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PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 68148

Title: Erythropoietin (EPO) as a protective mechanism in COVID-19.

Reviewer's code: 05382654

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Associate Chief Physician

Reviewer's Country/Territory: China

Author's Country/Territory: Thailand

Manuscript submission date: 2021-05-17

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-05-17 10:30

Reviewer performed review: 2021-05-22 11:57

Review time: 5 Days and 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

This MS mainly hypothesized that rhEPO/EPO analogs/LXA4/FGF23 antagonists may protect against COVID-19 at an early age through inhibitory action on the “proinflammatory state in predisposed adults through IL-6, PAI-1, and FGF23 induction and immune dysregulation, leading to ARDS, cytokine storm and/or autoimmunity”, which provided novel viewpoints for prevention and treatment of SARS-CoV-2 infection. However, as a Review article, “the status quo of the overall research in the field, the problems that have now been resolved and remain to be resolved, and the future research directions that may maximize the practical impact on a field” has not fully discussed. Some revisions are still needed before being published in World Journal of Stem Cells.

1. It is suggested that the title may be changed to “Protective mechanisms of Erythropoietin (EPO) in COVID-19”.
2. In page 5, line 2-4, “The novel coronavirus 2019-nCoV (SARS-CoV-2) infection, the cause of the coronavirus pandemic (COVID-19). has to date (May 11, 2021) infected over 160 million people worldwide” should be changed to “To date (May 11, 2021) severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection, the cause of the coronavirus disease 2019 (COVID-19)pandemic, has infected over 160 million people worldwide”. Throughout the text, please correct the syntax, tense and grammatical errors carefully.
3. Please refer to recent papers published in World Journal of Stem Cells and correct the format. In page 2, “Author Contributions” should be changed to “Author contributions:”. In page 3, “Keywords” should be changed to “Key Words”. Full name (such as COVID-19) should be given for the first time. In page 4, “Core tip” should be changed to “Core Tip”. In page 6, “[7]...[8]” should be changed to “[7, 8]” and should be placed at the end of a sentence. Other citations should be modified accordingly. In page 14, “Abbreviations” section should be deleted. All abbreviations should be provided full name for the first time in the text according to the journal’s requirements.
4. In reference 1, the title should be



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added, and is it “Cumulative confirmed COVID-19 cases per million people”? What is the cited date? In reference 2, “Med Sci Monit Basic Res. 2021; 27:e929207. doi: 10.12659/MSMBR.929207. PMID: 33397841; PMCID: PMC7796072.” should be changed to “Med Sci Monit Basic Res 2021; 27:e929207 [PMID: 33397841 DOI: 10.12659/MSMBR.929207]”. In reference 5, “Infect Genet Evol. 2010; 10(2):337-41. doi: 10.1016/j.meegid.2010.01.009. PMID: 20117248.” should be changed to “Infect Genet Evol 2010; 10: 337-341 [PMID: 20117248 DOI: 10.1016/j.meegid.2010.01.009]”. Please check other references including content and format carefully according to the journal’s requirements. 5. As a Review article, other mechanisms such as antiapoptotic and cytoprotective properties of EPO, potentiate mobilization of iron stores, causing interferon production, stabilizing endothelium, protecting the integrity of the pulmonary epithelial cell and attenuating pulmonary edema should also be discussed. Additionally, are there any results of cases report or clinical trials of EPO in COVID-19 so far? Please add some relevant discussion. Other suggestiones have been listed in the uploaded revised version.

PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 68148

Title: Erythropoietin (EPO) as a protective mechanism in COVID-19.

Reviewer's code: 05849063

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: India

Author's Country/Territory: Thailand

Manuscript submission date: 2021-05-17

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-05-21 08:27

Reviewer performed review: 2021-06-02 08:48

Review time: 12 Days

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input type="checkbox"/> Anonymous <input checked="" type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

Its a very interesting review looking at the evolving nature of the COVID-19 pandemic and rapidly changing etiopathogenesis and manifestations. The manuscript addresses the possible role of EPO on COVID morbidity and mortality through the involvement of Renin Angiotensin System. The possible protective roles of EPO at younger ages and the mechanisms thereof are described nicely and EPO's contribution to disease severity at older ages is also hypothesised convincingly. As mentioned, the COVID pathogenesis is an evolving field and the hypothesis may be explored further. However, there were many instances in the entire MS where the authors tried to over-simplify the issues, particularly those involving ACE and ACE2 polymorphisms and their effect on Angiotensin II levels. There were places that lacked more references. The detailed comments are shown as comments and track changes in the attached document. These need to be revised/addressed for a better clarity on the hypothesis that is definitely publishable after modifications.