

PEER-REVIEW REPORT

Name of journal: *World Journal of Hepatology*

Manuscript NO: 81063

Title: Clostridioides difficile infection in patients with nonalcoholic fatty liver disease-current status

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 06076623

Position: Peer Reviewer

Academic degree: PhD

Professional title: Research Associate

Reviewer's Country/Territory: China

Author's Country/Territory: Russia

Manuscript submission date: 2022-10-23

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-10-30 15:12

Reviewer performed review: 2022-11-02 13:30

Review time: 2 Days and 22 Hours

Scientific quality	<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 Grade E: Do not publish
Language quality	<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
Conclusion	<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
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No



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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

My detailed comments are as follows: 1.This manuscript only describes the correlation between CDI and NAFLD. Is there any further research? 2.How can CDI be treated and prevented, and which drugs are effective against CDI? 3. What is the molecular mechanism of CDI?

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Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03834342

Position: Editorial Board

Academic degree: PhD

Professional title: Professor

Reviewer's Country/Territory: France

Author's Country/Territory: Russia

Manuscript submission date: 2022-10-23

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-11-28 08:46

Reviewer performed review: 2022-12-04 20:18

Review time: 6 Days and 11 Hours

Scientific quality	<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
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 type="checkbox"/> Accept (General priority) <input checked="" 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="radio"/>] Anonymous [<input type="radio"/>] Onymous
	Conflicts-of-Interest: [<input type="radio"/>] Yes [<input checked="" type="radio"/>] No

SPECIFIC COMMENTS TO AUTHORS

Reviewer Comments to Authors The manuscript presented by Yana V Kiseleva et al. aims to give an overview about the current status of research on the association of NAFLD with *Clostridioides difficile* infection (CDI) severity. The paper sounds easy to read and presents a wealth of information with regard to such a complex area of research. However, there are few issues that remain to be addressed. Major comments:

1) In most studies related to *C. difficile*/NAFLD, patients with different NAFLD severity stages; often present with heterogeneous lesions and variable demographic characteristics including age, sex and ethnic background, various comorbidities (obesity, type 2 diabetes, ...), genetic susceptibility, which are known to influence the gut microbiome; are often overlooked. For example, it has been demonstrated that gut microbiota dysbiosis is exacerbated with increasing obesity severity [Le Chatelier, E. et al. Richness of human gut microbiome correlates with metabolic markers. *Nature* 500, 541 (2013); Aron-Wisnewsky, J. et al. Major microbiota dysbiosis in severe obesity: fate after bariatric surgery. *Gut* <https://doi-org.bases-doc.univ-lorraine.fr/10.1136/gutjnl-2018-316103> (2018)]. These observations suggest that patients need to be stratified for each metabolic confounding factor. Authors must comment on these questions. 2) A perspective section needs to be included in the text. There are new approaches including metagenomics and multi-omics studies, gut microbiome sequencing, system biology strategies that can be used to study in depth the suggested association of *Clostridioides difficile* with NAFLD and explore the potential use of microbiome signatures as biomarkers for future metabolic alterations diagnosis. 3) A figure or a table summarizing the main

information on *C. difficile*/NAFLD would help effective data presentation and make it easier for readers to understand the research in the manuscript. Minor comments: -

Title: No need for the abbreviation of nonalcoholic fatty liver disease in the title. -

Abstract section: first and second lines "Nonalcoholic fatty liver disease (NAFLD) is the most common chronic liver disease, leading to fibrosis, cirrhosis and hepatocellular carcinoma (HCC), factors known to be associated with increased....", the sentence is not clear (factors????). - Core Tip section: The sentence "More retrospective studies and systematic reviews are needed to examine this group of patients as a risk factor for CDI" is not clear, please rephrase. - Page 3, the title of the first paragraph is probably missing (Introduction?) - In this paragraph, the sentence "The current epidemiology of NAFLD is not totally understood" Is not clear, please clarify. -Page 4: line 6-7: the sentence ".... in 2017, the incidence was estimated at 223,900 with 12,800 deaths[14]." The citation needs to be checked. In the original reference (Ref #14 in this manuscript), it was written "In addition, nearly 223,900 people in the United States required hospital care for *C. difficile* and at least 12,800 people died in 2017." - There are still some grammatical mistakes in manuscript that need to be checked. For example: "Therefore, a low level of secondary bile salts (and consequently a low concentration of secondary bile acid-producing bacteria) and a high level of primary bile salts, results in CDI and its recurrence[38]."

RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Peer-review model: Single blind

Reviewer's code: 06076623

Position: Peer Reviewer

Academic degree: PhD

Professional title: Research Associate

Reviewer's Country/Territory: China

Author's Country/Territory: Russia

Manuscript submission date: 2022-10-23

Reviewer chosen by: Jia-Ru Fan

Reviewer accepted review: 2022-12-30 05:15

Reviewer performed review: 2022-12-30 05:25

Review time: 1 Hour

Scientific quality	<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
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
Peer-reviewer	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous



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statements

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

SPECIFIC COMMENTS TO AUTHORS

The revised manuscript is OK.