

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 82041

Title: Susceptibility patterns and virulence genotypes of *Helicobacter pylori* effecting eradication therapy outcome among Egyptian patients with gastroduodenal diseases.

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05753119

Position: Peer Reviewer

Academic degree: BSc, MSc, PhD

Professional title: Academic Research, Assistant Professor, Doctor

Reviewer's Country/Territory: Turkey

Author's Country/Territory: Egypt

Manuscript submission date: 2022-12-07

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-12-23 13:43

Reviewer performed review: 2022-12-26 12:30

Review time: 2 Days and 22 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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Peer-reviewer statements	Peer-Review: [<input checked="" type="checkbox"/>] Anonymous [<input type="checkbox"/>] Onymous
	Conflicts-of-Interest: [<input type="checkbox"/>] Yes [<input checked="" type="checkbox"/>] No

SPECIFIC COMMENTS TO AUTHORS

Dear Authors, The title and abstract are appropriate for the content of the text. Furthermore, the article is well constructed, the experiments were well conducted, and analysis was well performed. Similarity is very high. Similarity is very high. It should be less than 20 %. If you paraphrase it again, it is appropriate to publish.

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Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03699937

Position: Editorial Board

Academic degree: PhD

Professional title: Assistant Professor, Senior Lecturer, Teacher

Reviewer's Country/Territory: Iran

Author's Country/Territory: Egypt

Manuscript submission date: 2022-12-07

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-01-05 07:29

Reviewer performed review: 2023-01-05 13:36

Review time: 6 Hours

Scientific quality	<input checked="" type="radio"/> Grade A: Excellent <input type="radio"/> Grade B: Very good <input type="radio"/> Grade C: Good <input type="radio"/> Grade D: Fair <input type="radio"/> Grade E: Do not publish
Novelty of this manuscript	<input checked="" type="radio"/> Grade A: Excellent <input type="radio"/> Grade B: Good <input type="radio"/> Grade C: Fair <input type="radio"/> Grade D: No novelty
Creativity or innovation of this manuscript	<input checked="" type="radio"/> Grade A: Excellent <input type="radio"/> Grade B: Good <input type="radio"/> Grade C: Fair <input type="radio"/> Grade D: No creativity or innovation

Scientific significance of the conclusion in this manuscript	<input checked="" type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

Dear editorial office: WJG I should appreciate for inviting me to review paper entitled "Susceptibility patterns and virulence genotypes of *Helicobacter pylori* effecting eradication therapy outcome among Egyptian patients with gastroduodenal diseases.". I have read it and now you can find the review comments in below: 1- Please add the antibiotic in start of the title; 2- The English is fine and I think it is durable. 3- Novelty of the data is fine and I think the clinicians in the Egypt can earn from it to have better susceptibility profile of anti-hp treatment. 4- The main purpose of this study should be clearly stated in the introduction. 1. Reference 3 "Global Initiative for Cancer Registry Development. Lyon: International Agency for Research on Cancer; 2020. Available from: <https://gicr.iarc.fr/about-the-gicr/the-value-of-cancer-data/>. accessed February 2021" in introduction is quite wrong so I advise to add the proper reference which belongs to the 1994, etc. 5- I think there is no need to figure showing h. pylori among the samples from patients with gastritis and neutrophil. The proceeding fig is enough to show even the infiltration, so no need to it. Also please use the arrows to point the important keys in each figure, otherwise we have to dig up the whole picture. 6- I am not fine with this

