

November 10th, 2013

Dear Editor,

Please find enclosed, in Word format, the edited manuscript revised without (file name: 6367-review.doc) and with corrections inserted (file name: 6367-edited.doc).

Title: *Helicobacter pylori* infection in obesity and its clinical outcome after bariatric surgery

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Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 6367

The manuscript has been improved according to the suggestions of editor and reviewers:

1. The format of the manuscript has been updated according to the revision policies for Topic Highlight

2. Revision has been made according to the suggestions of the reviewers:

Reviewer 00004764:

This concise review summarizes a modest amount of controversial data on H. pylori in obesity focusing on pathophysiology as well as implications for obesity surgery. Several areas can be expanded with more critical evaluation of the studies and potential reasons for disparities of the findings.

1. *It is interesting that you note that African Americans and Hispanics have a higher probability of H. pylori. Interestingly, these are two populations at least in the U.S. which have the highest obesity rates.*

AUTHORS: The influence of race on prevalence of Hp infection in obese patients has been stressed and a new reference, concerning the race-related obesity rates, added.

2. *I would agree that the great differences in H. pylori infection rates amongst these studies are undoubtedly related to the method of detection. Perhaps you can scrutinize the studies once again to better define which studies use two methods for diagnosis which would be the gold standard or if not available which one used breath tests. Stool antigen was not mentioned. Also, we know of the ubiquitous use of proton pump inhibitors and its effect on the sensitivity of testing.*

AUTHORS: The studies included in Table 2 have been scrutinized once again in order to better analyze Hp diagnostic methods used. In this respect, relative comments have been included in the revised manuscript as well as a comment on the influence of antisecretory therapy on their diagnostic accuracy.

3. *You summarize a large amount of data relating ghrelin, H. pylori infection, and perhaps obesity pathogenesis. Suffice it to say this is controversial with clearly no evidence either way. One factor you did not mention perhaps is age. Significant gastric atrophy is more common in the elderly and most obesity is well defined at least at a younger age.*

AUTHORS: Data related to Hp infection and ghrelin have been extensively modified and synthesized. A comment on the relative impact of age added.

4. *Under Section 3 again there are differences among studies and perhaps one could better define why these differences are present.*

AUTHORS: As requested, possible further explanations of the differences between the studies have been added.

5. *Under # 4, we know that generally H. pylori does not cause any significant symptoms. It was interesting to note of the reduced eradication rates in obese subjects. Do we know anything about use of antibiotics based on weight?*

AUTHORS: According with the reviewer, even if data on antibiotics based on weight are lacking, a consideration on the need of a tailored therapeutic eradication regimen in obese patients has been added.

6. *It is interesting that there are no great recommendations from the societies of how to evaluate these patients preoperatively. One would suspect that eradication of H. pylori would be important given that a portion of the stomach will now not be available for easy endoscopic examination. Perhaps a recommendation that H. pylori should be looked for by two methods and careful follow-up after a vigorous antibiotic regimen, perhaps based on weight, should be performed.*

AUTHORS: As suggested, additional comments on difficulties to access to part of the stomach by upper endoscopy after bariatric surgery has been added.

Reviewer 00057868:

This a review paper. No new information is presented here. It is interesting in that it reviews the prevalence and outcomes of gastric bypass in patients with Helicobacter pylori infection. The association with reducing ghrelin levels has been reported elsewhere. It is a very nice literature review on the topic.

AUTHORS: The reviewer did not require any correction. However since data on the association of Hp infection with reduced ghrelin levels has been reported elsewhere, the paragraph inherent to these data has been extensively revised.

Reviewer 00504677:

Interesting study, however it needs some corrections:

1. *the references has to be re-written as reference 7 comes after 4 and 16 after 7 .it has to be in consequential order[1,2,3,4,.... and so on]*

AUTHORS: The numbers of the references are already in a consequential order, when considering the references cited in the Table2.

2. *PREVALENCE OF Hp INFECTION IN OBESE PATIENTS: ok*

3. *Hp INFECTION AND PATHOPHYSIOLOGY OF OBESITY: not only Ghrelin is playing a role in the pathophysiology of obesity but also other mechanisms such as endocrine pathology, genetics, socioeconomic, geographical distribution and other unknown factors. Therefore it is very difficult to accept that ghrelin is the major player in the obesity etiology.*

AUTHORS: The paragraph of the relationship between Hp and ghrelin has been extensively revised and its role have been reappraised. As requested, the other factors involved in the pathophysiology of obesity have been added.

4. *Hp AND BARIATRIC SURGERY: "Routine upper GI endoscopy studies, with concurrent Hp screening and biopsy to rule out pathologic abnormalities (e.g. esophagitis, polyps, hiatal hernia, gastritis, duodenitis), reported*

that abnormalities are present in up to 91% of bariatric candidates [10,14,20], with an higher incidence in patients with concomitant Hp. infection [9,12,61]. " The quoted studies were trying to push for gastroscopy before bariatric surgery. Majority of diagnosed problems on ogd are expected to be cured by bariatric surgery. HP as a cause of post bariatric surgery problem is hardly of clinical significance although some reports linked stomal ulcer to HP infection. Even though stomal ulceration is a rare complication of gastric bypass when performed by experienced surgeon. In conclusion the yield of gastroscopy before bariatric surgery is of negligible benefit.

AUTHORS: Accepting the remark of the reviewer, the controversies on the need of gastroscopy before bariatric surgery have been more extensively highlighted in the paragraph, as well as the need of more randomized control trials on this topic. However in this review, we endorse European guidelines that recommend to perform upper gastrointestinal endoscopy before bariatric surgery.

5.EFFECT OF HP INFECTION ON BARIATRIC SURGERY OUTCOMES: "Firstly, eradication should decrease the risk of gastro-duodenal peptic lesions in the remnant, and thus decrease early ulcer-related postoperative symptoms as well as later ulcer complications; " This is theoretical statement. post gastric bypass ulceration of remnant stomach is extremely rare and very difficult to prove as the bypassed stomach cannot reached by conventional gastroscopy, also late complication of gastric ulcer in remnant stomach is extremely rare or not reported.

AUTHORS: We agree with the reviewer's comment and the relative sentence has been changed. Furthermore the controversial points concerning Hp management before bariatric surgery have been more extensively highlighted. Nevertheless in the last part of the paragraph, the authors's position supporting an attempt to Hp eradication before surgery has been explained and substantiated.

Table 1 and 2: word should be world

AUTHORS: in Tables 1 and 2, "word" has been changed in "world".

3. References and typesetting were corrected. Due to the extensive changes in the paragraph "Hp infection and pathophysiology of obesity" reference order has been changed.

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,