

## PEER-REVIEW REPORT

**Name of journal:** *World Journal of Methodology*

**Manuscript NO:** 76138

**Title:** Growth Differentiation Factor - 15 (GDF - 15) as an emerging novel Biomarker in SARS-CoV-2 Infection

**Provenance and peer review:** Invited Manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 05630825

**Position:** Peer Reviewer

**Academic degree:** PhD

**Professional title:** Lecturer

**Reviewer's Country/Territory:** Romania

**Author's Country/Territory:** India

**Manuscript submission date:** 2022-03-05

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2022-04-03 09:50

**Reviewer performed review:** 2022-04-16 13:59

**Review time:** 13 Days and 4 Hours

|                    |   |
|--------------------|---|
| Scientific quality | <input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good<br><input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish            |
| Language quality   | <input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing<br><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 checked="" type="checkbox"/> Accept (General priority)<br><input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection             |
| Re-review          | <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No   |



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| <b>Peer-reviewer<br/>statements</b> | Peer-Review: [ <input checked="" type="radio"/> ] Anonymous [ <input type="radio"/> ] Onymous<br>Conflicts-of-Interest: [ <input type="radio"/> ] Yes [ <input checked="" type="radio"/> ] No |
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#### **SPECIFIC COMMENTS TO AUTHORS**

The article Growth Differentiation Factor - 15 (GDF - 15) as an emerging novel Biomarker in SARS-CoV-2 Infection - is a very well focused subject in a scientific interesting detail. The mini-review is well conducted, based PRISMA 2020 guidelines. The information is clearly synthesized and supportive in order to fulfill the established aim of the article. Despite all the presented limitations, this systemic review offers vital information on the risk stratification of SARS-CoV-2, and the goal of this study was not to create a predictive model but to investigate the potential importance of GDF-15 as a novel biomarker. As the objective was accomplished, The article can be accepted for publication in the actual form.

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**Peer-review model:** Single blind

**Reviewer's code:** 05229914

**Position:** Editorial Board

**Academic degree:** MD, PhD

**Professional title:** Chairman, Chief Doctor, Director

**Reviewer's Country/Territory:** Thailand

**Author's Country/Territory:** India

**Manuscript submission date:** 2022-03-05

**Reviewer chosen by:** Dong-Mei Wang

**Reviewer accepted review:** 2022-05-13 14:26

**Reviewer performed review:** 2022-05-15 02:18

**Review time:** 1 Day and 11 Hours

|                    |   |
|--------------------|---|
| Scientific quality | <input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good<br><input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish            |
| Language quality   | <input type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing<br><input checked="" 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)<br><input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection             |
| Re-review          | <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No   |

|                                     |   |
|-------------------------------------|---|
| <b>Peer-reviewer<br/>statements</b> | Peer-Review: [ <input type="checkbox"/> ] Anonymous [ <input checked="" type="checkbox"/> ] Onymous<br>Conflicts-of-Interest: [ <input type="checkbox"/> ] Yes [ <input checked="" type="checkbox"/> ] No |
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## SPECIFIC COMMENTS TO AUTHORS

please see corrections and suggestions in manuscript file and below: World Journal of Methodology Manuscript review of Manuscript NO: 76138

1. An interesting review. It spurred me to learn more about GDF-15. Especially interesting is the connection to erythropoiesis and iron metabolism. I would appreciate an enlargement on this in the discussion section which is too thin at the moment. If I would summarize, as it is, this review looks at existing studies on GDF-15 and lists their results, confirming what is already known. The only therapeutic advice deriving from the review is the potential use of iron chelating agents. There are no speculations on how GDF-15 impacts the pathogenesis of COVID-19, connections to erythropoiesis, inflammation, hepcidin and iron metabolism. The few sentences: from "Hyperactivity of the immune response in the pathogenesis.... to the end" are in my opinion too convoluted, and thin without making much sense either. How does the "imbalance" between immune response activation and cytokine response lead to all those conditions? Most of it is borrowed and rephrased, not much novel thinking? The associations between GDF-15 and FGF23 in kidney diseases could be discussed. The interactions between metformin and GDF-15 are interesting as GDF-15 mediates metformin effects and metformin is supposedly protective in SARS?! How is all this reconciled? Even if it is not, it is a worthwhile and stimulating discussion that will keep the reader interested in similar ways it did for me, but rather that looking for it myself I would have like to see it served right there.
2. Language is not captivating. At times, boring and incorrect. Needs the touch of a native speaker.
3. See suggestions and some language changes in the manuscript file.
4. After a major revision to correct the above, the manuscript can be reconsidered in my humble



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opinion.

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**Peer-review model:** Single blind

**Reviewer's code:** 05747309

**Position:** Peer Reviewer

**Academic degree:** MSc

**Professional title:** Research Associate

**Reviewer's Country/Territory:** Iran

**Author's Country/Territory:** India

**Manuscript submission date:** 2022-03-05

**Reviewer chosen by:** Dong-Mei Wang

**Reviewer accepted review:** 2022-05-13 14:38

**Reviewer performed review:** 2022-05-23 19:56

**Review time:** 10 Days and 5 Hours

|                    |   |
|--------------------|---|
| Scientific quality | <input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good<br><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<br><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 checked="" type="checkbox"/> Accept (General priority)<br><input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection             |
| Re-review          | <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No   |



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| <b>Peer-reviewer<br/>statements</b> | Peer-Review: [ <input checked="" type="checkbox"/> ] Anonymous [ <input type="checkbox"/> ] Onymous<br>Conflicts-of-Interest: [ <input type="checkbox"/> ] Yes [ <input checked="" type="checkbox"/> ] No |
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#### **SPECIFIC COMMENTS TO AUTHORS**

In my opinion, the introduction of the article could have been written more professionally, however, the manuscript is accepted.

## RE-REVIEW REPORT OF REVISED MANUSCRIPT

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**Reviewer's code:** 05229914

**Position:** Editorial Board

**Academic degree:** MD, PhD

**Professional title:** Chairman, Chief Doctor, Director

**Reviewer's Country/Territory:** Thailand

**Author's Country/Territory:** India

**Manuscript submission date:** 2022-03-05

**Reviewer chosen by:** Ji-Hong Liu

**Reviewer accepted review:** 2022-07-06 14:16

**Reviewer performed review:** 2022-07-06 15:29

**Review time:** 1 Hour

|                           |   |
|---------------------------|---|
| <b>Scientific quality</b> | <input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good<br><input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish            |
| <b>Language quality</b>   | <input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing<br><input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection |
| <b>Conclusion</b>         | <input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority)<br><input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection             |
| <b>Peer-reviewer</b>      | Peer-Review: <input type="checkbox"/> Anonymous <input checked="" type="checkbox"/> Onymous   |





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statements

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

#### **SPECIFIC COMMENTS TO AUTHORS**

the manuscript is certainly better now, better flow and more interesting. I made certain new linguistic changes in the manuscript. the metformin gdf-15 association in my opinion proves that GDF-15 is an effort by the host to alleviate endothelial injury; nevertheless a failed effort. I do not think that GDF-15 causes the storm or is involved in disease severity. I simply believe that it is a good marker. I suggest you read this: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8576656/> and then decide if you will delete the metformin section or write: " the finding that metformin, a SARS-CoV-2 protective repurposed drug, actually elevates GDF-15 poses the question whether elevated GDF-15 levels are a failed host response to alleviate SARS-CoV-2 endotheliitis. Clearly, more studies are needed to elucidate this hypothesis."