statement in the result section “In this study, eradication of *H. pylori* was obtained more frequently in patients with *vacA* s1 ($P = 0.02$), s2 ($P = 0.03$), or m1 ($P = 0.01$) positive strains.” WHY? why should a certain part of patients be more resistant to antibiotic therapy while the profile of virulence genes are quite different? ? What a biologic rationale behind? This should be reflected in the discussion. 7- Page 8 line 172, *vag*????????? something should be wrong please correct it. 8- Although the authors reported the susceptibility tests according the E test but I feel they needed to have method as agar dilution as control, at least for certain number of isolates. Their report is a bit high and I afraid to think more about it. I would blame the method for reporting such high rate resistance rate in this research. 9- Authors got 4 biopsies, two antrum and 2 corpus, thereafter they went to conduct biopsy bacterial culture, Giemsa staining and urease test. I can not see an enough consistency among this type of biopsy sampling. They should have taken samples from lonely antrum or corpus. I assume that the authors have a good explanation for this type of sampling. 10- 100% resistance report for the *hp* isolates? Why? How? Also 52% for clarithromycin? I am wondering about the method to measure the susceptibility profile. Authors need to explain the methods and also a good explanation in their discussion to convince the readers finely. 11- Page 10, line 216, “*H plyori*” please fix the mistake throughout the paper. 12- Table 1, where is the sequence for this primer? 13- Why authors have re-cultured the bacteria for 72 hours? “Each *H. pylori* isolate was sub-cultured and incubated for 72 hours” I am unclear about it. 14- There are high rate of resistance reported in this assay, I think the heteroresistance may be occurred since the sampling was a bit strange to me, there is a paper discussing the topic and I would mention them in below, please read and use them in your revised paper while authors are highly recommend to add up a explanation for this results. ** Rizvanov, Albert A., Thomas Haertlé, Lydia Bogomolnaya, and Amin Talebi Bezmin Abadi. "Helicobacter pylori and its antibiotic heteroresistance:

A neglected issue in published guidelines." *Frontiers in microbiology* 10 (2019): 1796. ***
Kao, C.Y., Lee, A.Y., Huang, A.H., Song, P.Y., Yang, Y.J., Sheu, S.M., Chang, W.L., Sheu, B.S. and Wu, J.J., 2014. Heteroresistance of *Helicobacter pylori* from the same patient prior to antibiotic treatment. *Infection, Genetics and Evolution*, 23, pp.196-202. 15- I think there is an urgent need to talk about application of this result in Egypt. I think there are a lot of people who can use them. This is lacking in the discussion section.

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Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 06463958

Position: Peer Reviewer

Academic degree: PhD

Professional title: Adjunct Associate Professor

Reviewer's Country/Territory: Brazil

Author's Country/Territory: Egypt

Manuscript submission date: 2022-12-07

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-01-05 13:58

Reviewer performed review: 2023-01-07 15:56

Review time: 2 Days and 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
Creativity or innovation of this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation

Scientific significance of the conclusion in this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

Title. It adequately reflects the sample, study location, methodology, and results.

Introduction. It reflects well the position of the literature concerning the objectives to be studied. Methodology. Proper. Results. The tables are well understood. Discussion. • The authors in the well-designed and performed study entitled “Susceptibility patterns and virulence genotypes of *Helicobacter pylori* effecting eradication therapy outcome among Egyptian patients with gastroduodenal diseases” investigate the eradication success of a 14-day triple therapy regimen in *H. pylori* infection. They declare that the low eradication rate is worrisome, and alarming cure rates in this study are unsatisfactory and disappointing. In addition, the high resistance to amoxicillin, clarithromycin, and ciprofloxacin is challenging and of great concern. Also, an alternative therapeutic regimen should be adopted in Egypt. • *H. pylori* were not eradicated in 27 patients. In Table 2 (Demographic and clinical characteristics of patients), we note that the study was performed at the National Liver Institute (NLI), and liver cirrhosis was present in 15 (20.8%) patients. How many patients have cirrhosis and poor response to treatment? Is there a possibility of a bias in the inclusion of these

patients? Please, add comments to the Discussion.

