



## PEER-REVIEW REPORT

**Name of journal:** *World Journal of Gastroenterology*

**Manuscript NO:** 86789

**Title:** Sequence of events leading to primary biliary cholangitis

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

**Peer-review model:** Single blind

**Reviewer's code:** 05848410

**Position:** Peer Reviewer

**Academic degree:** Doctor, MMed, PhD

**Professional title:** Chief Doctor, Chief Physician, Dean, Doctor, Professor, Surgeon

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

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

**Manuscript submission date:** 2023-07-07

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2023-07-13 14:00

**Reviewer performed review:** 2023-07-20 03:24

**Review time:** 6 Days and 13 Hours

<b>Scientific quality</b>	<input checked="" type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Novelty of this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
<b>Creativity or innovation of this manuscript</b>	<input checked="" type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation



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Scientific significance of the conclusion in this manuscript	<input checked="" type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

## SPECIFIC COMMENTS TO AUTHORS

As we know, the etiology of primary biliary cholangitis is unclear and the outcome is still vary a lot. This mini-review is excellent on discussing the molecular and cellular mechanism on the genesis and development of the primary biliary cholangitis, and the authors gave us a totally different view if this. The authors described the disease using the different period of the ones of PBC. In different period of this disease, the authors provided different studied results to inspire the readers.



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

**Peer-review model:** Single blind

**Reviewer's code:** 03294368

**Position:** Editorial Board

**Academic degree:** DSc, MD, PhD

**Professional title:** Dean, Professor

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

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

**Manuscript submission date:** 2023-07-07

**Reviewer chosen by:** Geng-Long Liu

**Reviewer accepted review:** 2023-07-31 05:44

**Reviewer performed review:** 2023-08-07 13:24

**Review time:** 7 Days and 7 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Novelty of this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
<b>Creativity or innovation of this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation



<b>Scientific significance of the conclusion in this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
<b>Language quality</b>	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input type="checkbox"/> Anonymous <input checked="" type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

**SPECIFIC COMMENTS TO AUTHORS**

The presented manuscript addresses a highly relevant topic, as primary biliary cholangitis (PBC) remains a challenging issue for both physicians and researchers. The paper is authored by a team with significant experience in the field of liver and biliary pathology, and their expertise is evident in their clear understanding of the subject's essence and importance, as highlighted in this mini-review. The abstract effectively summarizes and reflects the content of the manuscript, providing a concise overview of the study. The introduction aptly describes the background and significance of the research, setting the stage for the readers to understand the context of the study. The manuscript's text is well-drafted, supporting easy comprehension of the presented concept. However, it would be beneficial if the authors briefly described their method of selecting the literature reviewed. Additionally, in the conclusion, emphasizing the novelty of the paper and how it contributes to advancing our standard knowledge about PBC would be beneficial. Considering these minor points, I recommend publishing the presented mini-review after a few small polishing adjustments, should the authors and the editor agree with my suggestions.



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**Peer-review model:** Single blind

**Reviewer's code:** 05199192

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Deputy Director

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

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

**Manuscript submission date:** 2023-07-07

**Reviewer chosen by:** Geng-Long Liu

**Reviewer accepted review:** 2023-07-31 07:26

**Reviewer performed review:** 2023-08-08 16:07

**Review time:** 8 Days and 8 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Novelty of this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
<b>Creativity or innovation of this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation



<b>Scientific significance of the conclusion in this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

**SPECIFIC COMMENTS TO AUTHORS**

1. The manuscript mentions that "Escherichia coli and aromatic phenolic bacteria are associated with PBC" (Page 5, line 6). However, there is a lack of further explanation regarding the mechanisms underlying this association. The dysbiosis of gut microbiota affects the progression of primary biliary cholangitis (PBC) by regulating intestinal permeability, lipopolysaccharide production, and bile acid metabolism (PMID: 37408823, 28213609). Consequently, conducting a comprehensive review of this section may potentially enhance the readability of the manuscript.

2. When this manuscript refers to the impairment of bile duct epithelial secretion on page 6, it may be better to review the impact of the bile metabolic microenvironment on its secretion.

3. Page 4 of the manuscript, it is mentions that anti-mitochondrial antibody (AMA) initiates PBC. It is recommended to further review the mechanisms by which AMA causes PBC.



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**Peer-review model:** Single blind

**Reviewer's code:** 03664208

**Position:** Peer Reviewer

**Academic degree:** BCPS

**Professional title:** MHSc

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

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

**Manuscript submission date:** 2023-07-07

**Reviewer chosen by:** Geng-Long Liu

**Reviewer accepted review:** 2023-08-04 01:52

**Reviewer performed review:** 2023-08-14 05:35

**Review time:** 10 Days and 3 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Novelty of this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input checked="" type="checkbox"/> Grade D: No novelty
<b>Creativity or innovation of this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input checked="" type="checkbox"/> Grade D: No creativity or innovation



<b>Scientific significance of the conclusion in this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

**SPECIFIC COMMENTS TO AUTHORS**

As a consequence, approximately one-third of patients diagnosed with primary cholangitis will progress to cirrhosis. Traditional immunosuppressive therapy exhibits limited efficacy, necessitating liver transplantation as the ultimate treatment option. This review delves into the cellular and molecular mechanisms underlying the progression of end-stage primary cholangitis, ultimately leading to liver fibrosis and cirrhosis. The novelty of this study was general. In light of certain limitations within this study, the following inquiries are raised: 1.The abstract section fails to provide a comprehensive summary of the review's content. 2.The key terms do not accurately reflect the main focus, and it is recommended to revise them. 3.The references do not adequately represent the current state of research; therefore, it is suggested to remove them and instead cite articles from the past 3-5 years. 4. The discussion section does not address the core issues raised in the review, thus requiring further elaboration on the main points.



## RE-REVIEW REPORT OF REVISED MANUSCRIPT

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**Peer-review model:** Single blind

**Reviewer's code:** 03664208

**Position:** Peer Reviewer

**Academic degree:** BCPS

**Professional title:** MHSc

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

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

**Manuscript submission date:** 2023-07-07

**Reviewer chosen by:** Xin-Liang Qu

**Reviewer accepted review:** 2023-08-25 02:52

**Reviewer performed review:** 2023-08-25 12:25

**Review time:** 9 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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

This review discusses the disease background and possible preconditions of primary biliary cholangitis, and discusses in detail the sequential synergy of cellular/molecular events leading to end-stage primary cholangitis. This paper provides a new insight into the existing problems of primary biliary cholangitis, discusses the relationship with inflammation caused by liver fibrosis and bile secretion function, and provides a new idea for clinical diagnosis and treatment targets. The article is logical and has a prominent point of view. It may be considered for publication.