

Dear Editor:

Thanks very much for receiving the pertinent comments and suggestions from you and the reviewers. We have made response and modified our manuscript according to reviewers' each comment in the revised manuscript. Please see the details with yellow color in the revised manuscript in blue color. Besides, we have revised the manuscript according to the Editorial Office's comments and suggestions listed below.

Firstly, in terms of construction, we have revised the manuscript, tables, figures, and figure legends for formatting errors and adjusted them to the requirements of the journal.

Secondly, in terms of content, we corrected the title to a more specific and self-explanatory version, in accordance with one reviewer's comment. we have updated some authoritative and recently published references in our revised manuscript. We have re-written the duplicates and corrected the statement errors. During the submission waiting period, all subjects with incomplete treatments at the time had finished their treatments and had been off medication for one month. We tracked both these patients and those who had previously been lost to follow-up. This led us to refine and adjust the study results. The updated sample sizes, flow diagram, and eradication rates are marked in the manuscript.

Besides, we have added the "Core tip" section and the "Article Highlights" section.

Finally, in response to grammatical and formatting errors in the manuscript, we have edited it at a professional English language editing company recommended by the journal and have provided an English language certificate from the company.

We deeply appreciate the Editor/Reviewer's warm work earnestly, and hope that the modifications will meet with approval.

Sincerely,
Yiling Li.

The point-by-point responses to the concerns of the reviewers are as follows:

Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: Dear Editor, I should first thank for inviting me as potential reviewer to read and comment on paper entitled "High rates of secondary clarithromycin and levofloxacin resistance of *Helicobacter pylori* and susceptibility-guided eradication effect in Liaoning Province". In the current study, the authors aimed to collect information on individuals with failure eradication histories from Liaoning Province, in order to analyse the secondary resistance profile of clarithromycin and levofloxacin, demographic characteristics, along with assessing the effect of susceptibility-guided therapy in Liaoning, in the northeast of China. The main title accurately reflects the major topic and content of the study. The abstract summarizes and reflects the work described in the manuscript. Also, the abstract presents the significant points related to the background, objectives, materials and methods, results and conclusions. The materials and methods sufficiently described for the results and conclusions that are presented in the preceding sections. The study type and design were defined in the section of the materials and methods. Exclusion criteria are well defined. Figures and tables are sufficient

and well-organized. Ethics Committee approval was received. So, the section materials and methods is adequate. The statistical methods used are appropriate. The section of the discussion is well organized. The conclusions are drawn appropriately supported by the literature. The manuscript adequately describes the background, present status and significance of the study. The manuscript interprets the findings adequately and appropriately, highlighting the key points clearly. I think that it will contribute to the literature. I have some minor criticisms. - The manuscript appropriately cites the important and authoritative references but does not cite the recent published articles in the Introduction part of the manuscript. If the recent published article about helicobacter pylori prevalence in the world for example " Relationship between the severity of Helicobacter pylori infection and neutrophil and lymphocyte ratio and mean platelet volume in children. Argent Pediatr 2020;118(3):e241-243" are cited, the manuscript would be better.

Reply: Thanks for your recognition. Based on your suggestion, we have updated some authoritative and recently published references in our manuscript. We also thoroughly learned the reference " Relationship between the severity of Helicobacter pylori infection and neutrophil and lymphocyte ratio and mean platelet volume in children. Argent Pediatr 2020;118(3):e241-243". This article firstly investigated the association between Helicobacter pylori infection and neutrophil/lymphocyte ratio (NLR) and mean platelet volume (MPV) values, severity classification, and pre- and post-treatment status in pediatric populations. It concluded that there was no association between NLR and MPV values with Helicobacter pylori infection, severity classification, or pre- and post-treatment status. We surprisingly found it is very worthy of our study and has been cited at the Introduction section as follows:

H. pylori has also been implicated in the development of extra-digestive disorders, such as iron deficiency anemia, idiopathic thrombocytopenic purpura, nonalcoholic fatty liver disease (NAFLD), and Alzheimer's disease (AD)^[1-3]. *H. pylori* also elicits immune responses. Several researchers have investigated the association of *H. pylori* infection with mean platelet volume (MPV) and neutrophil/lymphocyte ratio (NLR) values in both adults and children ^[4, 5].

