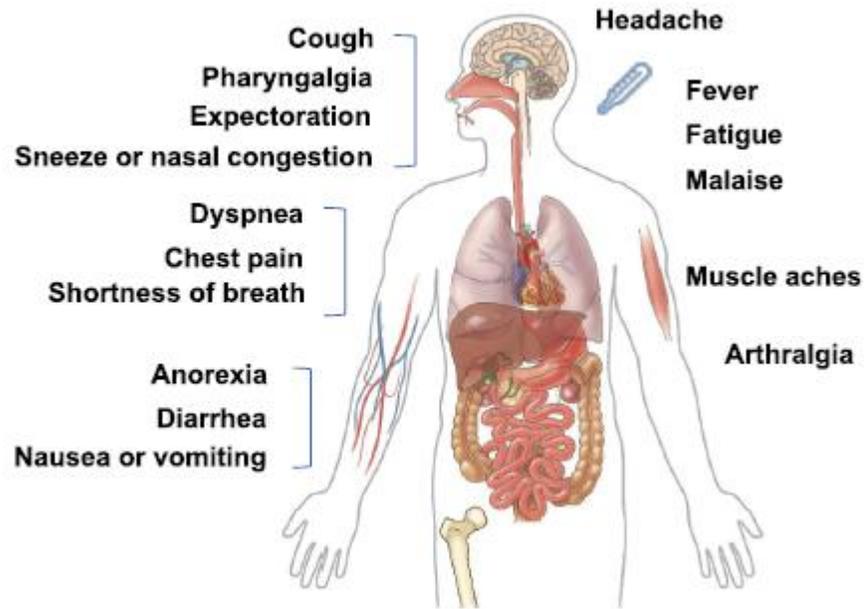
- Mild liver enzyme elevations relatively common.
- Severe elevations likely in severe disease.
- Initial work up recommended.
- Consider if there is underlying CLD.
- Exclude other causes of elevated liver enzymes in critically ill patients:
Sepsis, Ischemia, DILI etc.

COVID-19 and Liver Disease: Unanswered Questions

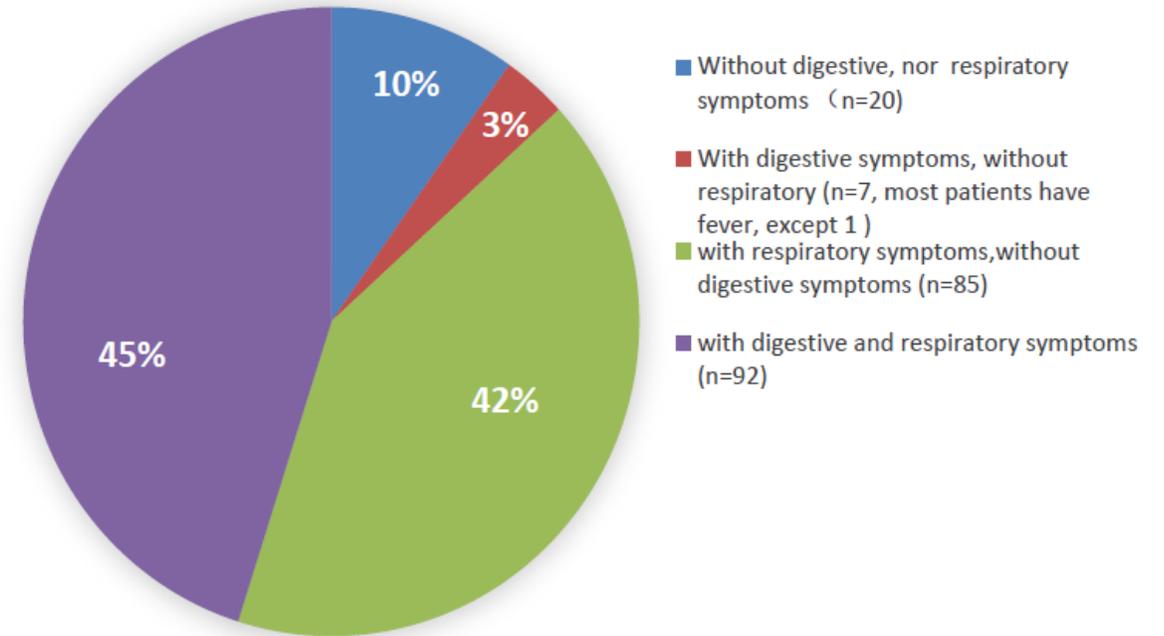


- Remains unclear at this point to what extent chronic liver diseases should be considered as risk factors for a severe disease course of COVID-19 infection.
- Does COVID-19 lead to ACLF in patients with compensated liver disease?
- Can patients with stable CLD be enrolled in therapeutic studies of COVID-19?
With caution.

COVID-19 and GI Symptoms



Frequency of COVID-19 patients with or without digestive symptoms



Nausea or vomiting (5.0%).

Diarrhea (2-10%).

Guan WJ, NEJM 2020

48% presented to hospital with digestive symptoms as their chief complaint.

Lei Pan, AJG 2020

Clinical characteristics of COVID-19 patients with digestive symptoms in Hubei, China



- Multicenter study of 204 patients with confirmed COVID-19 infection.
- Patients with digestive symptoms had a significantly longer time from onset to admission than patients without digestive symptoms (9.0 days vs 7.3 days).
- As the severity of the disease increased, digestive symptoms became more pronounced.
- Patients without digestive symptoms were more likely to be cured and discharged than patients with digestive symptoms (60% vs. 34.3%).
- The index of suspicion may need to be raised earlier in at-risk patients presenting with digestive symptoms.
- ACG- FOR IMMEDIATE RELEASE (Bethesda, Maryland, March 18, 2020)

Impact of COVID-19 on pre-existing GI diseases



- Given the use of biologics and immunosuppressive agents, whether patients with inflammatory bowel disease (IBD) are more susceptible to SARS-CoV-2 infection has raised great concern.
- Chinese IBD Society issued official guidelines for managing patients with IBD in early February 2020.

COVID-19 and GI diseases: Summary



- COVID-19 infection can present primarily with GI symptoms, well before respiratory symptoms develop. So be AWARE.
- COVID-19 can have prolonged shedding in the stool of recovered patients.
- Is this shedding infectious?
- Should we delay colonoscopy for at least 4-6 weeks?
- What effect can it have on IBD patients?