



PEER-REVIEW REPORT

Name of journal: *World Journal of Virology*

Manuscript NO: 76352

Title: Association of COVID-19 with Hepatic Metabolic Dysfunction

Provenance and peer review: Invited manuscript; externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 00053419

Position: Editorial Board

Academic degree: PhD

Professional title: Professor

Reviewer's Country/Territory: Spain

Author's Country/Territory: India

Manuscript submission date: 2022-03-13

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-03-15 16:24

Reviewer performed review: 2022-03-24 09:49

Review time: 8 Days and 17 Hours

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 Grade E: Do not publish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 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	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous



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

SPECIFIC COMMENTS TO AUTHORS

The authors have reviewed the metabolic implications of COVID-19 in the liver and the role this organ has in the progression of the disease. The manuscript is of interest as it provides discussion on relevant questions and some open questions that will surely boost further investigation. I have two comments for the authors: 1. The expression of ACE2 is very low in liver parenchyma (see, for example, data in the Human Protein Atlas). In light of this, do the authors think that hepatocytes are primary targets of SARS-CoV-2? Alternatively, is liver injury a secondary hit of the inflammatory response of the host to SARS-CoV-2 infection? These considerations must be taken into account throughout the manuscript in order to delineate an accurate molecular pathogenesis of COVID-19 and to define the relevance of the contribution of the liver. 2. It might be of interest to dedicate specific attention to one carbon metabolism. the authors make several independent references to different alterations associated with this central metabolic pathway in the hepatocyte, including folate cycle, methionine cycle, synthesis of phospholipids, polyamides and glutathione. Integrated discussion of all these aspects would provide a clearer view to the reader. 3. There are sections where the authors review several pathophysiological issues associated to COVID-19 but no link to metabolism is evident (see, pages13-16).



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Author's Country/Territory: India

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

SPECIFIC COMMENTS TO AUTHORS

The authors had touched on a very specific subject of the COVID-19 pandemic. SARS-Cov-2 had been proven to influence many bodily organs including the kidney, lungs, heart, and liver. This study adequately reviewed the association of COVID-19 to hepatic metabolic dysfunction. The paper is important and add to the COVID-19 specific literature. Findings from the current study explained the pathophysiology and can propose treatment methods in hepatic-metabolic dysfunction which is prevalent in COVID-19 patients. Matters that need to be improved on this paper are: (1) English language correction and (2) structural editing (i.e., some parts can be combined under subsections to improve clarity and readability)