

OPEN PEER REVIEW

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Advantages of "Open Peer Review" process

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- More motivations for all involved roles in the review process
- Authors' satisfactions from the review process: Increases honesty between authors and reviewers
- Education of both authors and new students
- Prevents reviewers from following their individual agendas and leading to the detection of reviewers' conflicts of interests

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Middle East Journal of Rehabilitation and Health Studies

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Peer Review Report for "Intra-familial Transmission of Hepatitis B and C Infections: A Systematic Review and Meta-Analysis"

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Review Timeline:

Submit Date: 17 Aug 2025

Revised Date: 3 Sep 2025

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Revision (0)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFeree : Reviewer

20 Aug 2025

Dear Editor

my comments:

1. Methodological Issues

1. Search extended until December 2024 while the manuscript is dated 2025 (chronological inconsistency).

2. No registration in PROSPERO or other registries is reported.

3. The eligibility criteria are too general, making study selection unclear.

4. Although the Newcastle-Ottawa Scale is mentioned, detailed scoring and justification are missing.

5. Important variables (e.g., participants' age, vaccination status) are missing in Table 1.
6. The risk of bias in primary studies is not addressed.

2. Statistical and Analytical Issues

1. I^2 values close to 99% indicate extreme heterogeneity, yet strong pooled conclusions are made.
2. Despite high heterogeneity, no sensitivity or leave-one-out analysis is performed.
3. Ambiguous definition of horizontal transmission – Sometimes includes sexual + non-sexual contacts, sometimes separated, leading to confusion.

3. Results and Interpretation Issues

1. Over interpretation of wide confidence intervals – For example, child transmission of HBV (16.3–61.7%) is too broad to justify strong claims.
2. Most studies are from developing/tropical countries, yet conclusions are applied globally.
3. No consideration of factors such as genotype, age, comorbidities, or cultural practices.
4. Strong public health recommendations are made despite acknowledged limitations.

4. References and Literature Use

1. Several references from the 1980s–1990s dominate, limiting relevance to current practice.
2. Some cited references do not match the statements in the text.
3. Limited consideration of modern therapies – Studies do not account for the effect of Direct-Acting Antivirals (DAAs) on HCV transmission.

REFeree : Reviewer

29 Aug 2025

Dear Associate Editor

my comments:

- 1- Although the title is clear, it suggested being more informative with a sentence showing the main findings of the study
- 2- Viral hepatitis in the article title should be changed to Hepatitis B and C infection. In this article, only Hepatitis B and C infection has been studied.
- 3- In the introduction, describe the impact of co-infection with hepatitis B and C on the severity of the disease and the liver.
- 4- In the introduction, the genotypes of hepatitis B and C should be mentioned.
- 5- What exactly is meant by non-sexual contact within the family? Do these contacts lead to disease transmission?
- 6- Considering intra-familial transmission, was sexual transmission between couples investigated? Why?
- 7- Considering the common transmission routes of hepatitis D infection with hepatitis B and hepatitis C, why has it not been studied?

8- Considering the phrase "Disrupting the mother-to-child" in the discussion section of abstract, why was vertical mother-to-child transmission not studied?
9- Also intrauterine, during birth and after birth transmission has been reviewed?
10- How contradictory and challenging outputs screened and what were the screening tool?
Best regards

REFeree : Associate Editor

30 Aug 2025

Dear EIC

According to the reviewers' comments, the article needs to be revised majorly.

Thanks

Fatemeh Ehsani : EIC

30 Aug 2025

Dear Authors

According to the reviewers and associate editor's comments, your article needs to be revised majorly. When revising your manuscript, please consider all issues mentioned in the reviewers' comments carefully: please outline every change made in response to their comments and submit the required files up two months.

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Revision (1)

Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

Reviewer 1:

The search is reported until December 2024, while the manuscript is dated 2025 (chronological inconsistency).

Response: We thank the reviewer for this observation. The literature search has been updated and extended until August 2025, and the revised manuscript now reflects this change to ensure consistency.

No registration in PROSPERO or other registries is reported.

Response: We acknowledge this point. While PROSPERO registration is not mandatory, we have clarified in the limitations section that this study was not prospectively registered in PROSPERO or similar registries.

The eligibility criteria are too general, making study selection unclear.

Response: We agree with the reviewer and have revised the eligibility criteria to make the study selection process more explicit and transparent in the Methods section.

Although the Newcastle-Ottawa Scale is mentioned, detailed scoring and justification are missing.

Response: We appreciate this valuable suggestion. The methodological quality of the eligible studies was assessed using the Newcastle–Ottawa Scale (NOS) across three domains: selection (maximum 4 stars), comparability (maximum 2 stars), and outcome/exposure assessment (maximum 3 stars). Studies with a score of ≥ 6 were considered high quality. To provide a concise summary, the final NOS score for each study has been added to Table 1.

The risk of bias in primary studies is not addressed.

Response: We agree with this important point. In the revised manuscript, we have included a qualitative assessment of potential sources of bias across studies (e.g., selection bias, misclassification of transmission route, and recall bias in self-reported exposures) to provide context for the interpretation of our findings.

I^2 values close to 99% indicate extreme heterogeneity, yet strong pooled conclusions are made.

Response: We agree that high heterogeneity warrants cautious interpretation. To address this, we have now included subgroup analyses and sensitivity analyses, which help explain potential sources of heterogeneity and provide more nuanced conclusions.

Despite high heterogeneity, no sensitivity or leave-one-out analysis is performed.

