

## **Responses to the issues raised in the peer-review reports**

Reviewer #1:

1.The title need to be more fascinating.

Answer: The title has been modified into “Remarkable gastrointestinal and liver manifestations of COVID-19: A clinical and radiologic overview”.

2.The article necessitate of some image to capture the reader.

Answer: I have added a few images (Fig.1-5) in the corresponding paragraphs (“radiographic manifestations of gastrointestinal tract injury” and “radiographic manifestations of liver injury”).

Reviewer #2:

1. The severity of the gastrointestinal and liver manifestations is unclear.

The authors should add comments on that point in addition to the impact of those complications in the management of patients with COVID-19.

Answer: Complement contents about the severity of the gastrointestinal and liver manifestations (paragraphs “pathogenesis of covid-19-associated gastrointestinal injury” and “pathogenesis of covid-19-associated liver injury”) as follows: “As has been reported before, nausea, vomiting, diarrhea, and loss of appetite were the main gastrointestinal symptoms of patients with COVID-19 infection. More severely, there were previous reports of esophageal bleeding, mesenteric artery embolism, intestinal perforation and hemorrhagic colitis of patients with COVID-19 infection.

If not promptly treated, these lesions can lead to shock finally. And coronavirus-infected patients presenting with gastrointestinal symptoms had longer duration from illness onset to hospital admission.

COVID-19 may do harm to liver and can finally result in severe body damage. On one side, as is known that non-alcoholic fatty liver disease (NAFLD) is a major cause of liver cirrhosis and hepatocellular carcinoma. On the other side, coronavirus-infected patients with metabolic syndrome and liver steatosis are more likely to develop drug-induced liver injury. In addition, it was revealed that coronavirus-infected patients with chronic liver disease (CLD) were at a higher risk of prolonged hospitalization and death. Besides, for those patients who complicated with CLD, decompensated cirrhosis and hepatocellular carcinoma may be predictors of higher overall mortality during the course of infection.”

2. The mechanism of fatty change of the liver should be discussed.

Answer: Complement contents about the potential mechanism of fatty change of the liver (paragraph “pathogenesis of covid-19-associated liver injury”) as follows: “So far, the mechanism of fatty change of the liver has not been certainly discussed. Potential association between novel coronavirus infection and hepatocyte steatosis may due to the following factors. Firstly, disorganized intestinal flora can increase the absorption of monosaccharides, which in turn promote the synthesis of fatty acids and triglycerides in the liver by increasing the activity of acetyl-CoA

carboxylase and fatty acid synthase. Secondly, the drugs. Patients with COVID-19 received medicine treatment by taking some kinds of drugs which may induce an acute energy crisis by interrupting adenosine triphosphate (ATP) synthesis by mitochondria, resulting in microvesicular steatosis. Thirdly, ACE2 plays an important role in releasing cytokines produced through the c-Jun N-terminal kinase (JNK) and I $\kappa$ B kinase- $\beta$  (IKK- $\beta$ ) pathways in COVID-19 patients, which induce insulin resistance and lead to ectopic accumulation of fat in various organs, including the liver.”