

Dear Editor-in-Chief, Science-editor and Peer-reviewers,

Thank you for assessing our manuscript, for the constructive comments made in your review notes and for the opportunity to revise and resubmit our paper "Pancreatic involvement in celiac disease". Your suggestions have been addressed on a point-by-point basis and changes have been made accordingly throughout the manuscript.

Review 1

The authors reviewed the association between pancreatic disease and Celiac disease. The manuscript is well-written and up-dated data & knowledge are extensively and concisely summarized. Therefore, it will be of interest to the readership of our journal. Thank you

Thanks for your reply.

Review 2

Many thanks for your mini review which I read with great interest. The manuscript requires changes as added as comments in manuscript.

Thanks for your reply.

Review 3

Point 1

The manuscript entitled "Pancreatic involvement in celiac disease" is an excellent review of the historical and proposed mechanistic association between celiac disease and various pancreas disorders. The authors put together a great summary of various published work about how celiac patients might be at risk for pancreatic glandular dysfunction and reflect on need to study the potential causative relationship between celiac disease and pancreatitis. Minor note: the authors didn't include author's/title page or an abstract. I encourage the authors to resubmit and adhere to the WJG minireview submission guidelines.

Author's reply

Thank you for the appreciation of our work and for pointing out the missing documents in our submission. Title page and abstract were now added in the submission system.

Point 2

“The systemic character along with its various clinical presentations however complicates case-finding and delays diagnosis, due to poor awareness among different medical specialties”.

Please re-phrase.

Author’s reply

Thank you for your comment, we’ve re-phrased the sentence in order to make it more clear.

Point 2

“none of the pancreatic-associated involvement in CD has been adequately reported in currently available guidelines”

The guidelines are self-explanatory for CD and pancreases related testing.

Author’s reply

We agree that guidelines are self-explanatory for CD and pancreas related testing as in the figure you presented, but this is limited only to considering pancreatic exocrine insufficiency in case of non-responsive CD. We believe the guidelines should cover pancreatic involvement in CD more thoroughly, as they do for some of the systemic manifestations of CD. We’ve updated the sentence in order to point out that pancreas-related involvement in CD is insufficiently covered in currently available guidelines.

Point 3

Freeman’s paper was published in 2007. Since than many researches have been done on CD and various associations between CD and PEI etc have been established.

Author’s reply

Thank you for this comment. We definitely agree that several papers have been published since 2007 regarding the various associations between CD and pancreas-related pathology, but this is a landmark paper where the need to further expand this relationship in terms of research was stated. In fact, the objective of our mini-review is to provide an update on the topic, with all the newly available data. We believe the Freeman paper is a reference timepoint for addressing pancreatic involvement in CD and should be covered in the background section.

Point 4

Please explain aim in more detail. What factors are you looking at? The aim of review is too general it needs to be more specific.

Author's reply

Thank you for this suggestion. We've updated the aims' paragraph accordingly, in order to better reflect the objectives of our review. We aimed to analyze the literature with regard to the magnitude of the association between CD and pathologies of the exocrine pancreas (acute pancreatitis, exocrine pancreatic insufficiency, autoimmune pancreatitis) and to assess the evidence on testing indications for CD in these conditions.

Point 5

The selection criteria is not defined. There were total of 889 papers with 145 excluded due to duplication. How selection was then carried out among more than 750 papers. What were inclusion and exclusion criteria? How many papers were finally included in study? Better to describe it in table format or flow diagram. The search strategy needs more explanation. Inclusion and exclusion criteria's? after taking out duplicated studies there are still more than 750 papers left. How were they narrowed down? What was the final selection? Other demographic findings to describe publication and study characteristics? Better to use a table or flow diagram to explain it.

Author's reply

Thank you for the above questions. We've added a flow-diagram and further explained how articles were screened and selected. We did not intend to do a systematic review to answer a specific clinical question, but a literature review on the topic.

Point 6

In reviews where there is conflicting information it is better to describe them in table form with other relevant demographics that could have resulted in a particular outcome. Unless we have some comparison, we cannot compare publication 21 with 24. Better to describe key features of the study in a table format. Also, at the end author should give his

own opinion. What they think about CD and risk of pancreatitis. This goes with other comparisons as well as described below under various headings.

Author's reply

Thank you for this suggestion. We've summarized data from the studies with discordant results in a table.

Point 7

The conclusion is also very general and what is already known. What different approach the author is suggesting for CD and pancreas association??

Author's reply

Thank you for the suggestion on including our viewpoint in conclusions. We've added a recommendation for CD testing in certain pancreatic conditions.

Point 8

The manuscript provides an excellent review of the mechanistic links between celiac disease and various pancreatic diseases. Respected authors, this is a well written paper and covers an interesting topic. Nevertheless, there are a number points that may deserve some revisions. 1. Add updated content. It would be better if it could be summarized into a table. 2. For the explanation of the mechanism, some charts will be more intuitive. 3. Missing Abstract section

Author's reply

Thank you for your kind appreciation. Manuscript has been updated according to reviewers' comments. A table summarizing studies looking at pancreatitis risk among CD individuals was added. Abstract was originally inserted during submission process in the corresponding form, and has now been added in the manuscript.

Point 9

Please be sure to use Reference Citation Analysis (RCA) when revising the manuscript. RCA is an artificial intelligence technology-based open multidisciplinary citation analysis database. For details on the RCA, please visit the following web site: <https://www.referencecitationanalysis.com/>. Please provide decomposable Figures (in which all components are movable and editable), organize them into a single PowerPoint file.

Author's reply

Thank you for suggesting RCA. I've added Figure 2 as PPT in my account and marked it as original.

Thank you again for all your comments, which were highly appreciated and taken into account for this revised, improved version of our manuscript. We hope that all changes made are satisfactory resolutions for your inquiries. We remain open to any further corrections.

We also confirm we will send the final version of the manuscript for language polishing depending on a second round of revision.

Best regards,
The authors