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To
The Editor
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Dear Sir/Madam,

Thank you very much for your mail dated March 1 regarding our submitted review article entitled “*dupA* of *Helicobacter pylori* as an important risk determinant for disease manifestation: An overview” (**Manuscript No: 54808**) for favour of publication in your esteemed journal. **My ID Number is “ID: 00036361”**.

We have gone through the comments from the reviewers very carefully and modified the manuscript especially the English language and grammatical part and it has been checked by a scholar. I am also sending you the response to reviewers’ comments point by point and all the modification has been in blue colour in the revised text.

The article has been read and approved by all the contributing authors and all authors declare no conflict of interest. Hope you will find this manuscript suitable in your revered journal.

Yours faithfully
Asish K. Mukhopadhyay

Responses to the reviewers' comments (Manuscript No: 54808)

REVIEWER-1:

Comment: This is a very good review paper, comprehensive analysis the DUPA. It has a good reference value for studying the toxicity of Helicobacter Pylori

Answer: Thank you very much to the erudite reviewer for the kind and encouraging words regarding our review article.

REVIEWER-2:

Comment 1: Abstract Line 39: etc is not scientific and should be removed

Answer: As advised by the reviewer, we have removed the word etc from Abstract line 39 in the revised manuscript.

Comment 2: Introduction Line 72: "duodenal ulcer (DU), peptic ulcer.... ", since peptic ulcer includes DU the authors should write "duodenal ulcer (DU), gastric ulcer

Answer: As advised by the reviewer, we replaced the peptic ulcer with gastric ulcer and duodenal ulcer in the revised manuscript.

Comment 3: At the end of Introduction the authors should add a section "Methods" where they should include the part reported in line 109-118, describing details of their search and also how they avoided duplicates

Answer: As suggested by reviewers, we have added the "Methods" section before line 108-118, describing the details of search. Proper care has been taken to avoid the duplicity of articles as each article was read carefully.

Comment 4 They could add as limits that this type of search is not able to detect congress abstracts

Answer: We have used the PubMed search engine where congress abstract were not available and we have focused mainly on full text articles so there is no chance of adding congress abstracts in this review manuscript

Comment 5: When the authors reported "Discrepancies of dupA with clinical outcomes" it should be better that the part beginning at line 194, dedicated to the technical approach, is separate from the epidemiologic part Line 174

Answer: In the revised manuscript, the line no. have been changed. Now, the line no. 174 and 194 should be read as 163 and 175 respectively. We want to inform to reviewers that the part beginning at line 194 (now 175) is also an epidemiological studies where RT-PCR was used instead of simple PCR method to detect dupA. We request the reviewers, allow us to keep the line 194 (now 174) onwards under section “Discrepancies of dupA with clinical outcomes”.

Comment 6: in the study by Kim et al is there a classification for DU and GU or is only described peptic ulcer?. It is better to highlight this point

Answer: As asked by the reviewer, we want to clarify that kim et al (2014) have classified the peptic ulcer into DU, BGU and dysplasia but we did not put DU and BGU in the manuscript. Together we put peptic ulcer. Now, we have replaced the peptic ulcer with duodenal ulcer (DU), benign gastric ulcer (BGU) and dysplasia in the revised manuscript.

Comment 7: Line 215 It begins with “The Tal. (2005)” please corrrige. Line 317 China is written china, please corrrige (and see other lines).

Answer: We apologize that for the mistake in line 215 “Some researchers of the above mentioned studies have supported the original finding of Lu *et al.* (2005)” was written like “The Tal. (2005)”. As suggested by the reviewer, we have changed the “The Tal. (2005)” with “Some researchers of the above mentioned studies have supported the original finding of Lu *et al.* (2005)”. We also replaced “china” as China in all other places like line 289, 291 and 297 in the revised manuscript.

Comment 8: Reference by Prof.Mégraud (1992) is very old. The same with its team has published a complete review in 2016. Please replace it with “Pellicano et al. A 2016 panorama of Helicobacter pylori infection: key messages for clinicians. Panminerva Med 2016;58:304-17”

Answer: As advised by the reviewer, we have replaced the Reference no. 7 (Megraud et al 1992) with “Pellicano et al (2016) in the revised manuscript.

Comment 9: Reference 10. A good reference to report the relevance of the infection in developing countries is the review of Prof. Smith from Nigeria on WJG “Smith S. et al. Infections with Helicobacter pylori and challenges encountered in Africa. World J Gastroenterol 2019;25:3183-95”. This could replace the old (2005) reference that discussed the issue in general terms.

Answer: As advised by the reviewer, we have replaced the references no. 10 (Czinn SJ , 2005) with recent one of Prof. smith from Nigeria. (Smith S et al., 2019) in the revised manuscript.

Comment 10: The reference number 1 is old (2000) and could be replaced by the more updated review ”Benign and malignant gastroduodenal diseases associated with Helicobacter

pylori: a narrative review and personal remarks in 2018. *Minerva Gastroenterol Dietol* 2018;64:280-96

Answer: As advised by the reviewer, we have replaced the references no. 1 (**Brown LM.** *Helicobacter pylori: epidemiology and routes of transmission. Epidemiol Rev* 2000;22:283-297) with the reference suggested by reviewers (**Buzas GM.** Benign and malignant gastroduodenal diseases associated with *Helicobacter pylori*: a narrative review and personal remarks in 2018. *Minerva Gastroenterol Dietol* 2018; 64: 280-296 in the revised manuscript.

Comment 11: English language requires a significant revision.

Answer: As suggested by reviewer, the manuscript has been thoroughly revised for the English language and also grammatical part was corrected by an English scholar.

REVIEWER-3:

Comment: *dupA* as a novel virulence gene since 2005 which may be related with the clinical outcome of *H.pylori* infection, even though there are contradictory findings. This is a review of 15 years' literature about the subject. It will help to raise the awareness of this gene and lead to new studies, indeed. This review deserve to be published in a more suitable journal

Answer: Heartfelt thanks to this reviewer also for the compassionate and inspiring words regarding our review article. We will be happy to publish this article to your esteemed journal "*World Journal of Gastroenterology*".