

Answer to Reviewer

Thank you for your important comments, which were extremely helpful for improving the quality of our manuscript.

Reviewer #1: This is an interesting and attractive manuscript describing the association between H. pylori antibody titer and 1) clinical characteristics and 2) endoscopic findings based on Kyoto classification. They concluded that nodularity, atrophy, and age 40–59 years (versus age ≥ 60 years) were correlated with a high serum antibody titer in H. pylori-infected patients in multivariate analysis. They also demonstrated that intestinal metaplasia and atrophy were related to age ≥ 60 years in group C. However, several concerns are listed below. The meaning of negative H. pylori serology is not simple. Group A (H. pylori antibody titer 60 and endoscopic finding? The obtained results seem to be confusing. In Group C, $>60y$ is associated with atrophy and IM, which is understandable because progression of atrophy is considered to occur in aged subjects, and their antibody titer spontaneously decreased by the profound atrophy. However, I can't understand the results that $>60y$ subjects in Group D are associated with IM, but not atrophy. IM is generally seen in advanced stage of atrophy. How can you explain this finding? Based on the author's result, aged subjects (>60) with high titer of H. pylori serology show IM, but the antibody titer does not decrease despite the advanced atrophy. Is it right? Thus, I recommend deleting these results (Table 4). Multivariate analysis also seems to be difficult in Group D because of the small sample size. The significance of high titer of H. pylori serology has been overlooked. Thus, I consider it important to investigate the association between high titer and endoscopic findings as describe in this manuscript. Because H. pylori antibody titer is an only method to predict the bacterial density of gastric mucosa, endoscopic findings with high H. pylori density are also clarified by this investigation, and may be useful.

Thank you very much for your insightful comments.

According to the reviewer's comments, we deleted Table 4 because of the small sample size. We made appropriate changes in the Abstract, the Core tip, and the Results according the deletion of Table 4. The paper has been accurate.

As the reviewer described, we also believe “Higher bacterial counts induce intense immune responses, resulting in subsequent higher antibody titers, while genetic

differences between human hosts may affect the antibody levels in response to pathogens”, as shown in the *Discussion*.

Thank you again.

Reviewer #2: The Authors describe an interesting association between anti-H. pylori antibody serum titers and specific endoscopic findings in a large series of patients. The manuscript is interesting, well written, with conclusions supported by results

Thank you very much for your comments.

Reviewer #3: Dr. Toyoshima, et al investigated 'Serum anti-Helicobacter pylori antibody titer and its association with gastric nodularity, atrophy, and age: A cross-sectional study'. The manuscript is informative and well-presented. The reviewer has no comments.

Thank you very much for your response.