

To the editor:

Thank you for sharing the remarks of the reviewer. We would like to make the following responses to the issues raised from the review of my submission:

1. Title reflects the main subject/hypothesis of the manuscript.

The review indicated that no specific changes should be made to the title.

2. The abstract summarizes and reflects the work described in the manuscript.

The review indicated that no specific changes should be made to the abstract.

3. The key words reflects the focus of the manuscript.

The review indicated that no specific changes should be made to the abstract.

4. The manuscript did not adequately describe the background, present status and significance of the study.

The PRISMA checklist indicates that the introduction to a systematic review should contain the following elements: 1) Rationale – which describes the rationale for the study in the context of what is already known, and 2) Objectives – a specific statement of questions being addressed. In this study the clinical utility of hematology laboratory testing was an important part of the background, and we described it, using up-to-date literature references. A second important part of the background was a discussion of liver injury in COVID-19 infection, which we described using current and, in many cases, highly cited references. Since we used references that were current as of the original submission date, we believe that the present status is adequately described. However, to update the background, we added an additional reference (Li et al *Int J Med Sci* 2021; 1285-1296) which states that there is a lack of consensus on the definition of liver injury in COVID-19.

We also added to following sentence to the last paragraph of the Introduction to more explicitly state the significance of this study: “These questions are significant, since the CBC and coagulation testing are among the most commonly ordered clinical laboratory tests, provide rapid results, and can be performed in virtually any setting, including resource-limited environments in which SARS-CoV2 testing is unavailable. “To emphasize that the Introduction contains a statement of the significance of the study, we have offset this paragraph with the subheading: “Objectives”.

5. Methods of this manuscript was not rigorous because all studies included were retrospective, and inclusion criteria for study groups was variable.

In response to this critique, we would like to clarify that this manuscript is a systematic review and not a narrative review. Although narrative reviews can provide guidance on a variety of subjects, they are prone to methodological flaws including: 1) selection bias, or lack of clarity about inclusion/ exclusion criteria for articles included in the review 2) potential low methodological quality 3) no evaluation of the included articles for validity. Systematic reviews differ from narrative (or traditional) reviews in several respects, including: 1) specific evidence-based criteria based on “explicit, pre-specified, and reproducible methods” (Gopalakrishnan S and Ganeshkumar P *J Family Med Prim Care* 2013; 2: 9-14). 2) demonstrate where knowledge is lacking 3) provide guidance for future research (Cook DJ, Mulrow CD, Haynes RB. *Ann Intern Med* 1997;126:376–80). Since our study was a systematic review, the aims of our study included an evaluation of the quality of the literature on this subject, a discussion of the current limitations of the literature, and guidance for further work on this subject.

The selection process for articles that were included in this study was based on an extensive and rigorous search of the literature, which we performed and documented based on the PRISMA checklist. The discussion of the structures of the included studies and their inclusion criteria is a standard part of

any systematic review. Based on our search of the literature, we conclude that all papers meeting our eligibility criteria were retrospective, and their inclusion criteria were variable.

6. Results are not accurate or convincing.

Again, the Results section of this manuscript was constructed using the PRISMA checklist and was compiled using standard methodology, as described in the Materials section. Accordingly, we believe that they are accurate. We would need further details to address any potential issues regarding accuracy of our findings.

7. The discussion section is of little value because of Less rigorous methods and designs.

We think the reviewer means that the discussion is limited by 1) the current literature, which consists entirely of retrospective studies, and 2) the lack of a clear definition for COVID-19 liver injury. We agree with this statement. However, this is a systematic review, one purpose of which is to demonstrate where information is lacking in the literature on a given subject. This is the focus of our discussion and in an effort to make this point we have modified the title of the Conclusions subheading to read: "Conclusions, including interpretation of results and implications for further research."

8. Biostatistics. The manuscript meets the requirements of biostatistics.

The review indicated that no specific changes should be made to the biostatistics.

9. Units. The manuscript meets the requirements of use of SI units.

The review indicated that no specific changes should be made to the abstract.

10. References. The manuscript did not cite appropriately the latest, important and authoritative references in the introduction and discussion sections.

The manuscript was composed using references indexed up to January 13, 2021 and to the best of our knowledge, used a number of highly cited papers in the introduction and discussion. We have reviewed the relevant medical literature published since the original submission date and have added an additional reference as noted in the answer to point #4. It would be useful to us if the reviewer could provide specific examples of references we should include in our manuscript.

11. The manuscript did not well, concisely and coherently organized and presented. there were many grammar errors.

Since this is a systematic review conducted using the PRISMA framework, we were required to organize our manuscript in a very specific way. This is particularly true for the Methods and Results sections. Accordingly, we have modified the subheadings of the Introduction, Methods, Results, and Discussion to emphasize that the format of the manuscript conforms to the PRISMA framework. Regarding the grammar and spelling, this manuscript was composed using Microsoft Word, and was checked for spelling and grammar before being submitted. In addition, the corresponding author is a native English speaker. Since it was stated that there were many grammar errors in the manuscript, we conducted a second grammar check using a widely regarded online editing program, online-spellcheck.com. This second spelling and grammar check likewise did not detect any errors. If we could be provided specific examples of these errors, they may be helpful for us to make any further corrections to the manuscript.

Our response to the Science Editor's comments is as follows:

1. Scientific quality: This manuscript is a systematic review, and it does not reach the publication standard of the WJG. Classification: Grade E

The manuscript is now under consideration by World Journal of Meta-Analysis.

2. Summary of the Peer-Review Report: Reviewer 05450115 pointed out that the manuscript did not adequately describe the background, present status and significance of the study and the

manuscript did not cite appropriately the latest, important and authoritative references in the introduction and discussion sections.

See the responses to points 4, 5, 6, 7, and 11 above.

4. Language quality: Classification: Grade D.

See the response to point 11 above.

In closing, we would like to thank the reviewer for his/ her thoughtful critique, which allowed us to improve our manuscript. We are hopeful that our clarifications have addressed the above concerns. If there are any further issues with the manuscript we would be happy to address them expeditiously.

Sincerely,

John L Frater, MD on behalf of the authors