Reviewer’s report

Title: Age at Menarche and Risk of Gestational Diabetes Mellitus: A Population-Based Study in Xiamen, China

Version: 0 Date: 03 Dec 2018

Reviewer: Clive Petry

Reviewer's report:

GENERAL COMMENT

Although this manuscript is not without interest as is, as such a large cohort is studied the way that the data is analysed could be improved whilst maintaining the ability to have plenty of statistical power. This could enhance the likely interest in and impact of the manuscript.

SPECIFIC COMMENTS

1. The cited literature in this area is incomplete at present.

2. Please comment on the fact that the average AAM is higher in this population than in many of the published studies in this area.

3. Please comment on how AAM was originally collected for the database.

4. Given that the cohort that was studied was so large, why was the age at menarche (AAM) studied as an ordinal rather than a continuous variable? I think that it would have been much more interesting to use it as a continuous variable and to be able to judge the presence or absence of any non-linearity etc.

5. There have been 3 recent systematic reviews and meta-analyses published in this area. One of them used a dose response approach and, as well as a linear negative association between AAM and GDM risk, also found a significant non-linear term (due to a slight u-shaped curve in the association between AAM and GDM risk). To be able to analyse these in the present data the AAM would have to be analysed as a continuous variable by polynomial logistic regression. Does this population show a (slight) increased risk of GDM in women with a late AAM? It would be worth commenting on.
6. One recently published study already showed a negative linear association between AAM and OGTT 60 minute glucose concentrations in pregnancy. This needs acknowledging.

7. In the confounder analyses, the statistical models of the associations between AAM and both GDM risk and OGTT fasting glucose concentrations lost significance when adjusted for maternal age, BMI and blood pressure (as well as educational level, family history of diabetes, and hepatitis B surface antigen in some circumstances). However it is not appropriate to adjust for BMI as many publications have already published strong associations between AAM and BMI in adult life. Negative associations have also been published between AAM and risk of pre-eclampsia in pregnancy, so adjusting for pregnancy blood pressures may also not be appropriate. Both increased BMI and blood pressures are likely to be associated with insulin resistance in pregnancy which has also been shown to be negatively associated with AAM. This needs careful discussion.

8. The BMIs of the study cohort are very low (at least by Western standards) and so the results may be less relevant to non-Asian populations (and vice versa). The “low” BMIs may explain why the effect sizes in this study are so much smaller than has been observed in other studies. It would be worth discussing this point.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics
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