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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 55147

Title: Lower expression of circulating mucosal-associated invariant T cells indicates poor prognosis in HBV-related liver failure

Reviewer's code: 00013213
Position: Peer Reviewer
Academic degree: MD, PhD
Professional title: Professor
Reviewer's Country/Territory: Egypt
Author's Country/Territory: China

Manuscript submission date: 2020-03-02
Reviewer chosen by: Jie Wang (Quit in 2020)
Reviewer accepted review: 2020-03-13 12:13
Reviewer performed review: 2020-03-17 09:42
Review time: 3 Days and 21 Hours

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish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) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[ ] Yes [ ] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

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SPECIFIC COMMENTS TO AUTHORS

-Your manuscript presenting status of peripheral circulating MAIT cells in CHB and HBV-related liver failure is interesting, however, There are some remarks that you have to respond to: 1- At results: You have presented data about levels and percentages of MAIT cells in patients with HBV-related liver failure and in CHB patients compared to HCs, however it is clear from your figures that the MAIT cells count and percentages had still significant lower values in patients with HBV-related liver failure when compared to CHB patients. These data are important as it may indicate that liver failure in such patients may represent a more advanced and aggressive state of inflammatory cascade that may be incriminated in the more depressive effect on the status of circulating MAIT cells. You have to demonstrate this issue statistically. 2- At table 1, it would be more informative to indicate the statistical significance in liver functions between CHB and HBV-related liver failure groups. 3-At discussion, you mentioned MAIT cells also play a critical role in liver diseases by promoting hepatitis and fibrosis, maintaining intestinal permeability, and responding to biliary epithelium cells and liver B cells.). These statements need more clarification to indicate how these cells do with the favor or against these situations. 4- It seems that the status of MAIT cells peripherally in circulation may not reflect their counts and percentage centrally inside the liver and hence the functional impact inside the liver may be totally different than the value of the peripheral expression of these cells in circulation. This may represent the phenomena of homing of lymphocytes in general inside the liver at the site injury with its depletion peripherally in the circulation. 5- Actually, discussion of your findings is lagging behind offering an explanation to the relevance of depleted MAIT cells peripherally on outcome of both CHB and HBV-related liver failure. Furthermore, the prediction needs cutoff values derived from ROC curve studies with sensitivity indices which is not

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present at your study and is difficult to perform due to small sample size.

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 55147

Title: Lower expression of circulating mucosal-associated invariant T cells indicates poor prognosis in HBV-related liver failure

Reviewer's code: 03728416
Position: Associate Editor
Academic degree: MD, PhD
Professional title: Assistant Professor, Surgeon
Reviewer's Country/Territory: Italy
Author's Country/Territory: China

Manuscript submission date: 2020-03-02
Reviewer chosen by: Jia-Ping Yan
Reviewer accepted review: 2020-04-13 08:54
Reviewer performed review: 2020-04-14 14:06
Review time: 1 Day and 5 Hours

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] 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) [Y] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
Re-review	[ ] Yes [ ] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

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SPECIFIC COMMENTS TO AUTHORS

I have with interest this manuscript, which concerns the role of of circulating mucosal-associated invariant T cells in patients with HBV-related liver failure. Overall, the paper is well-written and gives to the reader the right perspective on this topic. I believe that this manuscript will be of interest to the readership of WJG.

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 55147

Title: Lower expression of circulating mucosal-associated invariant T cells indicates poor prognosis in HBV-related liver failure

Reviewer's code: 04025443
Position: Editorial Board
Academic degree: MD, PhD
Professional title: Doctor, Senior Researcher
Reviewer's Country/Territory: Russia
Author's Country/Territory: China

Manuscript submission date: 2020-03-02
Reviewer chosen by: Jia-Ping Yan
Reviewer accepted review: 2020-04-13 06:57
Reviewer performed review: 2020-04-16 20:19
Review time: 3 Days and 13 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
Re-review	[ ] Yes [ ] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

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SPECIFIC COMMENTS TO AUTHORS