Reviewer #2:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors:

1. The title must be self-explanatory. Why "Liaoning Province"? "High rates of secondary clarithromycin and levofloxacin resistance of Helicobacter pylori and susceptibility-guided eradication effect in Liaoning Province" should be "? "Success of susceptibility-guided eradication of Helicobacter pylori in a region with high rates of secondary clarithromycin and levofloxacin resistance"

Reply: Thanks for your constructive suggestion. We realized the title should be self-explanatory and specific. The region mentioned in title should specify the prominent characteristics of high rates of secondary clarithromycin and levofloxacin resistance, by which the region was selected. Besides, the effect of eradication should be explained specifically. We have revised the title to "Success of susceptibility-guided eradication of *Helicobacter pylori* in a region with high rates of secondary clarithromycin and levofloxacin resistance".

2. Please use just one decimal in all values entire the manuscript. Prefer Age as 52.7±12.6 or even as 53±13. "The mean age and standard deviation of 132 adults was 52.69±12.585"

Reply: Sincerely thanks to this comment. We have carefully reviewed the manuscript and standardized the format of all values.

3. Use decimals in uniform format. (ie: as 15.7 and 11.0).

Reply: Sincerely thanks to this comment. We have corrected this problem and use decimals in uniform format, which have been marked in the revised version.

4. Re-write "Aim" and "Introduction" in "abstract section". Grammar errors and tautology should be corrected.

Reply: Thanks for your constructive suggestion. We have carefully reviewed the "Aim" in the "ABSTRACT" section and the "INTRODUCTION" section, and have re-written the duplicates and corrected the statement errors. We highlighted the modified section in the revised version.

5. "These two antibiotics analysed in this study" should be "Clarithromycin and levofloxacin were analyzed in this study"

Reply: Sincerely thanks to this comment. We have corrected this problem and marked in the revised version.

6. "Gastrointestinal symptoms included abdominal pain, fullness, heartburn, dysphagia, anorexia, and so on." Please remove "...so on." Instead list those other symptoms.

Reply: Thanks for your kind suggestion! We have removed "...so on."

7. "(rabeprazole 20mg/ilaprazole 5mg)" should be "(rabeprazole 20mg or ilaprazole 5mg)"

Reply: Thanks for your constructive suggestion. We have corrected this problem and marked in the revised version.

8. The comparison of treatment success for susceptibility guided eradication and empiric group (with non-completed level) should also given as Per Protocol (PP) and Intention-to-Treat (ITT).

Reply: Thanks for your constructive suggestion. During the submission waiting period, all subjects with unfinished treatments at that time had completed treatments and had been off medication for one month. We followed up with the above patients, as well as with those who had been previously lost to follow-up. We therefore refined and adjusted the results of this study. Updated sample sizes, Flow diagram, and eradication rates have been marked in the manuscript.

Reference

- 1 Dogan A, Ekinci O, Ebinc S. Effect of Helicobacter pylori infection on the first-line treatment outcomes in patients with immune thrombocytopenic purpura. *European review for medical and pharmacological sciences* 2022; **26**(11): 3995-4000 [PMID: 35731071 DOI: 10.26355/eurrev_202206_28970]
- 2 Mavilia-Scranton MG, Wu GY, Dharan M. Impact of Helicobacter pylori Infection on the Pathogenesis and Management of Nonalcoholic Fatty Liver Disease. *Journal of clinical and translational hepatology* 2023; **11**(3):

670-674 [PMID: 36969902 PMCID: PMC10037521 DOI: 10.14218/jcth.2022.00362]

3 Xie J, Cools L, Van Imschoot G, Van Wonterghem E, Pauwels MJ, Vlaeminck I, De Witte C, El Andaloussi S, Wierda K, De Groef L, Haesebrouck F, Van Hoecke L, Vandenbroucke RE. Helicobacter pylori-derived outer membrane vesicles contribute to Alzheimer's disease pathogenesis via C3-C3aR signalling. *Journal of extracellular vesicles* 2023; **12**(2): e12306 [PMID: 36792546 PMCID: PMC9931688 DOI: 10.1002/jev2.12306]

4 Sahin Y, Gubur O, Tekingunduz E. Relationship between the severity of Helicobacter pylori infection and neutrophil and lymphocyte ratio and mean platelet volume in children. *Archivos argentinos de pediatria* 2020; **118**(3): e241-e245 [PMID: 32470257 DOI: 10.5546/aap.2020.eng.e241]

5 Guclu M, Faruq Agan A. Association of Severity of Helicobacter pylori Infection with Peripheral Blood Neutrophil to Lymphocyte Ratio and Mean Platelet Volume. *Euroasian journal of hepato-gastroenterology* 2017; **7**(1): 11-16 [PMID: 29201765 PMCID: PMC5663767 DOI: 10.5005/jp-journals-10018-1204]