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PEER-REVIEW REPORT

Name of journal: *World Journal of Meta-Analysis*

Manuscript NO: 77053

Title: Difference in incidence of developing hepatocellular carcinoma between hepatitis B virus-and hepatitis C virus-infected patients mainly depends on varying impact of inflammation on hepatocarcinogenesis

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 02567657
Position: Peer Reviewer
Academic degree: MD
Professional title: Professor
Reviewer's Country/Territory: United States
Author's Country/Territory: Japan

Manuscript submission date: 2022-04-13

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-04-13 12:59

Reviewer performed review: 2022-04-29 06:58

Review time: 15 Days and 17 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Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish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) [ ] Accept (General priority) [ ] Minor revision [Y] Major revision [ ] Rejection

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

SPECIFIC COMMENTS TO AUTHORS

Major comments 1) Why was only ALT considered in hepatic inflammation? Why was aspartate aminotransferase (AST) not considered? Especially for HBV, the authors should also include AST in their assessment of inflammation. 2) To strengthen the study, the authors can include the duration of infection. If applicable, the authors should include in their analysis how HBV or HCV treatment can improve inflammation or if there are lasting effects of HBV or HCV infection in terms of causing long-term inflammation and/or changes, contributing to increased risk of HCC development. 3) Patients infected with HBV and/or HCV can have co-existing liver diseases, such as alcohol liver disease and/or fatty liver disease, which can also contribute to hepatic inflammation. The authors should indicate if any of these issues were mentioned in the articles that were included in their analysis. 4) What were the article inclusion/exclusion criteria? It would be helpful if the authors added a flow diagram to document the number of articles initially selected and how they were eliminated at each stage. 5) In Tables 3 and 4, a variety of additional factors were considered but were not included in the analysis. The reason why these were not included in the analysis should be provided. Minor comments 1) Please do not use abbreviations in the title of the manuscript. 2) Reference in Methods section needs to be formatted appropriately.

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Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 00504167
Position: Editorial Board
Academic degree: MD
Professional title: Associate Professor
Reviewer's Country/Territory: Italy
Author's Country/Territory: Japan

Manuscript submission date: 2022-04-13

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-05-04 07:45

Reviewer performed review: 2022-05-07 20:16

Review time: 3 Days and 12 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 [ ] Major revision [Y] Rejection

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

SPECIFIC COMMENTS TO AUTHORS

Revision manuscript n. 77053: Difference in incidence of developing HCC between HBV-and HCV-infected patients mainly depends on varying impact of inflammation on hepatocarcinogenesis: a meta-analysis In this meta-analysis the authors evaluated the impact of inflammation on the development of HCC. They considered the ALT levels in hepatitis B and C chronic patients excluding those treated with interferon. Furthermore, among the HBV chronic patients were also excluded those treated with nucleos(t)ides; and among the HCV chronic patients were excluded those treated with DAAs. Then, they calculated the HR in patients with abnormal ALTs. The authors concluded that the difference "in the incidence of HCC development between HBV and HCV patients may depend on the difference in the HR of ALT between HBV and HCV infections". I think there is an important bias in this study, that is, the role played by cirrhosis in the development of HCC. Among the studies selected by the authors for this meta-analysis, the HR for developing HCC in the presence of cirrhosis is missing in several reports. It has been calculated in 6 out of 11 reports in patients with HBV chronic infection, and in 1 out 8 reports in patients with HCV chronic infection. The two groups of patients are not comparable, and the conclusions of the authors are most likely wrong.