

PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Surgery

Manuscript NO: 69650

Title: Patients with Clostridium difficile infection and prior appendectomy may be prone to worse outcomes

Reviewer's code: 05824934

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: Singapore

Author's Country/Territory: United States

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Reviewer chosen by: AI Technique

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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 Grade E: Do not publish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 type="checkbox"/> Anonymous <input checked="" type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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SPECIFIC COMMENTS TO AUTHORS

This study investigates the possible link between prior appendectomy and the severity of *Clostridium difficile* infection (CDI). While the topic reported in this study is very interesting, several other factors may also be taken into consideration. As pointed out by the authors, *Clostridium difficile* infection occurs due to a dysbiosis of the gut (which may be manifested in two forms: reduced microbiota diversity and over-growth of certain strains like *Clostridium difficile*), and excessive use of antibiotics are the main risk factor of development gut dysbiosis and CDI. Thus, stronger antibiotics recommended in the conclusion of the manuscript should be further investigated. When we talk about microorganism infection, we need to take the human host immunity response into account, and not always thinking that antibiotic treatment being the sole mechanism responsible for the clearance of infections [1]. Thanks to the immune responses like phagocytosis and xenophagy, most of bacterial infections are self-limiting [1-3]. More importantly, our immune system will use these bacteria as source of essential nutrients [4,5] to support its proper functioning and to provide the essential nutrition needed by the whole body. The use of antibiotics actually deprives the patients of an indispensable source of essential nutrients. Nevertheless, as our immune system also contributes to nutrition acquisition by degrading human microbiota, pathogens and damaged body tissue cells, over-nutrition may occur, which may cause lipotoxicity and further tissue damage [6,7], promoting chronic inflammation and fuelling microbial dysbiosis (over-growth of specific microorganisms like *Clostridium difficile*). As the authors also collect socio-demographic data like weight and height of the patients and EMR information on patients' comorbidities in this study, it will be more captivating if the authors can investigate the contribution of BMI or metabolic comorbidity to severity of CDI, and test the link between nutrition disorder and CDI. The following references

may be included in the revision of the manuscript: 1. Levin, B.R.; Baquero, F.; Ankomah, P.P.; McCall, I.C. Phagocytes, Antibiotics, and Self-Limiting Bacterial Infections. *Trends Microbiol.* 2017, 25, 878–892. 2. Levin, B.R.; Antia, R. Why we don't get sick: The within-host population dynamics of bacterial infections. *Science* 2001, 292, 1112–1115. 3. Troisi, J.; Venutolo, G.; Pujolassos Tanya, M.; Delli Carri, M.; Landolfi, A.; Fasano, A. COVID-19 and the gastrointestinal tract: Source of infection or merely a target of the inflammatory process following SARS-CoV-2 infection? *World J. Gastroenterol.* 2021, 27, 1406–1418. 4. McFall-Ngai, M.; Hadfield, M.G.; Bosch, T.C.; Carey, H.V.; Domazet-Loso, T.; Douglas, A.E.; Dubilier, N.; Eberl, G.; Fukami, T.; Gilbert, S.F.; et al. Animals in a bacterial world, a new imperative for the life sciences. *Proc. Natl. Acad. Sci. USA* 2013, 110, 3229–3236. 5. Davari M, Moghaddam HR, Soola AH (2021) Identifying the Predictors of Self-Management Behaviors in Patients with Diabetes Based on Ecological Approach: A Systematic Review. *Curr Diabetes Rev* 17(6): e102620187197. DOI : 10.2174/1573399816666201026161009 6. Saltiel, A.R.; Olefsky, J.M. Inflammatory mechanisms linking obesity and metabolic disease. *J. Clin. Investig.* 2017, 127, 1–4. 7. Garbarino, J.; Sturley, S.L. Saturated with fat: New perspectives on lipotoxicity. *Curr. Opin Clin. Nutr. Metab. Care* 2009, 12, 110–116.