



## PEER-REVIEW REPORT

**Name of journal:** *World Journal of Hepatology*

**Manuscript NO:** 103839

**Title:** Research progress on the roles of complement in liver injury

**Provenance and peer review:** Unsolicited Manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 06109453

**Position:** Peer Reviewer

**Academic degree and professional title:** Associate Chief Physician, Associate Professor

**Reviewer's Country/Territory:** China

**Author's Country/Territory:** China

**Manuscript submission date:** 2024-12-02

**Reviewer chosen by:** Hong-Xin Jiang

**Reviewer accepted review:** 2024-12-06 01:34

**Reviewer performed review:** 2024-12-06 02:40

**Review time:** 1 Hour

Scientific quality	Grade B (Very good)
Novelty of this manuscript	Grade B (Very Good)
Creativity or innovation of this manuscript	Grade B (Very Good)
Scientific significance of the conclusion in this manuscript	Grade B (Very Good)
Language quality	Grade B (Very good)
Does this manuscript describe a study of the existing knowledge system?	Yes



Does this manuscript report a revolutionary innovation?	No
Does this manuscript report an unconventional innovation?	No
Conclusion	Minor revision
Re-review	No
Peer-reviewer statements	Peer-Review: Onymous
	Conflicts-of-Interest: No

#### **SPECIFIC COMMENTS TO AUTHORS**

This study provides a comprehensive review of the roles of the complement system in various liver diseases, including chronic hepatitis B, non-alcoholic fatty liver disease (NAFLD), and hepatocellular carcinoma. The manuscript not only summarizes current research advancements but also explores how different components of the complement system contribute to the pathogenesis of these diseases. By citing a substantial body of relevant literature from basic scientific research to clinical applications, it underscores the importance of interdisciplinary collaboration. For instance, it highlights molecular mechanisms linking viral hepatitis and hepatocellular carcinoma. The strength of this article lies in its comprehensive literature review, citing a large number of high-quality studies that cover a wide range from basic science to clinical applications. Examples include the study on complement C5a as a indicator of significant fibrosis and early cirrhosis in chronic hepatitis B patients [Deng et al., 2017], and a cross-sectional study on the association between complement C3 and the incidence of NAFLD in adults [Jia et al., 2015]. This provides readers with a detailed and up-to-date knowledge framework. Additionally, the article delves into the specific mechanisms by which the complement system operates in different liver diseases, revealing its dual role in immune responses, both enhancing immune reactions and potentially exacerbating liver damage



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through altered liver cell function. This in-depth analysis aids in understanding the complexity of the complement system and its critical role in disease progression. The paper also mentions the potential of the complement system as a new therapeutic target, listing promising directions for drug development, such as the protective effects of C5a receptor antagonists in reducing ischemia-reperfusion injury [Arumugam et al., 2004], providing valuable references for future treatment strategies. Finally, the authors not only summarize existing research findings but also point out important directions for future research and potential drug targets, such as exploring the role of the complement system in liver regeneration and repair [Mastellos et al., 2001], offering clear guidance for subsequent studies. Although the paper mentions several potential therapeutic targets, there is limited discussion on how these findings can be translated into practical clinical treatment strategies. Additionally, some sections lack clear logical connections between paragraphs. The authors are recommended to further explore the potential of the complement system as a therapeutic target and the challenges it faces, as well as refine the manuscript structure to ensure a smooth transition between different sections. Overall, this manuscript offers valuable insights into the role of the complement system in liver diseases, contributing significantly to the advancement of research in this field. However, addressing the aforementioned limitations would strengthen the manuscript and better serve both the academic community and clinical practice. By refining these aspects, the authors can provide a more robust foundation for understanding the complement system's role in liver diseases and potentially guide future research towards developing novel therapeutic strategies.



