

15 January, 2023

Editor-in-Chief

World Journal of Gastrointestinal Endoscopy

Manuscript No: 81165

Manuscript title: Gastroesophageal reflux disease in children: what's new right now?

Authors: Palittiya Sintusek, Mohamed Mutalib, Nikhil Thapar

Dear Editor,

Thank you for your letter dated 12 December 2022. We are pleased to know that our manuscript has been rated as potentially acceptable for publication in *World Journal of Gastrointestinal Endoscopy*, subject to major revisions and response to the Reviewer comments.

We would like to submit a revised manuscript that has been modified according to the instructions provided in the decision letter and reviewer comments. All changes made during the revision process are appropriately marked and highlighted in red. Also appended to this letter are point-by-point responses to the comments raised by the reviewers.

We would like to take this opportunity to express our sincere thanks to the reviewers who have identified areas of the manuscript that needed corrections or modifications. Their suggestions have indeed improved the

quality of our manuscript. We would also like to thank you for allowing us to submit a revised copy of the manuscript.

We hope that the revised manuscript is in order and that it can be accepted for publication in the World Journal of Gastrointestinal Endoscopy.

Sincerely Yours,

Nikhil Thapar

Department of Gastroenterology, Hepatology and Liver transplant,
Queensland Children's Hospital, Brisbane, Australia; School of Medicine,
University of Queensland, Brisbane, Queensland, Australia.; Woolworths
Centre for Child Nutrition Research, Queensland University of
Technology, Brisbane, Queensland, Australia.

Point-by-point responses to Reviewer comments

Response to reviewer 1

Reviewer #1: In this manuscript, the authors summarized Gastroesophageal reflux disease in children. This manuscript is clearly written and provides an objective presentation of the current literature. I do not have any substantial amendments to suggest. 1. Regarding pathophysiology, I am sure that TLESR is the main cause, but how about the involvement of other factors such as abdominal strain and free reflux? Also, the correlation between endoscopic findings and symptoms is not clear even in adults, but is there anything that mentions the usefulness of endoscopy aside from extra-esophageal symptoms? 2. Pharmacological

treatment describes the side effects of rate of respiratory and gastrointestinal infection, but how about references? 3. Regarding endoscopic management, which is mentioned at the end, I have the impression that the content only refers to surgical matters. If you write under this name, wouldn't it be better to write a little more about the usefulness of endoscopes?

Answer: Thank you for your insightful comments. We would like to answer your comments point-by-point as follow;

1. Regarding pathophysiology, I am sure that TLESR is the main cause, but how about the involvement of other factors such as abdominal strain and free reflux? Also, the correlation between endoscopic findings and symptoms is not clear even in adults, but is there anything that mentions the usefulness of endoscopy aside from extra-esophageal symptoms?

Answer: Thank you very much for your suggestions. We agree that the main pathogenesis of GERD is from TLESR. Hence, we added more information of TLESR in the pathogenesis part and retained the information of other factors. We hope that physicians will learn to recognize not only TLESR but also treat other factors associated with GERD in the meantime. In aspect of the usefulness of endoscopy in extraesophageal symptoms, a well-designed study reported the high prevalence of gross and histopathological abnormalities of the esophagus in extraesophageal symptoms (DOI: 10.1186/s12876-021-01658-z). We

recommend test (endoscopy and MII-pH) before treatment. In clinical practice, physician starts the treatment for extraesophageal symptoms that suspected from GERD and then test later if the symptoms do not improve. The treatment might modify the real gross and histopathology of esophagus making the poor correlation of endoscopic findings and symptoms.

2. Pharmacological treatment describes the side effects of rate of respiratory and gastrointestinal infection, but how about references?

Answer: We have added three referenced at this sentence, as follows:

Giuliano C, Wilhelm SM, Kale-Pradhan PB. Are proton pump inhibitors associated with the development of community-acquired pneumonia? A meta-analysis. *Expert Rev Clin Pharmacol* 2012; 5(3): 337-344 [PMID: 22697595 PCMID: 22697595 DOI: 10.1586/ecp.12.20]

Nguyen PA, Islam M, Galvin CJ, Chang CC, An SY, Yang HC, Huang CW, Li YJ, Iqbal U. Meta-analysis of proton pump inhibitors induced risk of community-acquired pneumonia. *Int J Qual Health Care* 2020; 32(5): 292-299 [PMID: 32436582 PCMID: 32436582 DOI: 10.1093/intqhc/mzaa041]

Chen Y, Liu B, Glass K, Du W, Banks E, Kirk M. Use of Proton Pump Inhibitors and the Risk of Hospitalization for Infectious Gastroenteritis. *PLoS One* 2016; 11(12): e0168618 [PMID: 27997598 PCMID: 27997598 DOI: 10.1371/journal.pone.0168618]

3. Regarding endoscopic management, which is mentioned at the end, I have the impression that the content only refers to surgical matters. If you write under this name, wouldn't it be better to write a little more about the usefulness of endoscopes?

Answer: We sincerely appreciate the reviewer's comments. We added more information about endoscopic and laparoscopic fundoplication in the treatment part already.

Response to reviewer 2

Reviewer #2: Well written review but it does not highlight what is new Very well Please add table for what is new in diagnosis and management and couple of flowcharts about steps in diagnosis and management

Answer: We would like to thank the Reviewer for the in-depth critique of our manuscript and for the constructive comments. The table and flowcharts were added in the manuscript already.

Response to reviewer 3

Reviewer #3: The review was well structured and of clinical value to both the gastroenterologists and the primary care pediatricians, however before acceptance revision is needed regarding the grammar and adding the references and correcting all tables and add them in the manuscript next to each corresponding paragraph. Please add a sentence from the following reference: proton pump inhibitors and risk of asthma in children. by Yun-Han Huang et al., JAMA pediatrics, 2021; 175(4):394-403 Also Please write

the full word in the text followed initially by the abbreviations, then down in the text you can use the abbreviations provided that it is NOT in the beginning of the sentence I added some corrections in RED, please revise the whole manuscript again

Response: Thank you for pointing this out. The grammar and typos were carefully correct as suggestion and the reference was added into the manuscript.

Response to Editor-in-Chief

I recommend the manuscript to be published in the World Journal of Gastrointestinal Endoscopy. Before final acceptance, when revising the manuscript, the author must supplement and improve the highlights of the latest cutting-edge research results, thereby further improving the content of the manuscript. To this end, authors are advised to apply a new tool, the Reference Citation Analysis (RCA). RCA is an artificial intelligence technology-based open multidisciplinary citation analysis database. In it, upon obtaining search results from the keywords entered by the author, "Impact Index Per Article" under "Ranked by" should be selected to find the latest highlight articles, which can then be used to further improve an article under preparation/peer-review/revision. Please visit our RCA database for more information at:

<https://www.referencecitationanalysis.com/>.

Answer: We sincerely appreciate the editor's suggestion. We revised the manuscript follow the comments of reviewers. We highlighted the latest cutting-edge research results into the table already.

Sincerely yours,

Nikhil Thapar

Department of Gastroenterology, Hepatology and Liver transplant,
Queensland Children's Hospital, Brisbane, Australia; School of Medicine,
University of Queensland, Brisbane, Queensland, Australia.; Woolworths
Centre for Child Nutrition Research, Queensland University of
Technology, Brisbane, Queensland, Australia.