Author's response to reviews

Title: Periodontal conditions, oral Candida albicans and salivary proteins in type 2 diabetic subjects with emphasis on gender.

Authors:

Fawad Javed (fawad.javed@ki.se)
Lena Klingspor (lena.klingspor@karolinska.se)
Ulf Sundin (ulf.sundin@karolinska.se)
Mohammad Altamash (draltamash@cyber.net.pk)
Björn Klinge (bjorn.klinge@ki.se)
Per-Erik Engström (per-erik.engstrom@ki.se)

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Author's response to reviews: see over
To,

The Editor,
BMC Oral Health

Dear Sir,

Thank you for your response and the comments from the referees concerning our manuscript titled “Periodontal conditions, oral Candida albicans and salivary proteins in type 2 diabetic subjects” (Manuscript ID: 3328842932290015).

The manuscript has been revised according to the referees’ comments and we have responded to the reviewers’ comments point by point in the following. Changes are highlighted in yellow in the revised manuscript.

We would like to express our gratitude to the referees for their valuable insight and you for your interest in our work.

Yours sincerely,

Fawad Javed
DDS, PhD
Corresponding author
Karolinska Institutet,
Institute of Odontology, Division of Research,
Box 4064, SE 141 04,
Huddinge. SWEDEN.
Ph: +46 70 430 4909 Fax: +46 8 711 83 43 Email: fawad.javed@ki.se
Reviewer 1: Elif E Sakalliolgu

We thank Reviewer 1 for thorough reading of the manuscript and for several relevant and constructive comments and good advices.

1- Materials & methods. Authors should refer the method used for unstimulated whole saliva collection.

The methods used for unstimulated whole saliva collection have been referred to in the revised manuscript as recommended by the Reviewer. The following references were entered in this regard.


2- Materials & methods. The year of diabetes in the patient population should be given.

The year of diabetes in the patient population has been entered in the revised manuscript as recommended by the Reviewer. The following information has been entered on page 9 in the revised manuscript:

The durations of T2D in individuals with and without C. albicans colonisation were 10.5 (range 8-14 years) and 10.8 years (range 8-12 years) correspondingly.

3- Results. The results in the text do not match with the results in “abstract” and it should be clarified regarding both DM and C. albicans and their statistical comparison. This paper and the statistical comparison are mainly based on DM (Candida levels, gender differentiation etc. are made in the diabetic group). However, “abstract” was written according to the comparison of gender and PI, BOP, PD, etc., of the C.albicans patient group (the main group of “abstract” was C. albicans).

Thank you for your observation. We have clarified the results in the abstract with reference to results in the text. Results in the abstract have been clarified as follows:

ABSTRACT: Results
Periodontal conditions (PI [p<0.00001], BOP [p< 0.01] and PD of 4 to 6 mm [p< 0.001], salivary IgG/mg protein (p< 0.001) and salivary total protein concentrations (p< 0.05) were
higher in type 2 diabetic females with *Candida albicans* (*C. albicans*) colonisation compared to males in the same group. Type 2 diabetic females with *C. albicans* colonisation had more teeth compared to males in the same group (*p* < 0.0001).

4- Some data discussed in “discussion” according to the statistical data but do not exist in “results”. For example, IgG levels compared between the genders of patients in *C. albicans*. All data presented in “results” are of the patients with DM. “Discussion” should be rewritten according to the data in “results”.

In the results of the submitted manuscript, Figure 2 (a) showed the differences in salivary IgG/mg protein, IgA/mg protein and total protein concentration in type 2 diabetic males and females with *C. albicans* colonisation. In this context, we discussed the possible associations between IgG/mg protein, number of teeth and oral *C. albicans* colonisation.

5- Page 12, first paragraph. The authors utilize BOP as the gingival blood flow. These 2 parameters are different and there are many other reasons that may affect BOP. Also, the results do not support this usage.

Thank you for the observation. The sentence has been clarified as follows:

Therefore, among type 2 diabetic subjects with *C. albicans* colonisation, the presence of more teeth seems to be the most likely explanation for the higher IgG/mg protein levels in females compared with males.

6- The mean values and SD should be added to all figures.

The mean and SD have been added to all figures as recommended by the Reviewer.

7- This paper needs some language corrections before publication.

The English language has been revised and edited as recommended by the Reviewer.

8- Data should be reevaluated by statistical means regarding the main subject (DM or Candida?) of the work.

After a methodical regression analysis, we observed that the number of teeth was mainly associated with the severity of periodontal conditions in diabetic females with *C. albicans*. However, to further evaluate whether T2D or Candida is responsible with inflammatory parameters, further studies are warranted.
Reviewer 2: Yutaka Seino

We thank Reviewer 2 for thorough reading of the manuscript and for relevant and constructive comments.

In this paper they do not show the diabetic state of the patients. The duration of the disease, the condition of microangiopathy and macroangiopathy, BP, and metabolic conditions of the patients such as mean HbA1c, total cholesterol, urinary protein should be shown and discussed. Further they should demonstrate the meaning of the presence of C. albicans for their diabetic state.

