June the 7th, 2021

To the Editors-in-Chief of World Journal of Clinical Cases

Dear Editor,

Please find attached a revised version of the manuscript entitled: *" Innate immunity – the hallmark of Helicobacter pylori infection in pediatric chronic gastritis*"**,** written by *Lorena Elena Meliț, Cristina Oana Mărginean, Maria Oana Săsăran***,** *Simona Mocanu, Dana Valentina Ghiga, Alina Bogliș and Carmen Duicu* Manuscript No 65984

COMMENTS TO AUTHOR:

Reviewer 1

Comment 1

The submitted paper analyzes the characteristics of children with H. pylori-induced gastritis and compares them with matched controls in order to identify risk factors, as well as the possible role of the TLR9 rs352140 polymorphism in the regulation of the inflammation generated in response to the infection. The obtained data identified low socioeconomic conditions as associated with *H. pylori* chronic gastritis, as well as higher leukocyte and neutrophils peripheral counts in children with the infection. The authors did not detect any significant difference in the distribution of the TLR9 genotypes between children with or without H. pylori, but associated higher leukocyte and neutrophil counts with the TT variant. Although the paper analyze children, these is an important issue that should be addressed, and it regards the possibility to detect a significant difference in the genotypes between the two groups due to the low number of subjects included.

Answer 1

We express our sincere gratitude for your valuable comments and time spent on assessing our manuscript. Following your suggestion, we introduced the following statement in the discussions section of our revised manuscript in order to underline that the significant difference might be due to the low number of subjects included in our study: 'Contrariwise the significant association between TT genotype and the increase in both leukocytes and neutrophils might also be influenced by the low number of subjects, but it definitely raises a major concern in this area that requires further studies on larger samples.'

Comment 2

Did the authors perform any a priori calculation regarding the number of subjects that had to be included in the study?

Answer 2

We did not perform a priori calculation of the sample since we included in this study only the patients that fulfilled the inclusion criteria within the study period and whose parents/caregivers signed the informed consent.

Comment 3

How did the authors evaluate the correlation between genotype and blood tests?

Answer 3

We sincerely apologize for our misinterpretation since statistically we did not analyzed the correlations, we compared the mean and median values of the laboratory parameters between the 2 groups. We corrected our statement in the revised form of our manuscript: 'We compared the mean and median values of the laboratory parameters between the two groups and we encountered a significant difference in terms of both leucocytes and neutrophils (p=0.0225/p=0.0292) for variant TT genotype of TLR9 rs352140.'

Comment 4

It seems to me that they compared the results only within the same genotype, but looking at the data it seems that higher levels were associate with the CC genetype if comparison was performed within controls or within the study group.

Answer 4

As we mentioned above, initially (Table II) we compared the laboratory parameters between the two groups irrespectively of the genotype, and we also compared the laboratory parameters for each genotype. Thus, we selected only the CC genotype carriers from each group and we compared the values of the laboratory parameters between these subjects. The same analysis was performed for the CT and TT carriers of each group.

Reviewer 2

Comment 1

Correct rs52140 to rs352140 in conclusion part.

Answer 1

We apologize for our mistake and we greatly appreciate your efforts in reviewing our manuscript. We corrected rs52140 to rs352140 as you recommended.

(1) *Science editor:*

Comment 1

1 Scientific quality: The manuscript describes a case control study of the innate immunity – the hallmark of Helicobacter pylori infection in children with chronic gastritis. The topic is within the scope of the WJG. (1) Classification: Grade C and Grade D; (2) Summary of the Peer-Review Report: The authors analyzes the characteristics of children with H. pylori-induced gastritis and compares them with matched controls in order to identify risk factors, as well as the possible role of the TLR9 rs352140 polymorphism in the regulation of the inflammation generated in response to the infection.

However, the authors did not detect any significant difference in the distribution of the TLR9 genotypes between children with or without H. pylori.

The questions raised by the reviewers should be answered; and (3) Format: There are 3 tables.

(4) References: A total of 50 references are cited, including 15 references published in the last 3 years;

(5) Self-cited references: There are 6 self-cited references. The self-referencing rates should be less than 10%. Please keep the reasonable self-citations that are closely related to the topic of the manuscript, and remove other improper self-citations. If the authors fail to address the critical issue of self-citation, the editing process of this manuscript will be terminated;

References recommend: The authors have the right to refuse to cite improper references recommended by peer reviewer(s), especially the references published by the peer reviewer(s) themselves. If the authors found the peer reviewer(s) request the authors to cite improper references published by themselves, please send the peer reviewer's ID number to the editorialoffice@wjgnet.com. The Editorial Office will close and remove the peer reviewer from the F6Publishing system immediately.

2 Language evaluation: Classification: Grade B and Grade B. A language editing certificate issued by AJE was provided.

3 Academic norms and rules: The authors provided the Biostatistics Review Certificate, the STROBE Statement and the Institutional Review Board Approval Form. Written informed consent was waived. No academic misconduct was found in the Bing search.

4 Supplementary comments: This is an unsolicited manuscript. No financial support was obtained for the study. The topic has not previously been published in the WJG.

5 Issues raised: (1) The title is too long, and it should be no more than 18 words;

(2) The "Article Highlights" section is missing. Please add the "Article Highlights" section at the end of the main text;

and (3) The scientific quality can't meet the requirement of WJG. 6 Recommendation: Transferring to the WJCC.

Answer 1

Thank you for taking into consideration our paper and for your valuable time spent on assessing our manuscript.

According to your recommendations we removed 2 of the 6 self-cited references.

Regarding the title, it had only 13 words, but we rephrased it as it follows: '**Innate immunity – the hallmark of *Helicobacter pylori* infection in pediatric chronic gastritis**'.

According to your recommendations, we introduced 'Article Highlights' section at the end of the main text: 'Article Highlights

- Environmental factors represent a major risk factor for *H. pylori* chronic gastritis in children
- Peripheral blood parameters might be reliable indicators of systemic inflammation triggered by *H. pylori* infection
- TLR9 polymorphisms seem to be involved in promoting or suppressing systemic inflammation in the setting of pediatric *H. pylori* chronic gastritis'.

Thus, by this letter and by the attached revised manuscript of our original manuscript, we hope to have fulfilled all the observations and recommendations made by the Reviewers.

Thank you for your time and consideration.

On behalf of all authors of this work,

Yours sincerely,

Prof Cristina Oana Mărginean, MD, PhD

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