

PEER-REVIEW REPORT

Name of journal: World Journal of Virology

Manuscript NO: 79269

Title: COVID-19 AND HEMOLYSIS, ELEVATED LIVER ENZYMES AND

THROMBOCYTOPENIA (HELLP) SYNDROME - ASSOCIATION OR CAUSATION?

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05401900 Position: Peer Reviewer Academic degree: PhD

Professional title: Associate Professor

Reviewer's Country/Territory: Iran

Author's Country/Territory: United Arab Emirates

Manuscript submission date: 2022-08-12

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-08-12 15:23

Reviewer performed review: 2022-08-12 20:45

Review time: 5 Hours

Scientific quality	[] Grade A: Excellent [] Grade B: Very good [] Grade C: Good [Y] Grade D: Fair [] Grade E: Do not publish
Language quality	[] Grade A: Priority publishing [Y] Grade B: Minor language polishing [] Grade C: A great deal of language polishing [] Grade D: Rejection
Conclusion	[] Accept (High priority) [] Accept (General priority) [] Minor revision [Y] Major revision [] Rejection
Re-review	[]Yes [Y]No



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Peer-reviewer

Peer-Review: [Y] Anonymous [] Onymous

statements Conflicts-of-Interest: [] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Thank you so much for submitting this article But unfortunately this manuscript is not well organized at all and does not follow a clear flow. The necessary standards for writing mini review articles have not been met. The scattering of unnecessary content is too much. Most of the content presented in this draft is on the two titles of (Pathogenesis of Pre-eclampsia and HELLP syndrome) and (Pathogenesis of COVID-19), so it is not necessary to present this volume of content and it can be summarized in the introduction section. But instead, the content presented on the two titles of (Evidence on COVID-19 and HELLP syndrome) and (Pathophysiology linkage between COVID-19 and HELLP syndrome) has been presented very, very briefly, As the main discussion of this manuscript is considered. Also, there is no information about the relationship between COVID-19, HELLP syndrome and pregnancy, which is the main topic of this mini-review. Due to the presentation of such materials in this manuscript, novelty was not observed.



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Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 06323782 Position: Peer Reviewer Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: Iran

Author's Country/Territory: United Arab Emirates

Manuscript submission date: 2022-08-12

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-08-13 06:48

Reviewer performed review: 2022-08-18 13:14

Review time: 5 Days and 6 Hours

Scientific quality	[] Grade A: Excellent [] Grade B: Very good [Y] Grade C: Good [] Grade D: Fair [] Grade E: Do not publish
Language quality	[] Grade A: Priority publishing [Y] Grade B: Minor language polishing [] Grade C: A great deal of language polishing [] Grade D: Rejection
Conclusion	[] Accept (High priority) [Y] Accept (General priority) [] Minor revision [] Major revision [] Rejection
Re-review	[]Yes [Y]No



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Peer-Review: [Y] Anonymous [] Onymous

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SPECIFIC COMMENTS TO AUTHORS



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Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 06139511 Position: Peer Reviewer Academic degree: PhD

Professional title: Assistant Professor

Reviewer's Country/Territory: India

Author's Country/Territory: United Arab Emirates

Manuscript submission date: 2022-08-12

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-08-14 06:07

Reviewer performed review: 2022-08-25 06:42

Review time: 11 Days

Scientific quality	[] Grade A: Excellent [Y] Grade B: Very good [] Grade C: Good [] Grade D: Fair [] Grade E: Do not publish
Language quality	[] Grade A: Priority publishing [Y] Grade B: Minor language polishing [] Grade C: A great deal of language polishing [] Grade D: Rejection
Conclusion	[] Accept (High priority) [] Accept (General priority) [Y] Minor revision [] Major revision [] Rejection
Re-review	[Y]Yes []No



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Peer-reviewer

Peer-Review: [Y] Anonymous [] Onymous

statements Conflicts-of-Interest: [] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The review entitled "COVID-19 AND HEMOLYSIS, ELEVATED LIVER ENZYMES AND THROMBOCYTOPENIA (HELLP) SYNDROME **ASSOCIATION** CAUSATION?" by Nasa et. al is a well written informative review of the risk of HELPP syndrome in the context of SARS CoV-2 infection. There are some minor suggestions, which if incorporated would help in better understanding of the review. The text does not refer to the figures provided at the end. There needs to be link between the figures and the text. An additional figure that summarizes the proposed mechanism by which COVID patients could be developing HELPP would help in better appreciation of the mechanisms.