The duration of the disease has bee entered in the revised manuscript (page 9) as recommended by the Reviewer.

In this study, we were more focused on the periodontal and salivary inflammatory parameters in subjects with type 2 diabetes (T2D). The aim was to investigate oral health.

It is known that oral Candida albicans (C. albicans) are commensal oral flora but can be opportunistic pathogens in subjects with a suppressed immune response, such as those with T2D. We hypothesized that periodontal and salivary inflammatory parameters may be influenced by the presence of C. albicans (which are more dominant in females compared to males) in subjects with T2D.

P10 l13 mean number of teeth 10.2? range 10-16 teeth, the mean is true?

Thank you for the observation. The value for the mean number of teeth has been corrected in the revised manuscript.
Reviewer 3: Ulvi Kahraman K Gursoy

We thank Reviewer 3 for thorough reading of the manuscript and for several relevant and constructive comments.

Methods: (4mm<6mm ) does that mean pockets with 4 to 6mm probing depth? This can be expressed as (4 to 6 mm, or #6 mm periodontal pocket) throughout the text.

Throughout the revised manuscript, the pocket depth has been expressed as recommended by the Reviewer.

Results: p value must be in lower case.
All p-values have been formatted in lower case throughout the manuscript, as recommended by the Reviewer.

Conclusions: It is the repetition of the results, not concluding.
The conclusions in the abstract and at the end of text have been written as follows:

Conclusions (Abstract) (page 2)
Clinical and salivary parameters of periodontal inflammation (BOP and IgG/mg protein) were higher in type 2 diabetic females with oral C. albicans colonisation compared to males in the same group. Further studies are warranted to evaluate the association of gender with these variables in subjects with T2D.

Conclusions (main text) (page 14)
Clinical and salivary parameters of periodontal inflammation (BOP and IgG/mg protein) were higher in type 2 diabetic females with oral C. albicans colonisation compared to males in the same group. These gender-specific features may offer a route to improve oral healthcare for females with T2D. However, further studies are warranted in this regard.

3rd sentence: Ref 2 is not suitable for this sentence, because that study is on Type 1 DM.
Reference no. 2 has been deleted from the revised manuscript.
4th sentence: Write *C. albicans* with full name, as it is first time used in the text (do not count the abstract).

Thank you for the observation. *C. albicans* has been written with full name the first time it was used.

5th sentence: ref 4 is not supporting this sentence.

Reference 4 has been deleted from the revised manuscript.

**MATERIAL METHODS:** Collection of oral yeast samples: (Kadir et al. 2002) give the ref. no.

Thank you for the observation. A reference number for the study by Kadir et al. 2002, has been entered in the revised manuscript.

**RESULTS:** Study population: there is a mistake in the data here. Number of *C. albicans* positive subjects is 29, with 17 male and 12 female. Number of *C. Albicans* negative subjects is also 29, with 6 male and 23 female. This makes the whole study population 23 male and 35 female. It was said to be 29 male and 29 female, before.

Thank you for your observation. We have corrected the figures in the study population in the revised manuscript as follows:

**Study population**

Fifty-eight consenting individuals (23 males and 35 females) satisfied the criteria and were admitted to the study. They were selected on a consecutive basis.

**Oral yeast colonization in subjects with T2D:** First two sentences belong to discussion, and again ref.no. must be at the end.

The sentences have been removed from the results as recommended by the Reviewer. The sentence has been moved to the discussion and the reference number is also entered at the end of the sentence as recommended.
In subtitles C. albicans are not in italic.

*C. albicans* has been written in italics throughout the manuscript as recommended by the Reviewer.

4th paragraph last sentence: Is it possible to come to this conclusion? We do not know the prevalence of denture-wearing between males and females. It is not true to conclude like that without giving the prevalence in the results. The results for denture wearing have been entered in the “Results” section as recommended by the Reviewer.

5th paragraph: It is giving a wrong impression like age does not effect C. albicans colonisation. So instead of saying “age does not seem to influence” it might be better to say “age can not be the effect on the differences in C. albicans colonisation, as it was adjusted in both groups”.

The sentence has been re-phrased as recommended by the Reviewer.

Last sentence: Confusing, better if it is simplified.
The last sentence has been re-phrased to improve clarity as recommended by the Reviewer.

FIGURES:
It would be better to put the subjects without C. albicans into the figures 2 and 3, so that we could make better comparisons.

Subjects without *C. albicans* colonisation have been entered in Figures 2 and 3, as recommended by the Reviewer.
Reviewer 4: Khalid Almas

We thank Reviewer 4 for thorough reading of the manuscript and for considering our manuscript as an article of high importance.

The sample size for future study should be based on power analysis.

Thank you for your valuable suggestions and we will consider your advice for future research studies.

The Conclusion at the end: Rephrase it as increasing number of teeth in female population does not reflect the finding of the paper. The conclusion in abstract is OK.

The conclusion has been re-phrased.