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**Peer-review model:** Single blind

**Reviewer's code:** 07755635

**Position:** Editorial Board

**Academic degree and professional title:** Associate Professor, MD

**Reviewer's Country/Territory:** China

**Author's Country/Territory:** China

**Manuscript submission date:** 2024-12-02

**Reviewer chosen by:** Hong-Xin Jiang

**Reviewer accepted review:** 2024-12-11 11:57

**Reviewer performed review:** 2024-12-20 14:08

**Review time:** 9 Days and 2 Hours

Scientific quality	Grade C (Good)
Novelty of this manuscript	Grade B (Very Good)
Creativity or innovation of this manuscript	Grade B (Very Good)
Scientific significance of the conclusion in this manuscript	Grade C (Good)
Language quality	Grade B (Very good)
Does this manuscript describe a study of the existing knowledge system?	Yes



Does this manuscript report a revolutionary innovation?	No
Does this manuscript report an unconventional innovation?	No
Conclusion	Minor revision
Re-review	Yes
Peer-reviewer statements	Peer-Review: Anonymous
	Conflicts-of-Interest: No

#### SPECIFIC COMMENTS TO AUTHORS

Thanks for the editor invited me to review the manuscript. It is my pleasure to review this manuscript. The manuscript " Research Progress on the Roles of Complement in Liver Diseases " offers a summary of the complex interplay between the complement system and liver homeostasis, emphasizing its dual role in liver disease pathology. The authors do not have academic integrity problems according to the peer-review rules, priorities, and standards. The manuscript topic fall within the scope of the journal. The manuscript structure is clear. The references consistent with or closely related to the subject of the manuscript. This is a very interesting study that will appeal to a lot of readers. This is a meaningful and interesting review. I still have the following questions about this manuscript. 1. First of all, the title of the article "Research Progress on the Roles of Complement in Liver Diseases" is too large. This review main summarizes the involvement of the complement system in liver injury, providing references and directions for future research. Therefore, the title of the article is not suitable and needs to be modified. 2. In fact the liver is responsible for producing 80%-90% of plasma complement components. The effects of complement and liver injury are mutual. However, this review only reviewed the effect of complement on liver injury, but did not mention the effect of liver injury on complement. 3. This review mainly reviews the



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relationship between complement and liver injury. Many studies are just phenomena, lacking the mechanism of complement in liver injury. 4. It is suggested that hepatitis B virus induced liver injury and hepatitis C virus induced liver injury should not be reviewed separately. 5. Finally, the primary and secondary titles of the article are not clear. For example “Complement and Alcoholic Liver disease (ALD)” including “The complement system is involved in alcoholic liver fibrosis and cirrhosis”.



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**Peer-review model:** Single blind

**Reviewer's code:** 08165212

**Position:** Peer Reviewer

**Academic degree and professional title:** PhD, Postdoctoral Fellow

**Reviewer's Country/Territory:** China

**Author's Country/Territory:** China

**Manuscript submission date:** 2024-12-02

**Reviewer chosen by:** Hong-Xin Jiang

**Reviewer accepted review:** 2024-12-23 00:48

**Reviewer performed review:** 2024-12-23 02:53

**Review time:** 2 Hours

Scientific quality	Grade D (Fair)
Novelty of this manuscript	Grade D (Fair)
Creativity or innovation of this manuscript	Grade C (Good)
Scientific significance of the conclusion in this manuscript	Grade C (Good)
Language quality	Grade B (Very good)
Does this manuscript describe a study of the existing knowledge system?	Yes



Does this manuscript report a revolutionary innovation?	No
Does this manuscript report an unconventional innovation?	Yes
Conclusion	Rejection
Re-review	No
Peer-reviewer statements	Peer-Review: Anonymous
	Conflicts-of-Interest: No

#### **SPECIFIC COMMENTS TO AUTHORS**

The review article titled "Research Progress on the Roles of Complement in Liver Diseases" offers an exploration of the complement system's multifaceted roles in liver pathophysiology, addressing its impact on various liver conditions. This manuscript should not be accepted for publication in the World Journal of Hepatology for the following reasons: 1. Lack of Novel Insights: The manuscript provides an extensive overview of the existing literature on the complement system's role in liver diseases but fails to offer new insights or significant advancements in the field. For a review article, it is crucial to provide a fresh perspective or new hypothesis that can advance the understanding or treatment of liver diseases, which this manuscript does not sufficiently achieve. 2. Incomplete Coverage of Recent Studies: The review does not adequately incorporate the latest research and findings, especially from the last one to two years. This omission is particularly notable in the sections on non-alcoholic fatty liver disease and viral hepatitis, where recent advancements have been pivotal. 3. Superficial Analysis: The manuscript often lists findings from various studies without deep analytical integration or discussion about the implications of these findings. A more thorough analysis and synthesis of how the complement system interactions vary between different types of liver diseases would be beneficial. 4. Methodological Concerns: There



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is a lack of transparency regarding the criteria for selecting studies included in the review, which raises concerns about the potential for selection bias. A more rigorous methodological approach to literature selection and analysis is needed. 5. Theoretical and Practical Implications: The discussion section lacks a critical examination of how the findings might influence current clinical practices or future research directions. The manuscript would benefit from a stronger focus on practical applications and potential therapeutic targets. Given these significant concerns, I do not find the manuscript suitable for publication in its current form. It would need substantial revisions to address the above points comprehensively.



