PEER-REVIEW REPORT

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [Y] Grade E: Do not publish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

Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

1. Authors mentioned in the abstract section that "The epicenter of this disease, China alone, carries a burden of 300 million chronic liver patients, which could deluge the death toll owing to Covid". The above description of defining China as the epicenter of Covid-19 is contrary to the current international data on Covid-19 and lacks essential scientific spirit, so please excuse the rejection of this manuscript.   2. Some currently used vaccines are listed in Table 2. However, the descriptions of the efficacy of some vaccines are quite different from each other and not specific enough, for example, "efficacy of 70.4%", "73.1% efficacy", and "95% protection against COVID-19", and the sources of these data is not apparent in this manuscript. Furthermore, the descriptions of doses in Table 2 are also confusing, which include "2 doses", "2 dose", "two doses", and a missing item.

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Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [Y] Major revision [ ] Rejection
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	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The idea of the review itself is innovative and will be useful for researchers planning experimental work. The authors were particularly successful in their comparative analysis of viruses. However, when authors reviewing the association of SARS-CoV-2 infection with the liver, they present numerous controversial claims that require more rigorous confirmation. Some of examples are presented below: "cytokine upsurge owing to multiorgan failure" 'Since liver is the primary site of synthesis of proteins associated with immunity" "After almost three years of corona panic, it is still disquietude as to what makes these viruses jump onto a human host and invade hepatocytes as a shared gateway - detection of the SARS-CoV-2 in the liver does not confirm virus enters the hepatocytes. It can be detected in the liver because of its presence in the bloodstream. Please, provide the journal readers with evidence that hepatocytes are SARS-CoV-2 gateway. "the liver serves as one of the favorite proliferation spots for coronaviruses since it is a common gateway for viruses entering the blood" – please provide a reference to the study in which viral proliferation in hepatocytes was confirmed. "Even autopsies and biopsies performed post-mortem on the liver reflected that corona virus-2 inflicted cholangiocytes, hepatocytes, and endothelial cells, causing severe liver damage." – infliction does not mean replication. Moreover, reference on the study with 11 deceased patients's autopsies is not sufficient to make conclusion about mechanisms of liver injury by SARS-CoV-2 virus.   Ischemic hepatitis is characterized by an extremely high elevation of transaminases, but that is not the case in SARS-CoV-2 patients. Drawing on our experience and that of other clinicians, most SARS-CoV-2 infected patients with elevated liver enzymes (including those with

underlining liver disease) do not experience a cytokine storm either. Please reconsider the liver involvement in the review.   In conclusion, as the authors make many controversial claims concerning mechanisms of liver injury in SARS-CoV-2 infected patients, it would be preferable to support these claims with references to the corresponding experiments rather than relying on reviews. Please check the reference for the proper PMID and DOI (11 reference – wrong DOI).

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SPECIFIC COMMENTS TO AUTHORS

The author reviewed the origin of corona virus detailly，as well as its transmission and mutation. Five SARS-CoV-2 strains were listed in Table 1. The liver is one of the favorite proliferation spots for coronaviruses. It has been evaluated in many studies that around 1/3rd of the Covid-19 patients complained about liver dysfunction. The article deduced mechanism of corona virus inducing liver dysfunction, that included hepatocyte ballooning majorly, eosinophilic action creating a cytokine storm, hypoxia, and ischemia leading to liver necrosis. Actually ACE-2 aided viral invasion and damage mediating immune response was the key factor. The article elaborated the molecular features after coronaviruses invaded liver cells, as well as the latest confirmed signal path. The author expounded the newest pharmacologic therapies specific to corona-associated hepatic injure, including immunomodulators and anti-inflammatory agents, anti-viral drugs and neutralizing antibodies. The article is very novel and contains many cutting-edge knowledge, which can be helpful for future basic and clinical research.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

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

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

SPECIFIC COMMENTS TO AUTHORS

Thanks for the author's reply, but I still can't accept the author's response and inaction to the first question. The authors mentioned in the abstract that "the epicenter of this disease, China alone, carries a burden of 300 million chronic liver patients, which could deluge the death toll owing to Covid". 1. Since the original manuscript was pointed out to be easily misunderstood and the authors mentioned "with no bias or any intentional content" in their response, why didn't the author adjust this sentence? 2. Could you please add references in the main text to the data mentioned in this sentence, and to deaths due to COVID-19 in patients with liver diseases? 3. The author highlighted the fully vaccinated data in the conclusion part. Could you please add some references?