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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 53988

Title: Type I and Type II Helicobacter pylori Infection Status in Stepwise Chronic Gastric Diseases and Their Impact on Gastrin and Pepsinogen Level In a High Gastric Cancer Prevalent Area

Reviewer's code: 02954019
Position: Editorial Board
Academic degree: MD, PhD
Professional title: Associate Professor
Reviewer's Country/Territory: Japan
Author's Country/Territory: China

Manuscript submission date: 2020-01-04
Reviewer chosen by: AI Technique
Reviewer accepted review: 2020-01-04 03:59
Reviewer performed review: 2020-01-04 13:15
Review time: 9 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [Y] Major revision [ ] Rejection
Re-review	[ ] Yes [ ] No
Peer-reviewer	Peer-Review: [Y] Anonymous [ ] Onymous

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

SPECIFIC COMMENTS TO AUTHORS

MS ID: 53988 TITLE Type I and Type II Helicobacter pylori Infection Status in Stepwise Chronic Gastric Diseases and Their Impact on Gastrin and Pepsinogen Level In a High Gastric Cancer Prevalent Area It is a potentially interesting study indicating that Type 1 H. pylori infection account for 84.2% of all gastric cancer, and has a significant impact on G-17 and pepsinogen levels. However, authors indicated that Type 2 H. pylori infection account for only 15.8% of all gastric cancer, and has a minimum impact on G-17 and pepsinogens. Based on these findings, the one possible reason why Type 2 H. pylori infection does not have a strong virulence, is that it has less serological impact compared to Type 1 H. pylori strains. However, there were several issues that concern me. Major points 1) Author should refer to the results of previous reports concerning the risk of Type 2 H. pylori infection on gastric cancer development. And if there were if there were previous reports, their data should be discussed. 2) Authors should refer to the histological type of gastric cancer both in Type1 and Type 2 H. pylori strains. 3) I consider that serological findings of CAG in H. pylori negative, Type1 and Type 2 positive subjects are especially important. It seems to be that PGII in Hp (-) subjects (N=51, 8.7± 4.3) is significantly lower ($p<0.01$) than that of Type 2 Hp (+) subjects (N=13, 15.4 ± 9.6) using student t test. Please re-evaluate the statistics especially in Table 5. 4) Authors should refer to the mechanisms of being a weak virulent factors of Type 2 H. pylori infection. It seems to me that the development rate of CAG in Type 2 H. pylori strains is low (Type 1: 79.7% vs Type 2: 20.3%), which is the main reason of low virulent factors. Thus, I speculate that it is understandable that type 2 strain have impact on PGII and PGI/II ratio. Please refer to the pathophysiological mechanisms of the difference of the virulent factors. 5) H. pylori negative gastric cancer is within 1% in

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Japan. Although authors stated in Discussion that "The current results are in line with these results, and indicate an important role of type I H. pylori in the development of upper gastrointestinal diseases and gastric cancer", 11.6 % seems to be relatively higher than that of Japanese report. I consider that H. pylori negative cases defined by this author are negative for serology and UBT, however, past infection cases or spontaneously disappeared cases are inevitably included. Authors should define it as at least subjects excluding PG positive cases. Data may be improved if definition of H. pylori more precisely.

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Name of journal: World Journal of Gastroenterology

Manuscript NO: 53988

Title: Type I and Type II Helicobacter pylori Infection Status in Stepwise Chronic Gastric Diseases and Their Impact on Gastrin and Pepsinogen Level In a High Gastric Cancer Prevalent Area

Reviewer's code: 00181048
Position: Peer Reviewer
Academic degree: MD, PhD

Professional title: Professor

Reviewer's Country/Territory: South Korea

Author's Country/Territory: China

Manuscript submission date: 2020-01-04

Reviewer chosen by: AI Technique

Reviewer accepted review: 2020-01-06 01:42

Reviewer performed review: 2020-01-14 07:04

Review time: 8 Days and 5 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [Y] Major revision [ ] Rejection
Re-review	[ ] Yes [ ] No
Peer-reviewer	Peer-Review: [Y] Anonymous [ ] Onymous

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

SPECIFIC COMMENTS TO AUTHORS

This manuscript studied H. pyroli infection and serum biomarkers for gastric cancer in the patients of various gastric diseases. Though enrolled cases were enough to support the conclusion, the results were not unique except the infection status of H. pyroli in Henan area. I recommend some suggestions to highlight the results. Major 1. Could you suggest diagnostic values (or ROC) for G17 and pepsinogen to DDx NAG, NAGE, CAG, PU and GC. 2. Change Table 2 and 4 into Figure 3. Table 5; Describe total level of G17, PG1, PG2 and PG1/2 in each group Minor 1. Abst line 72; expect in GC patients > except in GC patients 2. Line 308: diffuse type types of gastric cancer are > correct type types 3. Fig 1; Complete the sentence at 462 patients were 4. In Table 1 1) Describe Mean age ± SD in Hp +, Type 1 Hp+, Type II Hp+ and Hp- group 2) There were no clinically significant correlation Patients characteristics and H. pyroli infection. Change the title into Patient Clinical Data and H. pylori Infection Status (also in Text)

