Involvement of liver in COVID-19: systematic review and meta-analysis

We have read with interest the recent study by Qi et al.1 Currently, the impact of COVID-19 on the liver remains unexplored. Although majority of patients with COVID-19 have abnormal liver function, most studies on COVID-19 only attribute the severity of disease on the ground of respiratory complications. Thus, we aimed to perform a meta-analysis to estimate the prognosis of patients with COVID-19 stratified according to liver injury. Our meta-analysis includes nine studies2–10 with a total of 2115 patients (online supplementary file).

Abnormal liver function in patients with COVID-19 is possibly multifactorial; that is, drug-induced liver injury (DILI), severe acute respiratory syndrome coronavirus 2 replications in the liver10 and interorgan cross-talk in acute inflammation.9 Published studies on COVID-19 have shown that 37.2%–76.3% of patients have abnormal liver function.2,9 Similarly, the prevalence of liver injury is reported in about 21.5%–45.71% of patients.2,10 Generally, 7.14%–64.15% of patients with COVID-19 had increased aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyltransferase (GGT) and bilirubin levels, whereas albumin was decreased to 27.9–33.0 g/L in non-survivor patients.6 Besides, patients with COVID-19 with chronic liver disease (CLD) might develop decompensated liver as a systemic inflammatory response induced by COVID-19.1 We found that the prevalence of CLD was 4% (95% CI 1.5 to 6.4, I²=89%) among patients with COVID-19, with cirrhosis and hepatitis B being the most common. Likewise, the incidence of liver injury was 27% (95% CI 18.2 to 35.8, I²=97%; figure 1).2–10

Of note, older patients with COVID-19 had a higher risk of liver injury (standardised mean difference (SMD): −0.81, 95% CI −1.22 to −0.41, I²=0%, p<0.0001). Meanwhile, insignificant difference was observed in the usage of other drugs.8 Our analysis found that the liver injury group had considerably more use of lopinavir/ritonavir than the group without liver injury (OR: 4.15, 95% CI 2.36 to 7.29, I²=0%, p<0.00001). Moreover, patients with COVID-19 with liver injury had a high prevalence of liver injury,10 and patients with COVID-19 had increased inflammatory markers like interleukin-6, erythrocyte sedimentation rate (ESR), D-dimer, ferritin, neutrophil counts and C reactive protein (CRP), suggesting a ‘cytokine storm’. Concurrently, our meta-analysis showed a significantly lower absolute lymphocyte count (SMD: −0.81, 95% CI −1.82 to 0.20, I²=62%, p<0.0001) and higher ESR (SMD: 1.63, 95% CI 0.61 to 2.70, I²=90%, p=0.002) in the liver injury group compared with the non-liver injury group. However, no remarkable difference in CRP and absolute neutrophil count was observed between the two groups.

As evidence, DILI should not be overlooked in patients with COVID-19. Cai and colleagues found that the use of lopinavir/ritonavir was significantly associated with liver injury.2 Contrarily, Fan et al did not find any difference in the prevalence of liver injury among patients with and without medication.9 Our analysis found that the liver injury group had considerably more use of lopinavir/ritonavir than the group without liver injury (OR: 4.15, 95% CI 2.36 to 7.29, I²=0%, p<0.00001). Meanwhile, insignificant difference was observed in the usage of other drugs.

Furthermore, we also examined the prognosis of patients with COVID-19 with liver injury, and we found that patients with liver injury had obviously more severe disease (OR: 2.57, 95% CI 1.25 to 5.26, I²=62%, p=0.01), and a higher prevalence of mortality (OR: 1.66, 95% CI: 1.04 to 2.64, I²=35%, p=0.03) (figure 2).6–9 However, length of hospital stay was not significantly different among the groups (SMD: −0.61, 95% CI −2.37 to 1.15, I²=98%, p=0.50). The overall rate of severity and mortality in patients with COVID-19 with liver injury was 53.5% (130/243) and 23.5% (42/179),6–9 respectively.

To conclude, patients with COVID-19 have a high prevalence of liver injury, and patients with COVID-19 with liver injury are at an increased risk of severity and mortality. Thus, special attention should be given to any liver dysfunction while treating patients with COVID-19.
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