

Dear editor,

Thank you very much for sending us the valuable comments and critiques of the three reviewers on our manuscript (**Journal title:** *World Journal of Clinical Cases*. **Manuscript NO:** 62897. **Title:** *COVID-19 in gastroenterology and hepatology: lessons learned and questions to be answered, by Sun et al., 2021*), which is very helpful to improve the quality of our paper. The present manuscript has been revised thoroughly, and all the modifications were marked in red. We hope the revised version could meet the requirements for publication. The comments and the critiques of the reviewers have been addressed and itemized as follows:

Reviewer #1: The authors submit a review looking at COVID-19 in gastroenterology and hepatology. Overall, this is comprehensive, but there are major and minor points that the authors may consider. The elaboration part of Gastrointestinal Endoscopy in COVID-19 is not detailed enough, slightly vague. Consider including the three-level protection and infection monitoring strategy of endoscopic diagnosis and treatment during COVID-19 pandemic in this part. What is the difference between management of COVID-19 and the other infectious diseases? Please discuss this. Please put forward your own opinions and recommend the readers "How to apply this knowledge of COVID-19 in gastroenterology and hepatology in the community hospitals?" Finally, please define all abbreviations (eg GIT) at the first use.

Re: We really appreciate your insightful advice. We have now detailed elaborate the Gastrointestinal Endoscopy in COVID-19.

However, different countries have different incidences of COVID-19 and the

capacities for the performance of semi-urgent endoscopy. Hence there are heterogeneities among guidelines by leading organizations in different countries. In general, all organizations agree that cases should be individually assessed and reviewed pre-endoscopy, and elective non-urgent cases should be deferred depending on risk assessment, whereas for emergent cases, endoscopy should be performed in negative pressure room (*Teng M, et al. World Journal of Gastrointestinal Endoscopy, 2020*).” Polymerase chain reaction (PCR) testing should be performed before endoscopy to protect staff and prevent mass nosocomial infection.

To ensure a safe environment for patients and prevent infection to the endoscopy units, endoscopy staff are on the verge of significant changes and evolution. Cennamo et al. reported a practical model of GI endoscopy unit during the COVID-19 emergency, namely fast reorganization of the endoscopy department environment by means of a risk-based color-coding redesign of current spaces: waiting room, recovery room and endoscopy suites; implementation of new areas including check points, areas for changing personal protective equipment (PPE) and droplet areas; and create separate pathways and processes according to the new color-code design and dedicated areas (*Cenamo V et al, Digestive and liver disease : official journal of the Italian Society of Gastroenterology and the Italian Association for the Study of the Liver, 2020*). COVID-19 is likely to change the traditional mode of endoscopy to not only protect our patients, colleagues, and staff from COVID-19, but also help us to conquer future epidemic (*Peerly AF et al, Am J Gastroenterol, 2020*).

Moreover, we are deeply sorry for the careless mistake, and we have now defined all

the abbreviations at the first use.

Reviewer #2: A review that attempt to cover and contain everything about SARS-CoV-2. I think this article is vague and general in content and must be substantiated.

Re: This is really a thorny, but thought-provoking question. We really appreciate your valuable advice. Now we have revised the entire manuscript and tried our best to enrich the content of our manuscript.

Reviewer #3: I read with interest the manuscript by S. Liu et al. The article is a literature review, aimed to systematize current knowledge on gastrointestinal and liver manifestations of the novel coronavirus infection, SARS-CoV-2. The subject is actual, however, due to the current trend of priority publishing COVID-related data, a number of papers with most the same titles and that refer the same original articles are present in the global databases. Therefore, I would suggest to make the current paper more specific, at least in the title and also mention this information in the background section of the paper. According to the general recommendation for this type of papers (see PRISMA guidelines: <https://www.equator-network.org/reporting-guidelines/prisma>), there is a need for more detailed description of the process of data collection, assessment and handling. Please, add more details on the databases searched, types of papers enrolled, quality of the source paper assessment etc. The review would change to the better, in case the

flow diagram or more details on the total number of the source papers identified, and the number of papers excluded (and why) are provided. It seems that all the manifestations associated with SARS-CoV-2 infection may be divided to caused by COVID-19 itself, and those related to the provided treatment. Could you please mention how these manifestations were distinguished (otherwise, add this limitation to the appropriate section)? Please, consider to make a revision of points in "Answered Questions/Future research directions" section. To my knowledge, classification of grades of severity of gastrointestinal symptoms exists already. However, it is correct that these grades have not been widely used by the authors of original papers. This section also requires language polishing. Please, check whether all of the mentioned points of this section is really supported in the section of results.

Re: Thank you very much for giving us an opportunity to revise our manuscript. The manuscript was written as a narrative review. To revise it as a systematic review and follow PRISMA guidelines will require an extensive revision and time. If a narrative review is un acceptable, we would like to withdrawal the submission. Thanks.

As we said in manuscript, GI symptoms is the common adverse drug reactions. Moreover, drug-induced hepatotoxicity (antiviral medications, anti-malaria medications, antibiotics, steroids) were not uncommon. Other treatment such as the high levels of positive end-expiratory pressure (PEEP) implemented in COVID-19 infections may also cause hepatic congestion. Thus, it is difficult to distinguish whether the manifestations were caused by COVID-19 itself, or related to the provided treatment. An in-depth discussion of the past history and present history of

patients, clinical experience of doctors, and the understanding of ADR of pharmacists will all influence the judgement. We have added this point to limitation section according to your valuable suggestion.

We are very sorry for the unprofessional speaking, it's the truth that classification of grades of severity of gastrointestinal symptoms exists already. However, these grades have not been widely used by the authors of original papers. The misleading statement has been changed "Standardized criteria for diagnosis, and grading the severity of GI symptoms are missing in present original studies relate to COVID-19" to make it more rigorous.

In addition, we have carefully checked the language and syntax of this manuscript in an attempt to avoid any grammatical errors and badly worded/constructed sentences.

In addition, we have enlisted the help of several colleagues who are proficient in English. We believe that the language now is acceptable for review process.

Lastly, all of the mentioned points in Answered Questions/Future research directions have been carefully examined to avoid mistakes.

We hope that the level of our manuscript will meet the journal's desired standard in its current state.

Yours sincerely,

Shu-sen Sun

Department of Pharmacy Practice, College of Pharmacy and Health Sciences, Western
New England University, Springfield, MA 01119, USA.

Phone: 413-796-2424

Email: ssun@wne.edu