Author's response to reviews

Title: Periodontal disease and some adverse perinatal outcomes in a cohort of low risk pregnant women

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Author's response to reviews: see over
Dear Editor of
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Periodontal disease and adverse perinatal outcomes in a cohort of low risk pregnant women

First of all we would like to thank the reviewers who carefully checked the content of the manuscript. We are addressing the points they highlighted below, with the answers in bold. The text of the manuscript was changed accordingly, with the modifications indicated as yellow highlight.

Thank you again.

Sincerely yours

The authors

Reviewer’s report 1

Major Compulsory Revisions

1. Too many references, delete some unnecessary references.

OK, they are substantially reduced (from 45 to 33).

2. There should be information about at what gestational age that periodontal examination was performed.

This information is in page 5, methods session. The periodontal examination was always performed at below 32 weeks, generally during the second trimester of pregnancy.

3. Were treatment given for women with positive periodontal diseases? If no treatments were given, was this ethical? If treatments were given, then the two groups are perhaps not different.

No, treatment was not given to women with periodontal disease. At the time of the study this was not considered worldwide unethical, because there was not a strong evidence supporting treatment for reducing its occurrence and effects. The study protocol, as informed, was approved by the local IRB.

4. The diagnosis of PROM is usually tricky, what was your operational definition, how long was the interval between rupture of membranes and the onset of labor did you use to diagnose PROM?

The operational definition of PROM is provided now in page 7. The interval of time between the rupture of membranes and the onset of labor (latent period) was not recorded in this study because it was not a primary or secondary outcome of interest.
5. What factors were included in the final multivariate regression model?

This information is now provided in page 8 of the manuscript. For each main perinatal outcome, the correspondent model included the group plus all other predictors (control variables).

6. It is quite strange to see that the association between PD and preterm labor and LBW changed from “not statistically significant” to “statistically significant” after controlling for potential confounding factors by multivariate regression. Usually it is the other way round. Please explain.

Well, we don’t know but these are the numbers we got! We checked again with the statistician and they are OK.

7. The content of Paragraph 5 in the discussion part is not supported from this study and should be deleted.

OK, done.

8. Discussion should be more specific and concise.

OK, the discussion was shortened and more focused only on aspects related to the present study.

Minor Essential Revisions
1. The word "premature rupture of membranes" should be replaced by "prelabor rupture of membranes".

OK, it was changed in the whole text.

Reviewer's report 2

Major Compulsory Revisions
This paper adds more sound and high quality information about the relationship between periodontal disease (PD) and preterm birth (PTB) and should be published after some major revisions and replies from the authors.

Why did you use PARF for a presumed causal factor of PTB such as PD? The use of PARF is appropriate when causality is unquestionable or at least when the condition, PD, is clearly related to the outcome (you state in the discussion that the association between PD and PTB “is not necessary (substitute for necessarily) causal”) and it doesn’t seem to be the case for PD. Also, PARF must be used when there is a proven efficacious intervention, and again this is not the case for PD (check Oliveira, de Oliveira et al., 2010). It is questionable and the controversy surrounding PD as a direct and sole cause of PTB precludes you of doing another audacious statement like “the percentage of cases of PT that would be avoided with the exclusion of the PD is 29%, as well as 42% of PROM”, it doesn’t fit your results and is more a mathematical than scientific conclusion.

Well, here we did not completely agree with the reviewer. First because it is not a consensus that PARF could only be used when causality is unquestionable. Besides some controversy, there is a lot of scientific literature showing at least a statistical
association between PD and these adverse perinatal outcomes, being this relationship direct or not. The text makes clear that this was a theoretical exercise, trying to evaluate how would be the impact of eliminating the exposure of PD. This is completely different from doing “an audacious statement”.

One major concept in preterm birth pathophysiology is multicausality, and I think your sample is small (even being a low risk population) to assume that PD was the only probable cause of PTB.

Again, we never said that PD was the only probable cause of PTB. Just in case, this has been reinforced in the last paragraph of discussion session.

In results section of the abstract, the statement “PD explained 42.4% of cases of PROM” is not an appropriate remark and it is not possible to conclude it from the findings of the study.

OK, this phrase was deleted from the abstract.

Another question is the role of different degrees of PD severity, 83% (133 of 157) of PD patients were classified as P1, which seems to be a milder form of disease. This should be discussed in further detail.

As the reviewer pointed out, the present study has a relatively small sample size and it is underpowered to distinguish the effect of different degrees of PD severity. This analysis was not performed at all and therefore no discussion or conclusion could be drawn from that. But this is approximately the prevalence of mild PD severity found the majority of studies.

Minor Essential Reviews:

English: is well written in general but must be reviewed, avoid terms as fomented, hyperirritability (maybe “uterine tenderness” is more appropriate), use PTB as abbreviation for preterm birth, expression used more often in English, there are some minor typing and spelling errors.

OK, reviewed and corrected.

Adverse perinatal outcome: the outcomes addressed in the study are more related to prematurity and important outcomes are not cited such as stillbirth, neonatal mortality and morbidity and maternal morbidity. Therefore, it would be more appropriate to substitute adverse perinatal outcome for prematurity or describe in the title: low birth weight, premature rupture of membranes and preterm birth.

Again, the sample size of the study was not enough to study such other outcomes. However, PTB, LBW, SGA and PROM are still adverse perinatal outcomes. Then we added the word “some” before “adverse perinatal outcomes” in the title, abstract and objectives to make it clearer.

Page 5: there is no need to mention the seven excluded cases, inclusion criteria: why did you exclude 2 previous C-sections?

We think we should mention. They entered the study and signed an informed consent! In addition, in another manuscript exploring the factors associated with the presence of PD, in a cross sectional approach at the time of periodontal examination,
these 7 cases are included. The cases with 2 previous C-sections were excluded due to the fact that they have a higher likelihood of preterm birth, considering they are going to undergo a C-section when reaching term.

Page 6: it would be appropriate to clear why just one examiner is enough, how important is the inter-examiner variability for PD diagnosis? Considering the periodontal exam depends also on the subjective evaluation of the examiner, it is considered a good practice to have the capacity of the examiner to classify the periodontal status be checked by a second examiner (inter-examiner evaluation) or by the same in a second time (intra-examiner evaluation). This could be considered as a limitation of the study and is now clearly stated in the correspondent paragraph.

Page 7: did you check the information obtained by phone calls? You never state how many patients gave the information by phone, in table 2: Apgar 1st and 5th minute – you should make the numbers clearer. What was the mean gestational age of dental evaluation? Does it have any influence on the results? Is there progression of PD in pregnancy?

The information obtained by phone referred to a very short number of cases, no more than 5%, but we have not the exact number. We preferred to report the percentage of women in each group whose neonates had Apgar scores below 7 in the first and fifth minutes. Unfortunately it was not possible to evaluate the progression of PD during pregnancy because just one periodontal examination was performed at the beginning of the study.

Table 1: your sample size is 327
As already explained, the evaluation of periodontal status was performed during pregnancy, when 334 were enrolled. Seven of them were after excluded of the study.

Table 2: systemic disease – it was an exclusion criteria. What systemic diseases did you allow in your sample? Were any of them risk factors for PTB?
In the study design topic of the methods session we describe the systemic chronic conditions that we excluded from the sample. Therefore any remaining that was considered not related to PTB are allowed to remain in the sample.