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Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 06313768 Position: Peer Reviewer Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: Iran

Author's Country/Territory: United Arab Emirates

Manuscript submission date: 2022-08-12

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-08-15 16:22

Reviewer performed review: 2022-08-26 07:15

Review time: 10 Days and 14 Hours

Scientific quality	[] Grade A: Excellent [] Grade B: Very good [] Grade C: Good [Y] Grade D: Fair [] Grade E: Do not publish
Language quality	[] Grade A: Priority publishing [Y] Grade B: Minor language polishing [] Grade C: A great deal of language polishing [] Grade D: Rejection
Conclusion	[] Accept (High priority) [] Accept (General priority) [] Minor revision [Y] Major revision [] Rejection
Re-review	[Y]Yes []No



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Peer-reviewer statements

Peer-Review: [Y] Anonymous [] Onymous

Conflicts-of-Interest: [] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The presented manuscript entitled "COVID-19 AND HEMOLYSIS, ELEVATED LIVER ENZYMES AND THROMBOCYTOPENIA (HELLP) SYNDROME - ASSOCIATION OR CAUSATION?" (Manuscript NO: 79269) aims to establish a relationship between SARS-CoV-2 infection and HELLP syndrome by reviewing and summarizing some studies. The manuscript can be accepted for publication in "World Journal of Gastroenterology", after revision. The authors should revise the manuscript according to the following comments: 1. First of all, there are several grammatical errors and misspellings throughout the manuscript. Authors are obliged to take action to address these shortcomings. For example, in the abstract, the "unfavourable" is used incorrectly instead of the word unfavorable. Other examples: foetal tissue, high titre, analysed (analyzed), hospitalized (hospitalised), ... 2. The "Abstract" and "Conclusion" sections are very brief. The most important findings of this review need to be presented in Abstract section. 3. The manuscript seems too small to be published as a mini-review. Therefore, it is suggested that the authors logically try to increase the number of references used. If this is not possible and the number of suitable studies is small, it is recommended to change the type of article to commentary or perspective in consultation with the editor. 4. In the introduction section, after the sentences: (.......These include age above 75 years, male sex, preexisting cardiovascular disease, chronic lung, kidney or liver disease, sickle cell disease, diabetes, active cancer, severe obesity, and pregnancy), it is necessary to refer to the appropriate reference. 5. The statement that "Risk factors for developing severe COVID-19 in pregnant women include obesity, smoking history, and diabetes mellitus [1,2].) is incomplete. Other important risk



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factors, including pulmonary comorbidities, hypertensive disorders, etc. which are not mentioned here. Therefore, it is necessary for the authors to provide more complete and accurate information here and to refer to valid reports. 6.(Pregnancy, per se, does not increase the susceptibility to SARS-CoV-2 infection. However, being pregnant increases the risk of severe disease with SARS-CoV-2 infection and is associated with adverse pregnancy and perinatal outcomes [3]......). Comment: There are contradictions in the sentences and they are not well expressed. On the other hand, reference 3 does not seem appropriate here. 7. (Renin-angiotensin-aldosterone system (RAAS) plays a vital role in placenta homeostasis,..... ATII causes vascular constriction, endothelial injury, and vascular smooth cell proliferation, contributing to pre-eclampsia [12])........ Comment: In this of the article, part the relationship between the Renin-angiotensin-aldosterone system (RAAS) and pre-eclampsia is discussed. Some recent studies have investigated the relationship between the severe complications of the COVID-19 disease and the abnormal activation of the p38 MAPK signaling pathway, **RAAS** which is affected the disruption of the pathway (DOIs: by 10.1021/acsptsci.2c00045, 10.1016/j.yjmcc.2020.05.007, 10.1002/ddr.21961, 10.1080/15384101.2021.1982509, and 10.1080/15384101.2022.2100575). On the other hand, there are some studies that have established a logical connection between the abnormal activation of p38 MAPK and pre-eclampsia as well as HELLP syndrome (DOIs: 10.3109/14767058.2016.1144744, 10.1093/molehr/gal071, 10.1002/jcb.28778, 10.1007/s12192-009-0125-x). In this part of the article, I strongly suggest that the possible relationships between the p38 MAPK pathway and the mentioned cases (RAAS pathway, p38 MAPK, pre-eclampsia, and also HELLP syndrome) should be considered and described in a separate section. This suggested section can look at the etiology of the disorders mentioned in the title and introduction of the article from a new angle, which can potentially be interesting and useful for readers. 8. The contents of the studies



