

Dear Editor and Reviewer,

We appreciate the opportunity to allow us to revise our manuscript and thanks for reviewers' constructive comments and suggestions. We would like to submit our revised manuscript, entitled '**Assessment of the triglyceride glucose index in adult patients with chronic diarrhea and constipation**' for consideration for publication. In the revised manuscript, we have carefully addressed all comments and questions raised by reviewers' point-by-point. We greatly appreciate your time and efforts to improve our manuscript for publication.

Reply to Reviewer

Reviewer #1:

1. Your results showed a positive relation between TyG and diarrhea, but I couldn't find the time-relationship between both. To be predictive, a biomarker must be detectable time before symptoms. In the manuscript, I missed this information.

Reply: Thank you for the reviewer's suggestions; given the lack of data in some parts of the NHANES database, the authors have modified the conclusion section to be more cautious in concluding that higher TyG levels were positively associated with abnormal bowel health. The conclusion that TyG is a predictor of chronic diarrhea is not yet accessible and requires further investigation; this limitation is also mentioned in the DISCUSSION.

(See: page 3, lines 5 and lines 12-14; page 21, lines 15-20)

2. In case TyG could really predict a future gut dysfunction, which clinical applications do you foresee? How a biomarker of diarrhea or constipation could help people to avoid the development of such pathologies?

Reply: We thank the reviewers for their comments, and we have made improvements based on them. Subsequent well-designed randomized controlled trials will be required to determine whether TyG can be used as a reliable predictor of chronic diarrhoea and constipation, and with the current extensive study of the strong link between gut microbes and insulin resistance in pathological mechanisms, if TyG can be used as a reliable indicator of gut dysfunction, it suggests that in the future, early, comprehensive management of insulin resistance will be an essential measure to alleviate symptoms, which may provide novel drug-targeted treatments for such diseases.

(See: page 3, lines 13-16; page 9, lines 20-24; page 9, lines 10-12)

3. As you already mentioned, an important limitation of your study is the definition of chronicity (diarrhea and constipation) based solely on Bristol stool scale, which only gives a quantitative representation to fecal consistency but it does not inform for how long has been the patient reporting liquid or hard stools. It's not clear in the methodology if you

collected these data.

Reply: The database did not indicate, and the authors were unable to collect, the particular length of time patients reported liquid or hard feces during the NHANES 2013-2014 phase. MATERIALS AND METHODS has a more detailed description of the Bowel Health Questionnaire.

(See: page 5, lines 10-13)

BHQ060 - Common Stool Type

Variable Name: BHQ060
SAS Label: Common Stool Type
English Text: Please look at this card and tell me the number that corresponds to your usual or most common stool type.
English Instructions: HAND CARD BHQ2
Target: Both males and females 20 YEARS - 150 YEARS

Code or Value	Value Description	Count	Cumulative	Skip to Item
1	Type 1 (separate hard lumps, like nuts)	106	106	
2	Type 2 (sausage-like, but lumpy)	286	392	
3	Type 3 (like a sausage but with cracks in the surface)	1254	1646	
4	Type 4 (like a sausage or snake, smooth and soft)	2694	4340	
5	Type 5 (soft blobs with clear-cut edges)	464	4804	
6	Type 6 (fluffy pieces with ragged edges, a mushy stool)	389	5193	
7	Type 7 (watery, no solid pieces)	53	5246	
77	Refused	0	5246	
99	Don't know	31	5277	
.	Missing	782	6059	

4. There is another important question that arises from your results: statistical significance vs clinical

significance. Some of your results lacked statistical significance, but it doesn't imply a lack of clinical significance. You should strengthen on this point.

Reply: Thank you for your guidance. We have revised the text according to your suggestions. In the DISCUSSION section, the authors highlighted that statistical insignificance does not equate to clinical insignificance, in the non-linear association, when TyG is greater than 8.2 is positively correlated with chronic constipation, indicating that there may be a difference in the pathological mechanisms between TyG and chronic diarrhoea, constipation patients, so there is still a need for more basic research to explore this relationship. Therefore, further basic research is needed to explore this relationship.

(See: page 9, lines 20-24; page 10, lines 14-16)

5. Please provide the Informed consent statement.

Reply: Not applicable. The written informed consent was obtained from the patients/participants to take part in this study and human participants were assessed and sanctioned by the research ethics review board of the National Center for Health

Statistics. Therefore, we downloaded the Confidentiality Brochure from the NHANES website and uploaded this into the informed consent document during the submission process.

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- Your name will not be linked with your questionnaire answers and exam results. You will be given a unique participant ID for the survey.
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- NHANES databases are password protected and encrypted and can only be viewed by appropriate personnel.
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In conclusion, despite the difficulty in obtaining a true causal relationship between Ty G and diarrhoea and/or constipation, based on the positive results and theoretical analyses presented here, TyG has potential advantages in assessing the risk of abnormal gut health. We will discuss these observations and their potential clinical implications in more detail in the discussion section.

We hope that the above response meets your requirements.
Please feel free to let us know if you have any additional
questions or need further clarification.