## RE-REVIEW REPORT OF REVISED MANUSCRIPT

**Name of journal:** *World Journal of Hepatology*

**Manuscript NO:** 103839

**Title:** Research progress on the roles of complement in liver injury

**Provenance and peer review:** Unsolicited Manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 07755635

**Position:** Editorial Board

**Academic degree and professional title:** Associate Professor, MD

**Reviewer's Country/Territory:** China

**Author's Country/Territory:** China

**Manuscript submission date:** 2024-12-02

**Reviewer chosen by:** Li Li

**Reviewer accepted review:** 2025-02-07 09:47

**Reviewer performed review:** 2025-02-07 13:22

**Review time:** 3 Hours

<b>Content to be reviewed</b>	Does the manuscript's content fall within the scope of the journal? <b>Yes</b> Is there any Key Word that is not included in the manuscript title? <b>Yes</b> Do authors' affiliations correspond to the content of the manuscript? <b>Yes</b> Does the Abstract contain the contents of each part of the manuscript (IMRaD)? <b>Yes</b> Are the Key Words complete? <b>Yes</b> Is the content of the Introduction adequate? <b>Yes</b>
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	<p>Is the content of the Materials and Methods complete? <b>Yes</b></p> <p>Is the description of the experiments clear and complete? <b>Yes</b></p> <p>Are the experimental data presented in the manuscript's biostatistics content reliable? <b>Yes</b></p> <p>Are the experimental data of the Results true and reliable? <b>Yes</b></p> <p>Are the quality and resolution of the images up to standard? <b>Yes</b></p> <p>Do the selection and design of the figures and tables follow the principles of necessity and clarity? <b>Yes</b></p> <p>Is the content of the Discussion reasonable? <b>Yes</b></p> <p>Is the Conclusion reasonable? <b>Yes</b></p> <p>Are all references necessary and reasonable? <b>Yes</b></p> <p>Do authors omit important references? <b>No</b></p> <p>Are all references related to the topic of the manuscript? <b>Yes</b></p> <p>Do authors only cite their own earlier publications? <b>No</b></p> <p>Is the manuscript's text correct, concise, and clear? <b>Yes</b></p> <p>Will the manuscript's content be of interest to readers? <b>Yes</b></p> <p>Are additional experiments needed for the study? <b>No</b></p> <p>Does the research scope comply with ethics? <b>Yes</b></p>
<b>Scientific quality</b>	Grade B (Very good)
<b>Novelty of this manuscript</b>	Grade B (Very Good)
<b>Creativity or innovation of this manuscript</b>	Grade B (Very Good)
<b>Scientific significance of the conclusion in this manuscript</b>	Grade B (Very Good)



Language quality	Grade B (Very good)
Does this manuscript describe a study of the existing knowledge system?	No
Does this manuscript report a revolutionary innovation?	No
Does this manuscript report an unconventional innovation?	No
Conclusion	Accept
Peer-reviewer statements	Peer-Review: Anonymous
	Conflicts-of-Interest: No

#### SPECIFIC COMMENTS TO AUTHORS

Thanks for the editor invited me to review the manuscript. It is my pleasure to review this manuscript. The manuscript "Research progress on the roles of complement in liver injury " offers a summary of the complex interplay between the complement system and liver homeostasis, emphasizing its dual role in liver disease pathology. The authors do not have academic integrity problems according to the peer-review rules, priorities, and standards. The manuscript topic fall within the scope of the journal. The manuscript structure is clear. The references consistent with or closely related to the subject of the manuscript. This is a very interesting study that will appeal to a lot of readers. This is a meaningful and interesting review. The authours changed the title of the article "Research Progress on the Roles of Complement in Liver Diseases" to "Research progress on the roles of complement in liver injury". It is very good. In fact the liver is responsible for producing 80%-90% of plasma complement components. The effects of complement and liver injury are mutual. This review reviewed the effect of complement on liver injury and the effect of liver injury on complement. It is interesting.