Reviewer's report

Title: Smoking during Pregnancy and Risk of Abnormal Glucose Tolerance: A Prospective Cohort Study

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Reviewer: J Liu

Reviewer's report:

The authors used the data from a prospective cohort of 1,006 Hispanic pregnant women to examine the association between smoking during pregnancy and risk of abnormal glucose tolerance (AGT). The smoking status was self-reported by the respondents at recruitment (mean=15 weeks) and mid-pregnancy (mean=28 weeks). The outcome AGT was defined as >135 mg/dL on the routine 1-hour glucose tolerance test. The study found that women who smoked 0-9 cigarettes/day before pregnancy had an increased risk of AGT compared to the non-smokers after adjusting for age. The relationship was insignificant after additional adjustment of BMI, gestational weight gain (GWG), parity and education. Smoking in early and mid pregnancy was not associated with AGT. Quitters were about twice as likely to develop AGT compared to continued smokers but this association became insignificant after adjusting for GWG and other risk factors. The authors concluded that their findings do not support an association between smoking during pregnancy and AGT. Pre-pregnancy smokers who quit during pregnancy may have increased risk of AGT. Here are some comments and suggestions for its further improvement.

1. It would be useful to provide a flow chart to describe sample attrition process for the study. It is not clear why sample sizes for Table 2 were different from the statement "...a final sample size of 1,006 participants" (p5). If this is due to missing measurements at different visits, please specify. It is not clear why the sample size for pre-pregnancy and early pregnancy were different given that the information was collected at one time (first study visit).

2. Related to comment 1, due to various sample sizes for the analysis, it is hard to make comparison about the effects of smoking status on AGT at different time points. The authors only compared the characteristics of the sample of 1006 women who were screened for GDM with those who did not screened for GDM. In fact, due to the different sample sizes for different analysis, it is necessary to compare the differences between analytical samples as well.

3. I also noticed that the study may have limited power to detect the effect of light (0-9 cigarettes) and heavy smoking (>=10
cigarettes/day) on AGT (<10 AGT women in those categories per Table 2).
I wonder whether the authors have considered to categorize the smoking patterns in the following way: 1) non-smokers (never smoked in pre, early-, mid-pregnancy); 2) persistent smokers (smoked in all periods),
3) quitters (those who quitted smoking after pregnancy). This coding might be useful for you to do a unified analysis using all information available to you (~1,006 women). If a woman who has missing values in smoking status in early or mid-pregnancy, you will use whatever information is available to you to determine whether she is a smoker or quitters... You may need to consider how to code those weird smoking patterns (such as women might start to smoking during pregnancy) based on their answer etc.. The similar method of studying smoking patterns using PRAMS-questionnaire was used in prior study (Liu J. 2006, Am J of Public Health). If you have adequate sample size, you might consider to split category 3 into (early quitters, those who quit in early preg, mid quitters, those who quit in mid-pregnancy).
4. Re. the analysis, the authors stated the attenuation of the effects might be caused by gestational weight gain. This was not fully supported by the results presented because you did age-adjusted analysis first, then you adjusted multiple variables (GWG, parity, BMI, education) simultaneously. Thus, it would be useful to present a separate model to show the estimate was significant after adjusting for parity, BMI, education and it became insignificant after adjusting for GWG... This applied to all types of models presented in Table 2 and 3.
Per your results, GWG seems not different by AGT status. However, is GWG different by smoking status?
5. Authors may consider adding justification on why they selected AGT as the outcome instead of GDM, given that GDM is the focus of the main study. How did they decide the cut-off points of 135? Did the authors consider to use glucose as a continuous variable instead of a categorical AGT?
6. No information was provided on how quartiles of pregnancy physical activity were developed.
7. According to citation 9 (review article), it seems that more studies were published on this association in addition to what were cited in this article (#10-15).

1. Is the question posed by the authors well defined?
Yes, the study question is well defined although there is a need to justify why they studied abnormal glucose tolerance instead of GDM.
2. Are the methods appropriate and well described?
The methods are appropriate in general. However, they need to address some analytic issues suggested by the reviewer.

3. Are the data sound?
The data seem lack of power to detect the dose-response effect of smoking during pregnancy. It is confusing that multiple sample sizes were used for various analyses presented in the paper.

4. Does the manuscript adhere to the relevant standards for reporting and data deposition?
The manuscript needs more details about why and how analytical sample sizes were derived.

5. Are the discussion and conclusions well balanced and adequately supported by the data?
The discussion and conclusions the role of gestational weight gain in the association of interest are not supported by the data.

6. Are limitations of the work clearly stated?
Yes.

7. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished?
No. there are more studies to be cited related to this topic.

8. Do the title and abstract accurately convey what has been found?
Yes

9. Is the writing acceptable?
Yes

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.