Response: Thank you for pointing this out. We have now performed a leave-one-out sensitivity analysis, the results of which are presented in the supplementary materials. These analyses confirm the robustness of our findings despite the heterogeneity.

The definition of horizontal transmission is ambiguous – sometimes including both sexual and non-sexual contacts, sometimes separated, leading to confusion.

Response: We appreciate this observation. In the revised manuscript, we have clarified the definition of horizontal transmission: sexual transmission refers exclusively to husband–wife transmission, whereas non-sexual transmission refers to parent-to-child or other close household contacts. This distinction has been explicitly stated to avoid ambiguity and improve clarity.

There is over-interpretation of wide confidence intervals – for example, child transmission of HBV (16.3–61.7%) is too broad to justify strong claims.

Response: We thank the reviewer for this comment. The reported confidence intervals were calculated based on pooled eligible studies, and we have now emphasized in the revised manuscript that such wide intervals indicate variability and should be interpreted with caution.

Most studies are from developing/tropical countries, yet conclusions are applied globally.

Response: We acknowledge this limitation. In the revised discussion, we now highlight that most included studies originated from developing or tropical countries, and therefore the findings may not be fully generalizable to all settings.

No consideration of factors such as genotype, age, comorbidities, or cultural practices.

Response: We agree with this important point. However, the eligible studies do not reported results regarding genotype, age, comorbidities, or cultural practices to be investigated.

Strong public health recommendations are made despite acknowledged limitations.

Response: We appreciate this observation. The recommendations in the revised manuscript have been tempered to reflect the study's limitations, and they are now presented as suggestions for public health consideration rather than definitive conclusions.

Several references from the 1980s–1990s dominate, limiting relevance to current practice.

Response: We agree with the reviewer. The manuscript has been updated by replacing outdated references with the most recent and relevant studies, thereby improving the applicability of our findings to current practice. However, some eligible studies that match our selection criteria was related to 1980s to 1990s that we inevitable to be included within the studies. Our literature review has not restriction in publication date.

Some cited references do not match the statements in the text.

Response: Thank you for noting this. We carefully re-checked all references and revised the mismatched citations to ensure they accurately support the corresponding statements.

There is limited consideration of modern therapies – studies do not account for the effect of Direct-Acting Antivirals (DAAs) on HCV transmission.

Response: We appreciate this important suggestion. The impact of DAAs on HCV transmission has now been acknowledged and discussed in the revised discussion section to highlight the evolving context of viral hepatitis management.

Reviewer 2:

Although the title is clear, it is suggested to be more informative with a sentence showing the main findings of the study.

Response: We appreciate this helpful suggestion. The title has been revised to be more informative, now reflecting the main findings of the study.

“Viral hepatitis” in the article title should be changed to “Hepatitis B and C infection,” since only Hepatitis B and C infection has been studied.

Response: Thank you for pointing this out. The title has been revised to specify Hepatitis B and C infections, ensuring accuracy and clarity.

In the introduction, describe the impact of co-infection with hepatitis B and C on the severity of the disease and the liver.

Response: We agree with this important point. The introduction has been expanded to include the impact of HBV/HCV co-infection on disease severity and liver outcomes.

In the introduction, the genotypes of hepatitis B and C should be mentioned.

Response: We appreciate this suggestion. The introduction has been revised to briefly discuss HBV and HCV genotypes and their potential relevance to disease transmission.

What exactly is meant by non-sexual contact within the family? Do these contacts lead to disease transmission?

Response: Thank you for raising this point. We have clarified the definition in the revised manuscript: non-sexual transmission refers to parent-to-child or other close household contact, whereas sexual transmission refers specifically to husband–wife transmission. This has been stated more explicitly to improve clarity.

Considering intra-familial transmission, was sexual transmission between couples investigated? Why?

Response: Yes, this was investigated. We have clarified that sexual transmission refers exclusively to transmission between husband and wife, which was assessed in eligible studies.

Considering the common transmission routes of hepatitis D infection with hepatitis B and C, why has it not been studied?

Response: We appreciate this observation. Unfortunately, the eligible studies did not provide sufficient data on hepatitis D, and therefore it could not be analyzed in this review. This limitation has been noted.

Considering the phrase “Disrupting the mother-to-child” in the abstract’s discussion section, why was vertical mother-to-child transmission not studied?

Response: Thank you for noticing this. The abstract has been revised for clarity to avoid implying that vertical mother-to-child transmission was analyzed, since the included studies did not provide sufficient data on this route.

Were intrauterine, during birth, and after birth transmissions reviewed?

Response: We acknowledge this important point. However, the eligible studies did not report detailed data on intrauterine, perinatal, or postnatal transmission, and thus these could not be separately analyzed. This limitation has been indicated in the manuscript.

How were contradictory and challenging outputs screened, and what screening tool was used?

Response: Thank you for this comment. The manuscript already mentions that two independent reviewers screened all studies using predefined eligibility criteria, and disagreements were resolved through discussion or consultation with a third reviewer. This process has now been described more clearly.

OPEN PEER REVIEW

Revision (1)

REFEREE : Reviewer

8 Sep 2025

Dear AE

All questions have been answered well.

REFEREE : Reviewer

8 Sep 2025

Dear Editor

In my opinion, it is suitable for publishing.

REFEREE : Associate Editor

9 Sep 2025

Dear Chief Editor

Thanks the authors for improvement of quality of article. According to the reviewers' comments, the article is accepted for publication.

Fatemeh Ehsani : EIC

9 Sep 2025

Dear Authors

We are pleased to inform you that your article is accepted for publication in the MEJRHS. We hope to receive the other qualified articles from your group.