Author’s response to reviews

Title: Periodontal disease and spontaneous preterm birth: A case control study.

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Author's response to reviews: see over
To: The Editor(s) BMC Pregnancy and Childbirth,

Thank you for allowing us the opportunity to resubmit our manuscript. The reviewers comments were very helpful which have in resulted, we think, in an improved manuscript. The specific responses to the reviewer’s comments are outlined on the following pages. All the authors of the original manuscript have reviewed the changes and are in agreement with them. If you require any further information please don’t hesitate to contact me.

Sincerely,

Dr. Stephen Wood
Reviewer 1. GJ Linden

As requested the following changes/additions were made:

Comment 1: additional data as requested page 5 line 23.

Comment 2: Dr Cox has provided an explanation for our method of GCF volume measurement page 6 line 21 to page 7 line 2. We think it is also worth noting that any inaccuracies in the measurement of GCF volume and therefore enzyme concentration would be non-differential and therefore create bias toward the mean. This then could not account for our results.

Comment 3: We feel that this reviewer did not understand our reasoning for including the second control group, the undelivered antepartum controls. We had provided justification for our use of additional controls on page 7 line 17-20. Simply put a previous study (which we referenced) had documented decreasing probing depth with advancing gestation. Therefore, in comparing women who had delivered preterm (at earlier gestation) compared to term subjects could introduce substantial bias. Therefore, we designed our study to deal with this potential bias if we discovered similar findings in our population. As we did not find differences in attachment loss between the two control groups we felt justified in combining them. As indicated in the manuscript one of the undelivered subjects subsequently delivered preterm after her assessment. Obviously, it would be inappropriate for her to remain a control subject and we felt that the least potentially biased decision was to include her in the analysis as a control. This decision was taken before any analysis of our data or any review of this subjects examination and enzyme levels. With regard to the blinding, we are confident that the examiner was completely blinded to whether post partum subjects were cases or controls. We admit that the examiner may have been able to deduce the difference between undelivered controls and the post partum subjects (although many postpartum subjects would look similar to the undelivered subjects due to the usual delay in involution of the uterus post partum.) Therefore, as requested we have repeated our adjusted analysis separately for the two control groups Page10 LINE 8-9. However, as this additional data distracts from our primary apriori analysis and was not requested by the other reviewers we are leaving this section as “data not shown” but we are happy to make this analysis available on request.

With the undelivered controls only: OR=2.280 (0.468,11.10) With the postpartum controls only: OR=1.440 (0.22,9.38). Therefore, an extent severity score of (3,5) was not associated with premature delivery with analysis of each control group separately. (It may seem initially odd that with the control groups considered separately, the point estimates become positive our biostatistician has offered the following explanation: In this case, the change in sign can be attributed to multicollinearity, as evidenced by the very wide confidence intervals.)
However, we do not feel it is at all necessary to re-analyze the GCF enzyme data with the control groups separately as those performing the measurement (Dr. Cox and his assistants) were completely blinded to the patients group.

Comment 4: we have removed the inaccurate and contradictory statement on page 9.

Comment 5: In our discussion we think we are very cautious about interpreting our results. The reviewer’s statement that unlike in non-pregnant patients GCF enzymes may not be as predictive in predicting attachment loss may be correct but is pure speculation given the current state of the literature. On the other hand as several studies have documented a significant amount of attachment loss during pregnancy it is just as likely that they are highly accurate or even more so than in non pregnant patients. Finally, although it is possible the elevation of GCF enzymes may be due only due to hormonal changes in pregnancy this is again only speculative and as all our patients were pregnant, or recently so, it is difficult to see how this would account for our results.

Comment 6: The p values are recalculated in table 1 and 2 as requested using a Fisher’s exact test. As expected as the Fisher’s exact is a more conservative test most of the p values are slightly larger.

Additional minor comments: We thank the reviewer for his careful review of the manuscript and have made the changes as suggested to improve clarity.

Reviewer 2. Goepfert AR

Comment 1: As suggested we have included the reference to the reviewer’s study in the discussion, page 12 line 22. Although this study was much more rigorous than many previous studies, and focused on spontaneous preterm births and not an “amalgamated outcome” we still feel that variation in what is defined as the primary outcome may explain the variation seen in the literature. We of course, did not include this study as an example of studies that used an amalgamated outcome.

Comment 2: Additional information provided as requested page 8 line 21-22.

Comment 3: We did anticipate controlling for race as the majority of our population was/is Caucasian with no other preponderant racial group. Therefore, we did not feel control for this variable would be possible. We have provided data on our underlying population in the revised manuscript, page 4 line 1-3. Additionally, as the reviewer points out black race is associated with an increased risk of attachment loss and prematurity and therefore it can cause bias by increasing the proportion of subjects in the case group with attachment loss. As we did not find an association between case status and attachment loss this was unlikely to account for our results. Finally, our local population is made up of a very small proportion of black patients (1.5%) Also we feel it is worth considering that analysis controlling for race as not been performed in all similar studies in the literature 1-3.
Minor Essential revisions
2. revised as suggested.

Reviewer 3.

1. Made change as for Reviewer 1 comment 4.

Additional changes: One of our co-authors pointed out an error in the units of measurement for Figure 2. This has been corrected but the figure itself is unchanged.

Reference List

