May 29, 2017

Dear Reviewers:

Thank you for your valuable and helpful opinions and suggestions. We are pleased to answer your questions and the manuscript has been revised seriously according to your comments. The details are as following:

Question 1: TITLE: I would suggest the modification as above.

Answer: We have revised the title as your suggestion.

Question 2: INTRODUCTION: 8th line: Better to omit the statement "Hp is closely related to the occurrence and development of G-E reflux disease" because it is matter of debate and is not relevant to the topic.

Answer: We have omitted the sentence "Hp is closely related to the occurrence and development of G-E reflux disease" as your suggestion.

Question 3: METHODS: 1) Subjects: "…sera were stored at -75°C…"It is necessary to give information about the maximum time elapsed between blood withdrawing and storage and that elapsed between storage and testing. This because G17 could be influenced, being very instable.

Answer: We have added the information like this: "Blood sample was obtained and sera were stored (within 2 hours) at -75^{o}C until used for measurement of gastric biomarker levels (within 6 months)."

Question 4: METHODS: 2)Statistical analysis: The 1st paragraph should be modified: e.g."Serum biomarkers levels and serum biochemical tests were analyzed in Hp+ve and Hp-ve patients, separately in male and female subjects, by Student's t-test" or something like this.

Answer: We have revised this sentence as your suggestion.

Question 5: RESULTS: 1) Data must be provided with Standard Deviation

or Standard Error. As shown in the figure 1, PGI difference between 35-44 y group and >75 y group seems apparently higher than that observed in PGII for the same groups, which is statistically significant, as opposed to the PGI. The SD / SE for each value is probably the explanation, but this must be shown.

Answer: We have supplemented table 1 in the revised manuscript, which include data (mean **± SD**) of gastric biomarkers of each group in figure 1.

Question 6: RESULTS: 2) Biochemical tests: a) "Age positively correlated with serum levels of PGI and PGII; and negatively correlated with PGI/GII ratio". The AA have to explain this apparent contradiction.

Answer: In table 4 (in the revised manuscript) we can see that age positively correlated with levels of PGI and PGII, but the correlation is stronger with PGII. Meanwhile, table 1 (in the revised manuscript) showed that levels of PGII increased with age, and table 5 (in the revised manuscript) showed that age entered into the regression model of PGII and influenced its level. Therefore, the correlation between age and PGII is more strong and significant than that of PGI. On the other hand, we can also see in table 4 and table 5 that age negatively correlated with ratio of PGI/PGII and entered into the regression model of PGI/PGII, and table 1 showed that ratio of PGI/PGII decreased with age. So, the results of PGI, PGII and PGI/PGII are consistent and reasonable.

Question 7: RESULTS: 2) Biochemical tests: b) The AA should refer how many subjects show value of PGI < 35 microg/L, if any. This gives the measure of the clinical usefulness of this parameter in detecting chronic atrophic gastritis in general population, which is practically relevant.

Answer: There were 13 subjects showed value of PGI < 35 microg/L out of the whole 395 participants in our study.

Question 8: RESULTS: 2) Biochemical tests: c) The correlations between PGI and PGII with serum creatinine, cystatin, uric acid and LDL-Cholesterol levels are of little/null clinical significance if alimentary/dietary habits and BMI are not considered. The AA have to complete or justify this lack of information.

Answer: We have added BMI into the variables to carry out Pearson correlation coefficient matrix and multiple linear regression again, it was showed that there was no correlation between BMI and gastric biomarkers (table 4 in the revised manuscript), and Cr and FBG still entered into the regression models of gastric biomarkers (table 5 in the revised manuscript). Therefore, the correlations between FBG, Cr and gastric biomarkers are of clinical significance in our data.

Question 9: DISCUSSION: 1) In the first line "An European gastric biomarkers test…" should be linked in the References section to other works more representative (such as that of Storskrubb et al. Scan J Gastroenterol, 2008, and not to the n.17 cited by the AA).

Answer: We have replaced the reference as your suggestion.

Question 10: DISCUSSION: 2) 2nd line: "and IgA" should be deleted.

Answer: We have deleted "and IgA" as your suggestion.

Question 11: DISCUSSION: 3) An extensive study published in 2010 (Clin Chem Lab Med 2010;48(9):1327-1332) shows that a significant portion of dyspeptic young adults carry a chronic atrophic gastritis (PGI < 35), in Italy. A comparison between the Chinese population and the Italian one may be of interest, as far as the evaluation of this parameter is concerned.

Answer: Compared to the Italian dyspeptic population, there were 13 subjects (age 48-82 years) showed value of PGI < 35 microg/L out of the whole 395 participants in our asymptomatic Chinese population, the prevalence of

chronic atrophic gastritis is 3.3%.

Question 12: DISCUSSION: 4) The AA state that the PGI/PGII ratio decreased with age and this reflects the degree of atrophy in gastric mucosa. However, in the Results section they show that both PGI and PGII increase with age. How do they explain this? Does PGII increase more than PGI with aging (probably because of the increase in inflammatory status of gastric mucosa? Do they assume anti-inflammatory drugs? The AA should address this aspect.

Answer: The answer is the same to question 6, but why PGII increased more than PGI with age is not clear, maybe the distribution of PGII-secreting cells is more extensive, is one of the reasons. On the other hand, it was suggested in table 4 and table 5 (in the revised manuscript) that Hp infection had a more closely correlation with PGII than with PGI and may influence the levels of PGII more, this may be another reason. The participants didn't assume drugs. We have mentioned these in the 2nd and 3rd paragraphs of discussion in the revised manuscript.

Question 13: DISCUSSION: 5) The last paragraph: modify: "..the mechanisms involved are not clear" (delete "in which")

Answer: We have deleted "in which" as your suggestion.

Best Regards.

Sincerely Yours,

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