The paper describes the results of original prospective study aimed to assess the role of MAIT cells in HBV-associated conditions. I suppose that the obtained results may bring new information, though their relevance to clinical practice is quite doubtful. I have some concerns about methodology of the study and the interpretation of its results. First, patients with HBV infection represent a heterogeneous group. Despite the authors stated that they enrolled patients with chronic form of the disease, the SDs of ALT and AST values require some comments. Prothrombin activity is a good tool, but not the best one to describe decompensation of the liver function (especially when it is used alone). There are commonly used methods to assess decompensation of the liver function and assess prognosis in patient with chronic liver diseases (like Child-Pugh, MELD score, and others). It would be nice if these methods' results would be shown also to 1) better describe patients' population; 2) show correlation between previously described methods and MAIT cells counting. Could you please explain the absence of difference between studied groups by albumin level? This situation is strange, as low albumin concentration is one of the main parameters that are used to establish the presence of liver failure. Could this be caused by treatment (Albumin infusions)? I suppose, that more detailed description of clinical data is necessary for better understanding the results. Some of them may affect the results (presence of ascites, peritonitis, encephalopathy, causes of deaths). The "other reasons" of liver failure are not described, please, give more details to ensure that liver failure was not associated with, for example, presence of liver cancer, alcohol intake or something else. To make the paper closer to the requirements of the good publication practice, please consider to add patients' flow chart and study design graph. Please, disclose the information about study registration (required per ICMJE recommendations). At least some of the measurements were made

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twice. However there is no description in which time points this was made. No data on the mean time of follow-up is provide. Please, consider to add this information to the paper. Lymphocyte count is one of the parameters which is usually used to assess nutritional status. Taking into the account that patients with end-stage chronic liver disease in most cases have at least some degree of malnutrition and decreased protein synthesis, it may be logical to assume that MAIT cells' decrease in patients with liver failure may be associated with this factor also. Moreover, it has been described that in case of starvation or energy and protein deficiency, lymphocytes count in peripheral blood is decreased predominantly due to a dramatic fall of the number of CD3+ T-lymphocytes with relatively constant values of B-lymphocytes and null cells. It is clear that decreased protein synthesis and energy deficiency caused by liver failure are associated with poorer prognosis. But is there a need for relatively expensive and not widely available method to detect effects, that may be measured with much simpler tools? Please, consider to add this in the discussion. I disagree with the conclusion provided in the abstract that circulating MAIT cells may play a critical role in the PATHOGENESIS of HBV-related liver failure because it is more likely that on the contrary, liver failure and/or associated protein deficiency affect MAIT cells count. Based on the mentioned above, I conclude that major revision is necessary to make the obtained information cut clear and consistent.

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 55147

Title: Lower expression of circulating mucosal-associated invariant T cells indicates poor prognosis in HBV-related liver failure

Reviewer's code: 05077656
Position: Editorial Board
Academic degree: MBChB, MD, MSc, PhD

Professional title: Doctor, Lecturer

Reviewer's Country/Territory: Germany

Author's Country/Territory: China

Manuscript submission date: 2020-03-02

Reviewer chosen by: Jia-Ping Yan

Reviewer accepted review: 2020-04-14 22:26

Reviewer performed review: 2020-04-17 23:30

Review time: 3 Days and 1 Hour

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] 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) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[ ] Yes [ ] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

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SPECIFIC COMMENTS TO AUTHORS

I would like to thank the authors for the excellent study. However, I would suggest to add a comparative analysis regarding the prognostic power of circulating mucosal-associated invariant T cells as a marker and clinical scoring systems assessing the severity of the disease as they discussed in the introduction as MELD and CLIF scores.

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 55147

Title: Lower expression of circulating mucosal-associated invariant T cells indicates poor prognosis in HBV-related liver failure

Reviewer's code: 00505467
Position: Editorial Board
Academic degree: FRCS (Gen Surg), MD, PhD
Professional title: Academic Research, Adjunct Professor, Assistant Professor, Honorary Research Fellow, Surgeon, Surgical Oncologist
Reviewer's Country/Territory: Greece
Author's Country/Territory: China

Manuscript submission date: 2020-03-02
Reviewer chosen by: Jia-Ping Yan
Reviewer accepted review: 2020-04-13 17:11
Reviewer performed review: 2020-04-21 13:28
Review time: 7 Days and 20 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
Re-review	[ ] Yes [ ] No
Peer-reviewer	Peer-Review: [Y] Anonymous [ ] Onymous

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

SPECIFIC COMMENTS TO AUTHORS

In my opinion this observational study presents several pitfalls. The most import disadvantage might be the small sample of patients, which creates queries when it comes from a university institution, why this study is not a multi-center one to avoid bias? why the authors did not recruit more patients in order to have better sample for subgroup analyses? Why they did not correlate and compare their "biomarker" with the existing clinical scoring systems Like MELD and CLIF? The answers to all that questions would create a solid prospective randomized trial that would respond to many of our everyday clinical problems and might provide us with a novel prognostic biomarker. This study as the previous referred to by this one just presents a possibility which cannot stratify its results in clinical level safely and soundly. University institution should have higher targets and pave the way towards future not just record existing hypotheses.