Reviewer's report

Title: Frequency and risk factors for recurrent gestational diabetes mellitus in primiparous women: a case control study

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Reviewer: Barbara Daly

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Review for Journal of BMC Endocrine Disorders (Manuscript BEND-D-18-00127R1)

'Frequency and risk factors for recurrent gestational diabetes mellitus in primipara: a case control study BMC Endocrine Disorders'

General feedback

This manuscript investigated the reoccurrence of gestational diabetes (GDM) in subsequent pregnancies in 142 Chinese women attending an outpatient clinic in Shanghai. The results from this sample of women add an important adjunct to the global body of research on GDM given the unique 'one child policy' in China. Several important issues associated with insulin resistance have been raised in the discussion but these issues need to be considered in turn and logically in relation to insulin resistance. In general the manuscript has been reasonably well written with minor editing required (outlined below).

Abstract:

Methods: Please add study design. Review first sentence for clarity.

Results - add in significant result for first trimester HbA1c. If you have word space also add in results for HDL-C if close to significance in multivariate analysis.

Change 'index' to first or (first or index) for the first time.

Background

Lines 53-55 - Quantify the increase in GDM in Chinese women.

Line 75-76 Rewords sentence and check data - I thought most women only had one child. What proportion have more than one child.
Methods

Please explain how the sample of women were selected. Ie were all pregnant women who presented at the outpatients or medical clinic given an OGTT and all those who tested positive in first and returned with subsequent pregnancy included in the study. What was the total number of pregnant women attending the clinic during the study period. What proportion of women had GDM (first and following). What proportion of women had a second pregnancy?

Clarify details - outlined below.

Lines 87 - 89 - This is this is unclear - reword sentence. I suggest you change primipara to 'women undergoing a first pregnancy'; place quote marks around the name of the hospital and change 'consecutive births' to subsequent births… Clarify if the women were attending the medical centre attached to the hospital or the actual hospital.

Is this a large maternity hospital - does it represent most pregnant women in Shanghai?

Lines 90-93 - This is not clear. My understanding is that 142 women had elevated serum glucose following a OGTT challenge, then 78 women had a recurrent GDM in the subsequent pregnancy and 64 women did not develop GDM in their subsequent pregnancy - but I am unclear! Were all women who developed GDM in their first pregnancy included if they returned with a subsequent pregnancy (during the study period).

Line 99 - Remove 'anyone whose one or more …' - reword this sentence it is not clear!

Lines 112 and 114 - change 'conducted' to examined or analysed or measured!

Remove study design - if this was a case control study you should briefly explain why this design was used. Was this design (and analytical approach) chosen prior to the study? If all first pregnancy GDM women were followed up this would be a 'cohort' study.

Results

Lines 137-140 Move this into the methods section and avoid repetition. See my comment above - you need to clarify the two groups of women in the methods section.

Can you make a comment on the ethnicity of these women - you make reference to 'Asian and Pacific women' but it's important to know the ethnicity of your sample of women.. Did you collect information on ethnicity or can you make a statement that all women or most were Chinese from Shanghai? (Most researchers consider Chinese women 'Northern Asian' and they have a lower prevalence of type 2 diabetes (insulin resistance) than Southern Asian people!)
Line 140 - change to 55% - round percentages in the text for aiding comprehensive.

Tables

Table 1 - the right-hand side of the table is not visible. Ideally there should be a column for p values (or * and a footnote as to which ones are significant) to highlight these variables.

Line 150- add in 'although numbers are too small to detect potential significant differences.

Line 163 - 'Were not'…

Line 165-166 - change 'remarkable' to significantly elevated in women who developed GDM in their subsequent pregnancy compared with women who did not.

Refer to Table 2 in the text.

Table 3 - add in HDL-C or comment on this in the text. Was it close to significance?

Tables - add number of women at the end of each title i.e. (n=142)

Discussion

Line 181 - change 'our' to 'this'.

Line 182 … change 54.9% to 55% and add a phase about the sample i.e. 55% of all women who developed GDM in their first pregnancy who attended the medical centre at … hospital during the study period.

Line 185 - Refer to the ethnicity of your sample of women in context of their risk of GDM - see comment above.

Lines 194-195 - GDM does increase with the number of pregnancies - clarify this point.