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 53988

Title: Type I and Type II Helicobacter pylori Infection Status in Stepwise Chronic Gastric Diseases and Their Impact on Gastrin and Pepsinogen Level In a High Gastric Cancer Prevalent Area

Reviewer's code: 02537773
Position: Editorial Board
Academic degree: MD, PhD

Professional title: Academic Research, Associate Professor, Doctor, Lecturer

Reviewer's Country/Territory: Germany

Author's Country/Territory: China

Manuscript submission date: 2020-01-04

Reviewer chosen by: Jie Wang

Reviewer accepted review: 2020-01-26 20:33

Reviewer performed review: 2020-01-26 22:08

Review time: 1 Hour

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [ ] Grade B: Minor language polishing [Y] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [Y] Major revision [ ] Rejection
Re-review	[ ] Yes [ ] No
Peer-reviewer	Peer-Review: [Y] Anonymous [ ] Onymous

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

SPECIFIC COMMENTS TO AUTHORS

Yuan et al. studied the H. pylori status in a high-gastric cancer prevalence area. They focus on differ H. pylori types and evaluate them within the scope of histology and PGI, PGII and G17. This topic is interesting and there is an ongoing change in prevalence. Furthermore, there is a ongoing debate regarding the value of PGI, PGII and G17 in prediction of preneoplastic conditions and potential risk of gastric cancer. - Introduction: rather short and the last part of the introduction included some redundant result section. - Please explain what is the benefit to create a NAGE group, usually it is part of the NAG unless atrophy or ulcer is present. - Ethics: Research protocol number is not included. I have my strong concerns regarding the verbal consent which is inappropriate for the high-quality research, unless the all the analysis is a standard of care and the study had an exempt from the ethical committee, however, in this case it is a wrong statement in the paper. - Information to the H. pylori blot is not provided. Recently there is a report in WJG (World J Gastroenterol. 2017 Jul 14;23(26):4712-4723) showing that cagA antibody production is dependent on vacA genotype. In this regard, the authors may need to discuss the data in view of the published results. - In results, probably it is appropriate to mention the PU before CAG in results as CAG is already preneoplastic condition, while peptic ulcer not. - CAG is a mix of the atrophy types: corpus or antrum atrophy. The paper would benefit from more detailed data if possible. - How many of the H. pylori negative subjects had negative serology for cagA. It is for instance known that H. pylori-antibody disappear after eradication, while cagA-IgG antibody remain positive in a cohort of patients (World J Gastroenterol. 2017 Jul 14;23(26):4712-4723). - How many PU subjects were on PPI? This would explain increased G17 values. - I am quite surprised of the very high PG1 data and PG1/PG2

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ratio – as according to the manufacturing cut-offs these results do not support the CAG status, please explain and discuss. - Language needs editing - Biostatistics review certificate is with inappropriate language

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RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 53988

Title: Type I and Type II Helicobacter pylori Infection Status in Stepwise Chronic Gastric Diseases and Their Impact on Gastrin and Pepsinogen Level In a High Gastric Cancer Prevalent Area

Reviewer's code: 02537773
Position: Editorial Board
Academic degree: MD, PhD

Professional title: Academic Research, Associate Professor, Doctor, Lecturer

Reviewer's Country/Territory: Germany

Author's Country/Territory: China

Manuscript submission date: 2020-01-04

Reviewer chosen by: Le Zhang

Reviewer accepted review: 2020-04-13 12:55

Reviewer performed review: 2020-04-13 17:33

Review time: 4 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[Y] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

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SPECIFIC COMMENTS TO AUTHORS

The paper deals with a clinically relevant topic related to H.pylori Infection which is one of the most common burden in GI tract. The authors could successfully respond to my comments and made appropriate changes. I believe that in the present form the manuscript provides important insights to the H.pylori research. In particular, the data to serological biopsy with G17, PG1 and PG2 in relation to H.pylori infection are important.

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RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 53988

Title: Type I and Type II Helicobacter pylori Infection Status in Stepwise Chronic Gastric Diseases and Their Impact on Gastrin and Pepsinogen Level In a High Gastric Cancer Prevalent Area

Reviewer's code: 02954019
Position: Editorial Board
Academic degree: MD, PhD

Professional title: Associate Professor

Reviewer's Country/Territory: Japan

Author's Country/Territory: China

Manuscript submission date: 2020-01-04

Reviewer chosen by: Le Zhang

Reviewer accepted review: 2020-04-13 12:44

Reviewer performed review: 2020-04-15 02:21

Review time: 1 Day and 13 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [Y] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

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SPECIFIC COMMENTS TO AUTHORS

Although ROC analysis seen to be unnecessary, this study is generally good, and is acceptable for publication.