

# World Journal of *Hepatology*

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**ABOUT COVER**

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*WJH* mainly publishes articles reporting research results and findings obtained in the field of hepatology and covering a wide range of topics including chronic cholestatic liver diseases, cirrhosis and its complications, clinical alcoholic liver disease, drug induced liver disease autoimmune, fatty liver disease, genetic and pediatric liver diseases, hepatocellular carcinoma, hepatic stellate cells and fibrosis, liver immunology, liver regeneration, hepatic surgery, liver transplantation, biliary tract pathophysiology, non-invasive markers of liver fibrosis, viral hepatitis.

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## COVID-19 and liver disease: Are we missing something?

Tarana Gupta

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### Abstract

Since the coronavirus disease 2019 (COVID-19) has hit the world as a pandemic, researchers all over the world have worked on its diagnostics, prognosticating factors, *etc.* The present study showed liver enzymes, especially aspartate aminotransferase (AST) levels, to be high in non-survivors with raised AST/alanine aminotransferase ratio. Considering the non-specific nature of AST with its presence in organs other than liver such as muscle, heart, kidney and brain makes it difficult to interpret. Even pre-existing metabolic syndrome and non-alcoholic fatty liver disease are confounding factors for deranged liver functions detected during COVID-19 disease. Therefore, the results of the study should be taken with caution.

**Key Words:** COVID-19; Liver disease; Transaminases; Non-alcoholic fatty liver disease; Hepatocytes; Cholangiocytes

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**Core Tip:** The presence of angiotensin converting enzyme 2 receptors in liver endothelial cells makes it susceptible to severe acute respiratory syndrome coronavirus 2 injury. The authors have suggested raised aspartate aminotransferase (AST) levels in almost a third of non-survivors along with high AST/alanine aminotransferase ratio. Considering the presence of AST in organs other than liver such as muscle, red blood cells, heart and kidney, makes the interpretation difficult. Additionally, pre-existing non-alcoholic fatty liver disease has also been documented as a risk factor for severe coronavirus disease 2019 (COVID-19) disease. Therefore, more studies are needed for evaluation of AST as a predictive factor for severe COVID-19 disease.

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## TO THE EDITOR

We read with great interest the article by “Madian *et al*[1]”. Limited data is available for hepatic injury in coronavirus disease 2019 (COVID-19) disease. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus causes direct cytopathic effect on hepatocytes. It enters the cell through angiotensin converting enzyme 2 (ACE2) receptors which are ubiquitously present on alveolar epithelium, liver, kidney and blood vessels *etc.* ACE2 receptors are present on endothelium of smaller blood vessels in liver, however, sparse on sinusoidal endothelium. Chai *et al*[2] reported higher ACE2 expression on cholangiocytes (59%) than hepatocytes (2.6%). They also suggested that liver dysfunction in COVID-19 is predominantly due to cholangiocyte dysfunction. The profound cytokine storm generated by lung injury also results in liver dysfunction. The drug-related hepatotoxicity related to the use of acetaminophen, remdesivir, lopinavir/ritonavir, azithromycin *etc.* during treatment of COVID-19 disease plays an additive role in causing deranged liver functions[3]. In addition, use of steroids especially in moderate to severe cases can also cause hepatitis B flare in occult hepatitis B patients.

Only a few studies could highlight liver function tests in patients with COVID-19 in non-cirrhotic patients. Limited studies have shown acute liver injury in 14%-53% of COVID-19 cases. In the present study, aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels were elevated in 31% and 3% among non-survivors respectively with 48% having AST/ALT ratio > 1.2. Zhang *et al*[4] showed raised AST levels more frequently in intensive care unit (ICU) patients (62%) than in non-ICU (25%) settings. Interestingly, the present study revealed an increased in-hospital mortality up to 11-and 13-fold with AST levels > 1 ULN and > 2 ULN respectively. Chen *et al*[5] analyzed biochemical profile of 113 deceased and 161 recovered patients in Wuhan, and found abnormal AST levels in 59 (52%) *vs* 25 (16%) and lower serum albumin in 74 (65%) *vs* 22 (14%) patients respectively. In the present study, authors also mentioned the possibility of raised AST levels due to muscle injury resulting from profound cytokine storm in COVID-19 illness, though they have documented normal creatine kinase (CK) values indicating liver involvement. AST is an enzyme which is found in liver, muscle, heart, kidney and brain. Therefore, raised AST levels should be taken with caution. The pattern of liver injury in COVID-19 disease is elevated AST levels more than ALT levels with higher gamma-glutamyl-transferase (transpeptidase) (GGTP) values which is similar to alcoholic hepatitis.

We should not forget that non-alcoholic fatty liver disease (NAFLD) and obesity are associated with symptomatic, severe and complicated COVID-19 disease and is a potential confounder[6]. The studies assessing the role of liver injury on the course of COVID-19 illness have not screened patients for NAFLD, and we are not aware about their basic liver function tests before COVID-19. A pooled analysis of 8 studies in NAFLD and COVID-19 by Sachdeva *et al*[7] revealed NAFLD being a predictor of severe COVID-19 disease after adjustment of presence of obesity (OR: 2.3; 95%CI: 1.9-2.9, *P* < 0.001). Therefore, it may be too early to depend alone on AST levels for the severity and outcome of COVID-19 illness.

## FOOTNOTES

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