

Responses to reviewers' comments:

Reviewer #1

Question: 1 Introduction: The authors was show related problems about gastric cancer which ranked second for incidence rate and third for mortality rate among all cancers in China. In this cases I suggest the authors more explain the related data in others area of cancer ex: Western country or Africa.

Answer: Thanks for your suggestions.

In the revised manuscript, we had added the description of the incidence rate and mortality rate of gastric cancer in Western Europe and North America, which was “in Western Europe, the incidence rate ranks 9th and the mortality rate ranks 6th. In North America, the incidence rate and mortality rate of gastric cancer rank 13th and 9th respectively”.

Question: 2 Material and methods: multicenter retrospective study was conducted in 10 years, enrollment criteria with 6 items was clear and concern ethical issue to inform consent. I suggest the authors to explain about ethic committee in your institute to certify this research ex: This study was approved by.....in ethical committee.

Answer: Thanks for your suggestions.

This was a retrospective study. The use of data, including basic information and test results of *H. pylori* of patients, had been approved by the ethics committee of Taizhou Hospital of Zhejiang Province.

Question: 3 Results: In Multivariable analysis of *H. pylori* infection line 4 was incorrect "wasdetermined".

Answer: Thanks for your suggestions.

We had corrected this error.

Question: 4 Conclusion: The words "age and male gender" was not clear, I suuggest to described age group with related in study in couclusion.

Answer: Thanks for your suggestions.

We had revised the conclusion, that is, “The prevalence of *H. pylori* increased with aging, and male was at a higher risk of *H. pylori* prevalence. The resistance rate increased with aging, and *H. pylori* in female, age 21 to 50 years old, was at a higher risk of resistance to levofloxacin and clarithromycin.”

Reviewer #2

Question: 1 In the abstract, several things should be noted: a mention that it refers to "naive patients", the years of the study as well as the trend of evolution of resistance for clarithromycin, metronidazole and levofloxacin rather than the global rate.

Answer: Thanks for your suggestions.

We added the mention that “Gastric mucosal specimens were collected from naive patients”. In the abstract, we revised the expression of the resistance rate for the four antibacterial drugs, which is “The average resistance rate of *H. pylori* to amoxicillin and metronidazole was 0.21% and 93.72%, which remained stable. The average resistance rate to clarithromycin was 23.99% with an increasing trend from 14.43% to 38.24%. The average resistance rate to levofloxacin was 30.29%, which increased from 17.07% to 39.42% and mostly stabilized after 2017.”

Question: 2 In the Material-Methods, it would be good to know the number of gastric biopsies used as well as the type of grinding fluid. Was the culture time systematically extended to 7 days when there was no growth after 3 days?

Answer: Thanks for your suggestions.

Taking into account the patient's tolerance, one patient in this study only collected a gastric mucosal tissue sample for testing, and the site was the lesser curvature of the gastric antrum or the greater curvature of the gastric body, or the tissue adjacent to the lesion. We used the brain heart infusion as grinding fluid. The culture time would be extended to 7 days if there was no growth after 3 days of cultivation. We had added these description in the article.

Question: 3 Replace "drug sensitivity test" with "antimicrobial susceptibility testing" which can be abbreviated AST.

Answer: Thanks for your suggestions.

We had replaced the “drug sensitivity test” with “antimicrobial susceptibility testing” or “AST”.

Question: 4 Peptic ulcer disease is a specific disease including duodenal ulcer and gastric ulcer only but not gastritis, gastric MALT lymphoma, etc. Please correct these.

Answer: Thanks for your suggestions.

We had changed the sentence to “*H. pylori* cause substantial morbidity from various peptic ulcer diseases, gastritis and even gastric lymphoma.”

Question: 5 What is "a concentration of 0.5 McDaniel"? This reviewer is only aware of the McFarland scale of opacity.

Answer: Thanks for your suggestions.

We had corrected the error from “0.5 McDaniel” to “0.5 McFarland”.

Question: 6 Could you also provide some information on the Dr. Ehrenstorfer GmbH for the amoxicillin cut-off MIC?

Answer: Thanks for your suggestions.

The cut-off MIC of amoxicillin bought from the Dr. Ehrenstorfer GmbH is the same as the reference MIC of amoxicillin, which is 2 µg/ml. The purity of the amoxicillin standard from Dr. Ehrenstorfer GmbH, Germany is 96.68%, which has sufficient effective content and is suitable for antimicrobial susceptibility testing.

Question: 7 Replace "age brackets" with "age groups".

Answer: Thanks for your suggestions.

We had replaced the “age bracket” with “age group”.

Reviewer #3

Question: 1 This is an interesting and nicely large data set. But the authors views on the subject is largely flawed. *H. pylori* infection rate is not affected by age as it s primarily acquired during childhood. But it is affected by age cohorts, meaning the prevalence rates differs according to age cohorts and the prevalent rate of antibiotic resistant strains, in that specific cohort. On another note gender is not considered a risk factor for the infection or antibiotic resistance, but the overused antibiotics in any gender or society, can select for antibiotic resistant strains. I, therefore, suggest that the authors, revise the paper with this view and submit it for another round of review, to avoid misunderstandings.

Answer: Thanks for your suggestions.

We had carefully considered your suggestions and modified some of the descriptions in the article. We had changed “Age and gender were risk factors for *H. pylori* prevalence and resistance” to “*H. pylori* prevalence and resistance rate was increased with age. Male was at a higher risk of *H. pylori* prevalence, and *H. pylori* in female was at a higher risk of resistance.”