Line 196 Avoid referring to women by their ethnicity i.e. state Caucasian women …/ Chinese women

Lines 200-202 - Please write a sentence or two about the women in your sample having a mean 'normal' prepregnancy BMI for Asian women. This is very important in that despite half the women having a BMI <23 they actually developed GDM. They are very susceptible to GDM and type 2 diabetes (later) despite not being overweight or obese! This highlights the difficulty in reducing the prevalence of GDM as more women develop 'western lifestyles' associated with increasing wealth in China and globally.
Line 207 - change 'high' to higher.

Line 209 remove 'Besides'

Line 211 - this is not clear suggest … the severity of hyperglycaemia following an OGTT …

Lines 212 - 214 - can you suggest why FPG was lower in the second GDM pregnancy? Did these women receive any lifestyle advice or were they more likely to be followed up early in pregnancy?

Lines 217-223 - this section is not clear. Be confident in your postulations and reference. It is assume if women are insulin resistance they will have fewer (and less) functional insulin receptors.

Line 226-228 - Triglycerides are also highly predictive of the development type 2 diabetes. This is a hallmark of insulin resistance. Lack of glucose entering adipose cells and ATP --> activates Hormone Sensitive Lipase and increases the section of triglycerides from adipocytes into the serum.

Line 230 - delete 'two'.

Line 229 - It is well accepted that insulin resistance underlies GDM and type 2 diabetes. Perhaps add a sentence explaining that insulin resistance increases in all women during pregnancy to ensure sufficient glucose is transferred through the placenta for fetal growth. However, in women who develop GDM the increase in insulin resistance elevates serum glucose levels that meet diagnostic criteria (or words to this effect). Also link triglycerides levels to insulin resistance (as explained above).

Line 234 You need to reference the association between BMI and triglyceride levels. I would argue that this is not necessarily the case in European women who can carry more body weight but not become insulin resistant. Triglyceride levels are far more strongly associated with insulin resistance. Physical activity also reduces against insulin resistance.

Line 239 - Please review! Elevated serum triglycerides indicate insulin resistance (i.e. lack of glucose into adipose cells) not high dietary fat intake. You can comment of the higher LDL-C level in women with subsequent GDM (but not significant probably due to the small difference and study sample) as this is directly related to dietary saturated fat intake.

Clarify dyslipidaemia and is strong association with insulin resistance and discuss the results in your study in relation to this. Elevated triglycerides and low HDL-C are most strongly predictive of insulin resistance and subsequent development of type 2 diabetes. Your results fit in with this spectrum. In fact your univariate HDL-C levels are almost significantly different.

Line 245 - be specific re cholesterol (which lipoprotein or total).

Line 246 - Remove 'prevent'… reduce
Line 248 - this study…

Line 250 - this is not clear… Pregestational diabetes = type 2 diabetes - rewrite this sentence clearly.

Line 251 - what is common - this is unclear.

Line 252 - however, we excluded

Line 253 delete 'another one is.. Start with 'Missing data for a ??reasonable proportion of women for prepregnancy weight… … self-reporting body weight is less accurate than measurement and recording at the clinic…

Conclusion

Line 259 - …GDM recurred in more than half of the women in their second or subsequent pregnancy …

If HDL is close to significance you could add this in.

I suggest an overall statement in line with your 'novel' along the line of …the dyslipidaemia profile identified in this sample of Chinese women strongly correlates with insulin resistance and the development of subsequent GDM development.

Editing required

Check spacing for in-text citation. Review Journals reference list style.

Line 63 - remove 'pretty'

Line 68 - remove 'racial'

Line 74 - have not instead of haven't

Line 76 Remove 'paid more attention to' … suggest 'documented'

Line 79 - Remove 'on the other hand'.

Line 80 - reword 'provide clues' and 'prevent' (it is impossible to 'prevent' GDM… suggest 'Identify additional modifiable risk factors …

Round percentages in the text (particularly in the discussion) or describe in words i.e. over half of the women in the study sample developed GDM again in their second pregnancy.
Avoid using ethnicity as the 'noun' to describe women i.e. Caucasian women, Chinese women…

Avoid using shortened versions of two words i.e. it is not 'it's' - please check all.

Line 244 - always write in the third person… remove 'we found'

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

Yes

**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.

Yes

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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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