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Editorial

COVID-19 and liver dysfunction

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Dear Editor,

It's been a year now since the beginning of the COVID-19 pandemic which has wreaked havoc in the healthcare delivery system and economic devastation. There has been a race against time for the discovery of vaccine which has finally resulted in the war footing approval and usage of vaccines globally. The world salutes the healthcare professionals but we stand looking poignantly into life and salute the true hero of the pandemic "the common man" with the elated sense of social responsibility, camaraderie and survival. With the globe affected, it's the common man who stayed home, maintained social distancing and cooperated with healthcare authorities and Governments through the difficult times. Each country is affected with distinct demographics and with varied presentations of the individual disease.

The increase in mortality and morbidity is observed with advanced age and existence of comorbidities like obesity, diabetes mellitus, hypertension and chronic lung disease.[1] Fever, cough and dyspnea are the usual symptoms associated with the onset of COVID-19 progressing to acute respiratory distress syndrome and complications.[2] Apart from this constellation of symptoms, gastrointestinal symptoms including nausea and vomiting, and diarrhea are also noticed.[3] Various studies have demonstrated abnormalities of liver function tests revealed by elevated alanine aminotransferase (ALT) and aspartate aminotransferase (AST) with marginal increase of total bilirubin.[4, 5]

This affliction of liver function may be either due to direct effect of COVID-19 or secondary liver injury. The direct effect might be attributed to SARS-CoV-2 directly binding to Angiotensin-Converting Enzyme (ACE2) positive cholangiocytes and causing liver damage leading to liver test dysfunction in COVID-19 patients.[6]

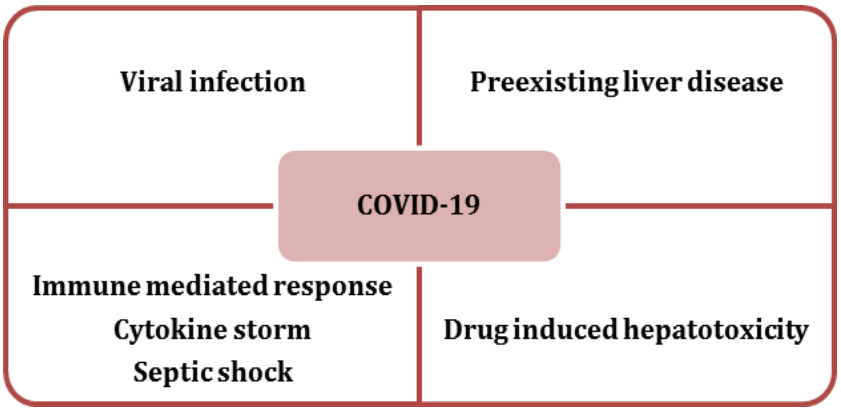
The overall frequency of various abnormalities in liver function in COVID-19 is depicted in the table below[7]

Liver function parameter	Pooled prevalence (%)	95% CI & I^2 statistics
Hyperbilirubinemia	10.98	95% CI 6.87–17.08; I^2 94%
Alanine aminotransferase	23.28	95% CI 19.92–27.01; I^2 90%
Aspartate transaminase	23.41	95% CI 18.84–28.70; I^2 95%
Alkaline phosphatase	7.48	95% CI 3.91–13.83; I^2 75%
Gamma glutamyl transferase	27.94	95% CI 18.22–40.27; I^2 93%
Hypoalbuminemia	61.27	95% CI 48.24–72.87; I^2 91%
Increased globulins	20.17	95% CI 4.73–56.25; I^2 95%

In a study by Saini RK et al, it was observed that out of the 89 patients with raised liver enzymes, Intensive Care Unit (ICU) facility was required for 33 patients (37.07%), while in patients with normal liver enzymes only 21.15% required ICU care. ICU requirement was found to be more pronounced in patients with liver injury, where 23 out of 43 (52.48%) were admitted in ICU (p=0.0005).[8]

The etiology of this liver injury in COVID-19 might be due to the viral infection of the liver. There is also possibility of drug induced hepatotoxicity as evidenced by the varied manifestations of liver injury across different population.[9] Cytokine storm arising due to the immune mediated inflammation might also be the cause of liver injury and even leading to liver failure in COVID-19 patients who are critically ill.[10] The spectra of biologically induced liver injury and chemically induced liver injury include viral hepatitis, non-alcoholic fatty liver disease and alcoholic liver disease. These already have a significant health burden on the society.[11] Persistent liver injury due to preexisting liver disease might be exacerbated during active viral replication following COVID-19. Individuals with systemic immunocompromised status due to liver cirrhosis or liver cancer are more susceptible to COVID-19 infection.[12]

Figure 1: Etiological factors of liver injury in patients with COVID-19



Considering these, liver function should be meticulously evaluated in COVID-19 with a focus on the comorbidities, immunocompromised status, advanced age and preexisting liver disease. This in turn puts the impetus on tailored therapeutics for each group and the need for predictive biomarker in liver injury which is an evolving area of research in hepatology.

According to the National Institute of Health, a biomarker is defined as "A characteristic that is objectively measured and evaluated as an indicator of normal biologic processes, pathogenic processes, or pharmacologic responses to a therapeutic intervention".[13] The advent of instrumentation and technology has led to the mining of biomarkers in the de novo approach of metabolomics, transcriptomics, proteomics and lipidomics. Mechanism based biomarker discovery has also benefitted with the advancement of technology leading to identification of specific relevant markers in various diseases. Novel biomarkers predictive of liver injury in COVID-19 may be identified through large scale multiomics based biomarker detection. However, validation of such biomarkers poses a greater challenge.

The impairment of ALT, AST and other liver function test parameters is not salient feature of COVID-19 and these changes are acute nonspecific due to inflammation.[14] However, further research into the pattern and characteristics of the traditional markers of liver function test could provide useful insight in COVID-19 management. There is also a forecast of increased rates of obesity, increased alcohol consumption and may be the cause of liver disease burden on society and healthcare delivery services following the pandemic which is not quantified. Hence, health education is also a priority which should be highlighted along with the preventive measures of physical distancing, use of sanitizers and wearing masks.

Authors would like to end our opinion stating that COVID-19 a multifaceted disease shall not spare any organ or individual. "Social distancing, Hand hygiene and Face masks" should be the priority beyond vaccination.

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