ANSWERING REVIEWERS

7 of July 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 11269-review.doc).

Title: Performance of ASGE guidelines for Dyspepsia in Saudi Population: Prospective Observational Study

Author: Nahla Azzam, Majid A Almadi, Hessah Hamad Alamar, Lamis Atyah Almalki, Rehab Nawaf ALRashedi, Rawabi Saleh Alghamdi, Waleed Al-hamoudi

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1. The manuscript has been improved and revised according to the suggestions of reviewers.

1st reviewer

(1) The article from Saudi Arabia is aim to evaluate the adherence of primary care physicians to dyspepsia guidelines, to describe the common endoscopic findings, to evaluate the importance of "red flag" symptoms and to estimate the prevalence of H. pylori in dyspeptic patients. The title is "Performance of the ASGE guidelines for Dyspepsia in a Saudi Population: A Prospective Observational Study". There have some questions and uncleared issues. The authors should to be clarified and be added the following issues in the text.

1. This study is a prospective observational study. Some limitations might be occurred.

We agree with the reviewer, and we added the limitations in our manuscript.

2. Several factors influence the performance of the ASGE guidelines. Please clarify and add these issues in the text.

We thank the reviewer for his feedback and have added the factors influencing in our manuscript.

3. The variety of primary care physicians.

All are family physicians.

4. Please also add the difference of the performance of the ASGE guidelines between the eastern and western countries including between the developed and the developing countries in the text.

We have added the difference in the discussion-section. Thank you.

5. The clinical application of the study is very important. The authors should to be recommended the readers to apply this knowledge into routine clinical practice.

We thank the reviewer, and have added the recommendation at the end of the discussion section.

6. Please revise the manuscript into the WJG style. Thank you so much.

Format has been updated.

2nd reviewer

(2) 1. The sample size is too small for such a dyspepsia study. Conclussions about such a prevalent condition need to be based in a sufficient sample size. However, there no previous sample size calculation in the methods section, that should always be present in this type of study.

Although we do agree with the reviewer that the sample size is small, but we know a priori that the prevalence abnormal findings in our dyspepsia population is high (more than 60%) based on prior literature [25]

We do thank the reviewer about the point that we had overlooked to state in the methods section about the sample size calculation. We included the following statement in the statistical analysis section

"Based on an a priori baseline prevalence of abnormal findings on endoscopy of 60% and given we wished to include up to 9 variables in our multivariable model, we estimated that 150 individuals would be needed to provide sufficient accuracy within the multivariable analysis"

2. Some issues about patient's selection are concerning, as mean age, of 40.3 years, young for endoscopy in a dyspeptic population, a high proportion of patients with a prior endoscopy, even with more than one endoscopy, which could bias the results.

The demographics of the patient population in Saudi Arabia is very different from others as there is a very high proportion of the population below the age of 20. Again this is evident in the previously cited paper where the mean age was 45.3 years (SD 18.1 years)[25]

Again we would like to remind the reviewer that the whole notion of this paper was to challenge the ASGE guidelines performance "One of which is age" in our patient population with all its peculiarities.

We again thank the reviewer for his note about the proportion of patients with a prior number of endoscopic evaluations prior to the index endoscopy in this study. Although it is true that this fact might introduce bias to the results; we could not discern the direction of the bias as if these were normal endoscopies it would induce bias to an opposite direction compared to if these were abnormal endoscopies. Unfortunately we do not have data on these prior endoscopies as these were performed at other institutions and again we want to point out that these patients were referred directly to endoscopy without being seen by a specialist representing "real life practice" in an open access endoscopy unit.

3. Abnormalities should be defined and listed in a table. It is surprising to find GERD as an endoscopic finding in 17% of patients, even more when GERD (which is a syndrome, but not an endoscopic finding) was an exclusion criterion.

We have included a figure that displays the findings on endoscopy as well as their proportions. We opted for a graph to relay the results rather than a table as there would not be much to be gained with a simple listing of findings and their proportions when compared to a graph.

We thank the reviewer to pointing out our misrepresentation of the finding on endoscopy. It is true that we excluded those with predominantly GERD related symptoms but we found signs of GERD in the form of reflux esophagitis. We have reworded the findings to the following, more clear, expression

"The most common endoscopic findings were gastritis in 52%, duodunitis in 10%, hiatus hernia in 7.8%, ulcers in 3.9% and malignancy in 2.6% of the patients; the remaining 17% were found to have refulx esophagitis signifying GERD. Furthermore, 6.5% had endoscopic features suggestive of celiac disease "

4. It is surprising to find a previous endoscopy as an independent risk factor to have endoscopic findings. Previous findings should be listed and I think patients with abnormalities in a previous endoscopy should be excluded from the analysis.

We respectfully disagree with our kind reviewer. To the contrary to his note, we think it is only natural for a history of a prior endoscopy to be a predictor of an abnormal finding, as the reason for a repeat procedure would usually signify a persistent complaint that the patient was not has been relieved from. It might even be

thought of as a selection bias where those who had a prior endoscopic procedure being at an increased probability of having an abnormal finding on a repeat endoscopy. Unfortunately we do not have data on these prior endoscopies as these were performed at other institutions.

If we exclude those with a prior endoscopic procedure then we would lose above one quarter of our study population and we would be severely underpowered to detect any predictors of an abnormal endoscopy. Thus we refrained from the suggestion by the reviewer. Nonetheless, we performed a sensitivity analysis after excluding those who had a prior endoscopy and the results were more or less the same "Data available upon request".

5. The sample size and the number of patients with relevant findings do not allow the author to make statements about the validity of alarm symptoms. Of note, multivariate analysis was irrelevant, maybe due to the short sample size.

We thank the reviewer for his comment. We do acknowledge his concern have addressed it in our response to the prior reviewer. We also added a segment on the sample size calculation as the prior reviewer has pointed out.

6. The final part of the discussion is reiterative.

We thank the reviewer for his comments and has been notified and corrected.

7. English is very good except some isolated spelling mistakes ("duodunitis").

It has been notified and corrected .thank you.

3rd reviewer

(3) In this study, the authors have tried to demonstrate factors related to the positive endoscopic findings based on the ASGE guideline/ Study design is nice and analysis is clear. Their results should be useful for the general readers.

We thank the reviewer for his valuable feedback.

References and typesetting were corrected.

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

Sincerely yours,

Dr. Waleed Al-Hamoudi,
Division of Gastroenterology,
King Saud University,
Riyadh, P.O Box 2925(59),
Riyadh 11461, Saudi Arabia.
E-mail: walhamoudi@gmail.com