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Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05196053

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Professor

Reviewer's Country/Territory: Japan

Author's Country/Territory: Egypt

Manuscript submission date: 2022-12-07

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-01-05 01:59

Reviewer performed review: 2023-01-09 01:06

Review time: 3 Days and 23 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input checked="" type="checkbox"/> Grade D: No novelty
Creativity or innovation of this manuscript	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation

Scientific significance of the conclusion in this manuscript	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input checked="" type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

1. While the aim of this study is mentioned as "to assess the impact of H. pylori virulence genetic determinants on the eradication success" in Aims , nothing was referred about that in Conclusions or Core tip. Title is also out-of-focus. 2. The manuscript seems to consist of two stories. One is the relation between the virulence genotype of H. pylori isolate and eradication sensitivity. The other is the influence of anti-microbial sensitivity of H. pylori isolates on eradication efficiency. However, the both stories are not clearly defined, moreover, the relation between both stories remains obscure. 3. The most impressive and interesting finding in this study would be that the H. pylori isolates bearing VacA-s1 genotype are significantly more conducive to eradication therapy. Actually, multivariate analysis in Table 4 showed that aOR and pValue of s1 are 0.003 and 0.507, respectively. The figures are impressive. However, this evidence regarding the relation between s1 and eradication sensitivity was already demonstrated in a meta-analysis in a previous report (The association between vacA or cagA status and eradication: A meta analysis. PLOS ONE 2017;12:e0177455). 4. Therefore, some further analysis concerning the s1 and eradication should be added to the manuscript.



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Otherwise, an advantage to be published in international standard gastroenterology journals like WJG might be little. Because the mechanism why s1 genotype is more sensitive to eradication therapy using anti-microbials is thought to be elucidated with high priority, the following analyses might be fruitful; 1) the difference between the severity of gastric mucosal inflammation (eg, Updated Sydney System Score) and s1-/s2 genotypes 2) the difference in sensitivity to AMX/CLR and s1/s2 genotypes

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Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05112530

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Chief Doctor, Professor

Reviewer's Country/Territory: Russia

Author's Country/Territory: Egypt

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Reviewer chosen by: AI Technique

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Review time: 17 Days and 17 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No

Peer-reviewer statements	Peer-Review: [<input checked="" type="checkbox"/>] Anonymous [<input type="checkbox"/>] Onymous
	Conflicts-of-Interest: [<input type="checkbox"/>] Yes [<input checked="" type="checkbox"/>] No

SPECIFIC COMMENTS TO AUTHORS

I carefully read the paper Susceptibility patterns and virulence genotypes of *Helicobacter pylori* effecting eradication therapy outcome among Egyptian patients with gastroduodenal diseases

- 1 The title reflect the main subject of the manuscript
- 2 The abstract summarizes and reflects the work described in the manuscript
- 3 The key words reflect the focus of the manuscript
- 4 The manuscript rather adequately described the background, present status and significance of the study. But authors postulated that treatment could be prescribed for 7 to 14 days which is not correct. Current Maastrich VI recommended the only 14 days treatment. By the way, authors cited previous consensus Maastrich V, which also recommended 14-days treatment. Also, the deadline for standard therapy with clarithromycin is 15% resistance rate but not 20% as written in the paper. The aim of the study is to investigate the prevalence of *H. pylori*... The study included 86 patients of one hospital, so authors should use term frequency, but not prevalence.
- 5 The manuscript describes methods in adequate. The only RUT for *H. pylori* primary diagnostics and as a control test after therapy could be criticized because of low sensitivity.
- 6 The main contribution of the study is the new data regarding high prevalence of resistance of *H. pylori* in Egypt to most of the antibiotics currently used for eradication therapy and as a result unacceptable eradication rate.
- 7 The manuscript cited not the latest reference. Authors didn't cite important recently published papers like Maastrich VI consensus report and papers on European registry on management of *H. pylori* infection.

Overall quality of the paper is rather good. it would be recommended to publish after corrections.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 82041

Title: Susceptibility patterns and virulence genotypes of *Helicobacter pylori* effecting eradication therapy outcome among Egyptian patients with gastroduodenal diseases.

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05196053

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Professor

Reviewer's Country/Territory: Japan

Author's Country/Territory: Egypt

Manuscript submission date: 2022-12-07

Reviewer chosen by: Geng-Long Liu

Reviewer accepted review: 2023-02-20 03:52

Reviewer performed review: 2023-03-07 02:16

Review time: 14 Days and 22 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Peer-reviewer	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous



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E-mail: bpgoffice@wjgnet.com
<https://www.wjgnet.com>

statements

Conflicts-of-Interest: [] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

My decision is that the manuscript should be accepted.