mentioned above can also be used to describe the next sections of the manuscript, such as "Pathogenesis of COVID-19" and "Evidence on COVID-19 and HELLP syndrome", and "Conclusion".



RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Peer-review model: Single blind

Reviewer's code: 06313768 Position: Peer Reviewer Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: Iran

Author's Country/Territory: United Arab Emirates

Manuscript submission date: 2022-08-12

Reviewer chosen by: Li-Li Wang

Reviewer accepted review: 2022-09-08 04:44

Reviewer performed review: 2022-09-08 05:53

Review time: 1 Hour

Scientific quality	[] Grade A: Excellent [] Grade B: Very good [] Grade C: Good [Y] Grade D: Fair [] Grade E: Do not publish
Language quality	[] Grade A: Priority publishing [Y] Grade B: Minor language polishing [] Grade C: A great deal of language polishing [] Grade D: Rejection
Conclusion	[] Accept (High priority) [] Accept (General priority) [] Minor revision [Y] Major revision [] Rejection
Peer-reviewer	Peer-Review: [Y] Anonymous [] Onymous



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statements

Conflicts-of-Interest: [] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The authors of the article "COVID-19 AND HEMOLYSIS, ELEVATED LIVER ENZYMES AND THROMBOCYTOPENIA (HELLP) **SYNDROME ASSOCIATION** OR CAUSATION?" (Manuscript NO: 79269) have made some changes in the revised manuscript, but they have not considered the mentioned comments well. It is recommended that the authors refer to the previous comments and consider the requested items better. Especially, in the revised manuscript, the p38 MAPK signaling pathway is not sufficiently discussed and even the p53 MAPK pathway is wrongly mentioned, which should be corrected. As suggested in the previous review, it is necessary to mention the importance of p38 MAPK inhibition in the article in more detail. Some recent studies have discussed the relationship between severe complications of COVID-19 and abnormal activation of the p38 MAPK signaling pathway and have investigated the remarkable potential of p38 MAPK inhibitors such as papaverine, chelerythrine, losmapimod, and dilmapimod in the treatment of COVID-19, which are useful to cite here (DOIs: 10.1002/ddr.21961, 10.1080/15384101.2021.1982509, and 10.1080/15384101.2022.2100575).



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Peer-review model: Single blind

Reviewer's code: 05401900 Position: Peer Reviewer Academic degree: PhD

Professional title: Associate Professor

Reviewer's Country/Territory: Iran

Author's Country/Territory: United Arab Emirates

Manuscript submission date: 2022-08-12

Reviewer chosen by: Li-Li Wang

Reviewer accepted review: 2022-09-08 04:30

Reviewer performed review: 2022-09-09 14:09

Review time: 1 Day and 9 Hours

Scientific quality	[] Grade A: Excellent [] Grade B: Very good [Y] Grade C: Good [] Grade D: Fair [] Grade E: Do not publish
Language quality	[] Grade A: Priority publishing [Y] Grade B: Minor language polishing [] Grade C: A great deal of language polishing [] Grade D: Rejection
Conclusion	[] Accept (High priority) [Y] Accept (General priority) [] Minor revision [] Major revision [] Rejection
Peer-reviewer	Peer-Review: [Y] Anonymous [] Onymous



statements

Conflicts-of-Interest: [] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Thanks for submitting and reviewing this manuscript. The above items were reviewed and revised and modified to the extent acceptable.