

Dear Editor,

Revised version is being uploaded with references formatted as per guidelines.

Highlighted green references do not have either PMID or DOI

Highlighted yellow references are weblinks.

Please let us know how can we upload the powerpoint for the figures and first page of articles that do not have PMID or DOI as there is link or way to upload these files?

Kind regards,

Dalbir S Sandhu, MD

Dated – April 25, 2020

Dear Reviewers.

We sincerely appreciate your efforts to review our paper in an expedited manner.

Please find below description of each reviewer's comment and how it has been addressed.

Kind regards,

Dalbir S Sandhu, MD

#### **Reviewer # 1**

This is a narrative review of the gastrointestinal manifestations of SARS-CoV-2/COVID-19. This topic is obviously of great interest currently and the field is rapidly evolving.

This appears to be a fairly comprehensive review of papers published to date on this topic and will therefore likely be of interest to readers.

We thank the reviewer for this generous comment.

I have a few comments/questions that I think should be addressed prior to publication.

These are generally minor. 1) What methods were employed to identify pertinent articles?

Was a systematic review undertaken with a formal search strategy? If so, then please include these methods. (If not the case, this is still acceptable).

***A separate section on methodology is added. Briefly, we queried PUBMED and also searched GOOGLE for all published and in-press papers using the search terms as described.***

2) I have some concern about how the recommendations of the IOIBD group on IBD therapies are presented. For example, the authors state that it is recommended that patients who develop COVID-19 illness NOT stop medications like anti-TNF and ustekinumab. The IOIBD guideline available

at [https://www.gastrojournal.org/article/S0016-5085\(20\)30465-0/pdf](https://www.gastrojournal.org/article/S0016-5085(20)30465-0/pdf) in fact recommend that anti-TNF and ustekinumab (and others) be stopped in patients who develop COVID-19 (in contrast to patients who only test positive for the virus without COVID-19 disease). Care should be taken to ensure that the recommendations from this guideline are accurately presented in this review. For example, it is recommended not only that prednisone >20 mg/day be stopped in patients with proven infection but also as a precaution to PREVENT infection.

***We sincerely thank the reviewer for this detailed comment. As the situation is evolving the recommendations from IOIBD are also getting updated. We have included the most up to date recommendations in the revised version and have included all suggestions pertaining to anti-TNF, ustekinumab and steroids.***

3) There are several instances of acronyms appearing throughout the text without being spelled out (WHO, SIRS, TNF). Please spell out at first mention.

***We thank the reviewer for this comment. This has been addressed in the revised manuscript.***

4) A description of reports of COVID-19 in patients with underlying liver disease and IBD is given. A comment on whether outcomes/mortality rates are higher in these patients compared to the general population would be very informative and of great interest to readers (i.e., how do the outcome rates in patients with underlying GI disease compare to outcomes rates (severe disease, mortality) in the general population?

***We thank the reviewer for this comment. Based on current published literature no statistically significant association has been reported in the outcomes of COVID-19 in patients with underlying chronic liver disease or IBD. This statement has been added on page 8***

The abstract states: Lastly, patients with underlying gastrointestinal diseases such as chronic liver disease and inflammatory bowel disease may at higher risk of developing more severe disease. It is difficult to make this claim without comparing outcome rates to those in the general population.

***We thank the reviewer for this comment. This statement has now been revised to state ‘Further research will help elucidate the association between patients with underlying gastrointestinal diseases such as chronic liver disease and inflammatory bowel disease and severity of COVID-19’.***

5) It is stated: Although there is anecdotal mention of a more severe course of COVID-19 in patients with concurrent gastrointestinal symptoms, no definite association has been established. Please provide a reference.

***We thank the reviewer for this comment. Since this was a controversial statement and was generated from case reports we deleted this sentence in the revised manuscript.***

6) It is stated: it is important for clinicians to not be distracted by minimally elevated liver enzymes and focus on viral control and supportive care. What is meant by “viral control” as there are no proven antiviral therapies, as I understand it.

***We thank the reviewer for this comment. There are currently no proven antiviral therapies (although several are being tested). We changed this sentence to now state 'focus on general management and supportive care'.***

7) Suggest using the term “healthcare workers” or “healthcare providers” rather than caregivers.

***Thank you for this comment. This has been now changed to healthcare providers.***

8) Are there any guidelines or position statements on the approach to FMT during the pandemic (i.e., should elective FMT be suspended?). If so, please add a brief mention of recommendations.

***Thank you for this comment. Added information is now provided in the revised manuscript under FMT on page 8.***

9) In Figure 1, is it known that hepatic dysfunction is the cause of elevated LDH?

***Thank you for this comment. It is postulated that the cause of elevated LDH is likely related to hepatic dysfunction so we included it in the figure.***

**Reviewer #2:** It is well-written reviews about gastrointestinal and hepatic manifestatins of COVID-19. It's important to get this kind of paper out soon, so I reviewed it in a hurry. There are only some minor points the author should. In the abstract, SARS-Co-V-2, AST, ALT, ACE2 should not be abbreviated because they are written only in once.

***Thank you for this comment. This has been addressed in the abstract section of the revised manuscript.***

In page 5, it is better to change title of the "Hepatobiliary manifestations" to "Hepatic manifestations" because biliary manifestaton is not reported in this section

***Thank you for this comment. This has been changed to hepatic manifestations in the revised manuscript.***

In page 8, SECURE-Cirrhosis should be abbreviated and

***Thank you for this comment. This has been addressed in the revised manuscript.***

In line 13, Americas is correct ?, not the US ?

*Thank you for this comment. Americas is a term used for including both North and South America so we used Americas (<https://www.britannica.com/place/Americas>)*

**Reviewer #3:** Nowadays , COVID-19 become a global pandemic. The authors discussed gastrointestinal and hepatobiliary manifestations, the concern for fecal-oral transmission and the impact of COVID-19 on underlying gastrointestinal diseases. There are some new information in this review.

*We thank the reviewer for this comment and for reviewing our manuscript.*