

## PEER-REVIEW REPORT

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

**Manuscript NO:** 66092

**Title:** Helicobacter pylori infection: how does age influence the inflammatory pattern?

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

**Peer-review model:** Single blind

**Reviewer's code:** 05072111

**Position:** Peer Reviewer

**Academic degree:** PhD

**Professional title:** Assistant Professor

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

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

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**Reviewer chosen by:** AI Technique

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<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 Grade E: Do not publish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>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 checked="" 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</b>	Peer-Review: <input type="checkbox"/> Anonymous <input checked="" type="checkbox"/> Onymous

## SPECIFIC COMMENTS TO AUTHORS

The aim of the article titled "Helicobacter pylori infection: what can influence gastric inflammatory pattern?" was a description of the changes and differences in the host's immune response to H. pylori infections, with particular emphasis on the effect of the patients' age. I find the article interesting and worth publishing, however, some corrections should be made to improve its quality. Below I present a list of changes and suggestions which, in my opinion, will improve the quality of the manuscript: - In general, the manuscript is written correctly in terms of language, while the Abstract, Core tip and Conclusions need to be improved -> these are the most important parts of the article (or at least those that are checked by readers as the first ones) Especially: "During childhood, it is possible to observe a predominant regulatory response, evidenced by several studies when they found high concentrations of key cytokines for the maintenance of this type of response such as TGF- $\beta$ 1 and IL-10..." [Abstract] "... the high levels of TGF- $\beta$ 1 and IL-17 found in that context, ..." [Abstract] "This can be explained based on the gastric inflammatory pattern against the disease, which changes as long as the infected individual gets older; favoring, initially, the persistence of the infection and then the gastric damage." [Core tip] Conclusions -> All Additionally: - "Helicobacter pylori is a microaerophilic, gram-negative, bacillus-shaped, mobile bacterium of great clinical importance and capable of colonizing an extremely hostile environment, due to its low pH, the stomach" -> Helicobacter pylori is a microaerophilic, gram-negative, rod-shaped, mobile bacterium of great clinical importance and capable of colonizing an extremely hostile stomach environment [Introduction] - "Studies, when analyzing the adult population ... child population is or will be infected with the bacterium" -> This entire part should be moved to the "Prevalence" section - especially

because that part was reused by authors in this fragment of the text [Introduction] - "H. pylori are part of Group I of carcinogens ..." -> H. pylori belongs to a Group I of carcinogens ... [Introduction] - "This predominantly regulatory pattern makes the gastric mucosa of children more easily colonized with H. pylori, but with less inflammation, when compared to what occurs in the mucosa of infected adults." -> This predominantly regulatory pattern makes the gastric mucosa of children more easy to be colonized by H. pylori, but is associated with a lower grade of inflammation, when compared to what occurs in the mucosa of infected adults. [Introduction] - "Interestingly, the pattern of immune response against the pathogen observed in children is not able to eliminate the infection, and the bacterium persists in the gastric environment if left untreated." -> As a result of this, the immune system of pediatric patients is not able to eliminate the H. pylori infection, and the bacterium persists in the gastric environment if left untreated. [Introduction] - "a lower concentration of TGF-B1, which, despite participating in the Treg and Th17 responses" -> a lower concentration of TGF- $\beta$ 1, which, despite participating in the Treg responses (without "Th17") [Introduction] - "A higher prevalence of the disease is usually observed among male subjects than in females" -> it is worth adding a sentence or two explaining why this is the case, e.g., a higher level of hygiene among women [Prevalence] - "The analysis of the expression of cytokines in the gastric environment evidenced that IL-10 and TGF- $\beta$ 1 are expressed in higher levels in the former group than in the latter" -> please delete "than in the latter" [Cytokine concentrations in the gastric mucosa] - "Taken together, the aforementioned results show that age, indeed, influences in the immune response" -> Taken together, the aforementioned results show that age, indeed, influences the immune response [Cytokine concentrations in the gastric mucosa] - "enhanced levels of Foxp3 and Latency Associated Peptide by T regulatory cell" -> enhanced levels of Foxp3 and Latency Associated Peptide by T reg cells [Cytokine concentrations in the gastric mucosa] -

“Therefore, we hope that, along with the advances in the clinical analysis of genetic and epigenetic backgrounds, the future approaches of H. pylori infections and the decisions on the necessity of bacterial eradication be carried out in a more individualized manner, instead of the generalized, but necessary, treatments preconized by current guidelines.” -> too long sentence; please separate into two shorter ones [Cytokine concentrations in the gastric mucosa] - “In a study that added neutralizing antibodies to IL-12 in gastric biopsy cultures, he observed” -> In a study that added neutralizing antibodies to IL-12 in gastric biopsy cultures, authors observed [Gastric histology and cytokine concentrations] - As aforementioned, gastric environment colonization by H. pylori leads to a polarization of Th1/Th17 responses whereas Treg cells are responsible for regulating the inflammatory process. -> As aforementioned, gastric environment colonization by H. pylori leads to a polarization toward Th1/Th17 responses, whereas Treg cells are responsible for an induction of anti-inflammatory responses. [Gastric histology and cytokine concentrations] - “Along with the cytokine pattern in children previously discussed in this paper ...” -> Along with the cytokine pattern in pediatric patients previously discussed in this paper [Gastric histology and cytokine concentrations] - Figure 2: If possible, I think that it is worth introducing additional colors, e.g., the child should be marked red and the adult should be blue-green (it would facilitate faster interpretation)

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

statements

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

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This Frontier paper is mainly analyzing the inflammatory pattern of cytokines during *Helicobacter pylori* induced gastritis. The differences of the inflammatory response and cytokine profile between children and adults are emphasized. The presented data are based on author's own research works and publications. The data from other authors are also presented and analyzed. The analysis of cytokine inflammatory patterns in childhood and adulthood is quite comprehensive, interesting and important. Authors conclude, that the age is one of most important factors. The data presented in the manuscript generally are corresponding the requirements of "FRONTIER TYPE" article. But the title is too extensive for such manuscript as it does not respond to the TITLE question: "*Helicobacter pylori* infection: what can influence gastric inflammatory pattern?" Gastric Inflammatory pattern is usually dependent on: host factors, pathogen factors and environmental factors. In this manuscript, only the host inflammatory cytokine pattern is analyzed. I could not find the analysis of genetic host factors, neither *Helicobacter pylori* related factors, nor nutrition or environment related factors. All these factors are also important to the expression of inflammation, activity of gastritis and the progression to atrophic and metaplastic changes in the gastric mucosa. Therefore I strongly recommend to change the title and to limit it on the data analyzed. The conclusions also must be changed and limited to the data which are analyzed in the manuscript I would like also to make some notices to the "Prevalence" chapter. I would like to suggest to add some new data from Eastern- Central European countries. Reference: Medicina 2021, 57(3), 254; <https://doi.org/10.3390/medicina57030254>

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<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
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statements

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

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

This manuscript brings important information from which medical community may benefit so I think it is worthy to be published. A manuscript is within the scope of the Journal. Title reflects the content of the article. Abstract is adequately structured.