Author’s response to reviews

Title: Screening for Celiac Disease in Poorly Controlled Type 2 Diabetes Mellitus: Worth it or not?

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Author’s response to reviews:

We express our special thanks to the reviewer for his/her careful reading of the paper, and for providing valuable comments and suggestions which have helped improved both the content and the presentation. We believe that the revision has been successful and the paper has been improved. The responses to reviewer's comments are available in this document.

Response to the comments of Reviewer

Thank you for your insightful assessment of the manuscript. We have addressed the issues you noted in this revision.
Methods Section:

1. Please explain how the healthy controls were recruited from the diabetes clinic.

--Diabetes clinic changed as endocrinology outpatient clinic (Page 4, line 1)

2. There is no mention of sample size or power calculations. How was sample size decided?

--We did not calculate sample size or power calculation before starting the project. We consecutively enrolled patients according to inclusion criteria during six months period which was the predicted study time when applying for the approval of ethical committee.

Results section:

1. Repetitive text—there are 2 statements that 2 pts in the DM group were diagnosed with celiac.

--The second “Two patients (1.45%) in DM group were diagnosed with CD (Table 1 and 2)” sentence in the results part was removed.

2. Text states: "The cut-off point of 0.6 was assumed." and then says normal c-peptide range was 0.51-2.7 ng/ml. The first group included those with c-peptide <0.51 so please clarify how the cut off of .6 was used.

--We used the cut-off of 0.51 and we wrote 0.6 by mistake. Thank you for your attention. We modified the “The cut-off point of 0.6 was assumed” as The cut-off point of 0.51 was assumed”

1. It does not seem relevant to point out that the mean C-peptide differed by C-peptide group, considering that the groups were created based on C-peptide value.

--We compared c-peptide levels, after dividing diabetic patients into 3 groups, to show mean c-peptide levels are statistically significantly different between groups. P value of <0.0001 suggest this. However, if the reviewer wants to us to remove that part from the results section and table 4, we can do it.
2. For 2nd half of Results section, it's not clear what groups are being compared—DM vs healthy or c-peptide groups. Please clarify.

--The results in the second half of results section (a second paragraph was created which starts with “The DM group was divided into three groups according to the C-peptide concentrations” are all related to c-peptide groups (Page 6, line 15-25).

3. In last sentence of Results, text says C-peptide did not differ by groups, but previous text and Table 4 show that it did. This needs to be corrected (or removed since not relevant).

-- “c-peptide concentrations” was removed from “Age, SBP, DBP, BMI, WC, duration of diabetes, total insulin dose and hsCRP, FPG, PPG, HbA1c, c-peptide concentrations were similar between groups (p>0.05) (Table 4)” sentence (Page 6, line 23-25).

Discussion/Conclusion:

1. Much of the text is background information and could be moved to the Introduction section.

-- First paragraph of the discussion part was summarized as “High-fat diet induced secretion of proinflammatory cytokines (), endoplasmic reticulum stress via activation of toll like receptors (), endoplasmic reticulum stress via activation of toll like receptors (), activation of NLRP3 inflammasome upregulation () and promotion of glucose homeostasis by TNF-α blocker (), association of insulin resistance and dietary fatty acids with activation of B and T lymphocytes () are all evidences which may suggest the role of autoimmunity in etiopathogenesis of T2DM” and this part was added to introduction part (Page 3, Line 21-26).

2. The authors state in both the Discussion and Conclusion that the prevalence of CD was slightly higher in their study than in the normal population. As you could argue that 1.45% and 1% are similar, please state the actual prevalences (1.45% vs 1% in general population).

--The sentences were modified as “In our study, the prevalence of CD disease was slightly higher than the actual prevalence of CD in general population” and “The prevalence of celiac disease among patients with type 2 diabetes, with poor glycemic control despite insulin therapy, is slightly higher than the actual CD prevalence in general population.”
3. The authors state: "Positive correlation of tTGA IgA with HsCRP and HbA1c might show the DM with worser prognosis could be associated with higher levels of tTGA IgA and possibly higher incidence of Celiac disease." The authors should add the caveat that while positive, the correlations were very weak (both $r \leq 0.21$).

We agree with the reviewer idea. We removed that sentence since it is not suitable based on that much correlation (Page 8).

Tables:
1. Add Ns to tables 2-4

Ns were added to table 2 and table 4.

2. Specify that Table 4 is limited to DM group

The explanation of table 4 was modified as “Demographic, biochemical and clinical characteristics of diabetic patients when they divided into 3 categories based on their c-peptide concentrations”