

Response to Reviewers

Reviewer 1

1) Reviewer comment: Title “Renal Manifestations of Hepatitis E Among Immunocompetent and Kidney Transplant Recipients” In this manuscript, the authors describe renal manifestations of hepatitis E among not only kidney transplant recipients, but also immunocompromised and the other solid organ transplant recipients. It is not clear whether we need to discriminate them.

Response: We appreciate reviewers’ comments. We agree that we described renal manifestations of solid organ transplant. We changed the title of manuscript to “**Renal Manifestations of Hepatitis E Among Immunocompetent and Solid Organ Transplant Recipients**”. We have changed “kidney transplant” to **Solid Organ transplant in the manuscript.**

2) Reviewer comment: Are there any differences in terms of clinical manifestations, diagnosis, and therapy?

Response: We have stated in manuscript “However, it is unclear if renal manifestations and presentation differ among various organ transplant recipients”. We also included in “Treatment section” “With non-sustained virological remission, ribavirin is recommended to continue for 6 months. Among Liver transplant recipients, Interferon (IFN) α has shown to achieve sustained virological remission among patients with hepatitis E after liver transplant. However, use of IFN α is not recommended among other solid organ transplant recipients secondary to the risk of graft rejection”.

3) Reviewer comment: The section “Glomerular manifestation of hepatitis E” needs to be included in the section “Renal manifestations of Hepatitis E infection”

Response: We agree with the reviewers’ comments. Have included Glomerular manifestations of hepatitis E under “Renal manifestations of Hepatitis E infection”

4) Reviewer comment: Figure 2: Does “Immunocompromised” include only “Kidney Transplant”? How about “Pegylated Interferon for 3 months in liver transplant patients” (Kidney Transplant)? Please clarify

Response: Thank you for a very valid point. We have modified Figure 2: Included “solid organ transplant” instead of “kidney transplant”. Also added “Pegylated Interferon” can be given for 3 months in liver transplant and not in other transplant patients secondary to risk of rejections.

5) Reviewer comment: There are some typos to be corrected (Introduction “uncooked meet (meat?)” “fetal (fatal?) outcomes” etc.). Proofreading by native English speakers is required

Response: We apologize for the typos. We thank reviewer for the corrections. We have made all the necessary corrections in the manuscript.

Reviewer 2

1)Reviewer comment: Following suggestions are there to enhance the manuscript: 1. Add the following reference: Hering T, Passos AM, Perez RM, Bilar J, Fragano D, Granato C, Medina-Pestana JO, Ferraz ML. Past and current hepatitis E virus infection in renal transplant patients. J Med Virol. 2014 Jun;86(6):948-53. doi: 10.1002/jmv.23915. Epub 2014 Mar 12. PMID: 24619955.

Response: We are thankful for reviewers’ suggestions. We have included the above-mentioned reference in section 2: Clinical course.

2) Reviewer comment: Please add a Table reflecting studies and data of Chronic HEV infection in immunocompromised. It will substantiate the problem statement of the entity and summarize the topic too !

Response: We appreciate reviewers’ suggestion. We have added Table-1 including the reports of renal manifestations of Hepatitis E virus among immunocompetent and solid organ transplant recipients.

Reviewer 3

1)Reviewers’ comments: In the introduction section the authors mention Hepatitis E virus belongs to Herpesviridae family, but actually the HEV belongs to Hepeviridae family.

Response: We apologize for the typo. We have corrected to “Hepeviridae” in Introduction.

2)Reviewers’ comments: The section ‘Renal manifestations of Hepatitis E infection’ should be Renal manifestations of Hepatitis E virus infection.

Response: Totally agree with reviewer. Made changes as ‘Renal manifestations of Hepatitis E virus infection’.

3)Reviewers’ comments: G6PD should be defined at its first appearance

Response: We thank reviewers’ suggestions. Defined G6PD at its first appearance.

4) **Reviewers' comments:** In the figure title 1, AKI should be defined or shown its elaborative form in its first use.

Response: We thank reviewers' suggestions. Have defined AKI in figure:.

5) **Reviewers' comments:** There are some typos that should be carefully checked. For example, Interestingly, In the subgroup who received anti- viral therapy, cryoglobulinemia was detected in 70%....; HEV mediated (should be HEV-mediated) renal manifestations were thought to be a result of direct cytopathic injury

Response: we agree with reviewers' suggestion. Have change to HEV-mediated renal manifestations.

6) **Reviewer's comment:** In Immunocompetent patients, it advised..... (Should be In immunocompetent patients, it is advised)

Response: We apologize for the typo. Have made recommended changes in the manuscript.

7) **Reviewer's comment:** In patients with severe acute infection or acute on chronic liver disease ribavirin therapy is considered (please confirm the highlighted part)

Response: We confirm that In patients with severe acute infection or acute on chronic liver disease ribavirin therapy is considered.

8) **Reviewer's comment:** Guinault [32] et al reported a case of hepatitis E virus-induced cryoglobulinemic glomerulonephritis in a immunocompetent patient (a should be an)

Response: We are thankful for reviewers' comments. Made suggested changes in the manuscript.

Response to Editors

- 1) **Science editor** comments: Summary: The authors stated that they reviewed clinical course, pathogenesis, renal manifestations, diagnosis and management of hepatitis E among immunocompetent and kidney transplant recipients. Scientific quality: Grade D; Grade B; Grade B Language quality: Grade C; Grade B; Grade A Conclusion: Major revision; Minor revision; Minor revision References: 10 of the references were published within the last 5 years Self citation: No Language certificate: No provided Summary of peer review reports: The reviewers emphasized some important points in the article, which are very important in my opinion. Authors should revise the article taking these suggestions into account. After the necessary revisions, the article can be published. Recommendation: Conditional acceptance

Response: Thank you very much for taking time in reviewing our manuscript and providing valuable feedback. We appreciate the support and encouragement. We have revised our manuscript according to reviewers' suggestions.

(2) **Company editor-in-chief** comments: I have reviewed the Peer-Review Report, full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Hepatology, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors.

Response: We appreciate the opportunity of submitting our manuscript to your journal. We have revised manuscript based on reviewers' suggestions.