Author's response to reviews

Title: Associations of maternal prepregnancy obesity and excess pregnancy weight gains with adverse pregnancy outcomes and length of hospital stay

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

Subject: Re-submission of article (MS ID: 1202231925528765, correspondent author Abdullah Al Mamun)

Dear Editor(s),

We are writing to thank you for your review to the submission of our article “Associations of maternal pre-pregnancy obesity and excess pregnancy weight gains with adverse pregnancy outcomes and length of hospital stay” manuscript # 1202231925528765. We give a point by point response to reviewer’s comments below and have uploaded a revised version of the paper showing tracked changes. All authors have seen and approved the final version of the paper and we look forward to hearing further from you.

Yours sincerely,

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Response to reviewer 1

Major compulsory revisions

1. One of my major worries is about the generalisability of this study of women delivering almost 30 years ago to outcomes of women giving birth now. The authors acknowledge this as a study limitation, but I feel do not fully discuss differences between their cohort and women delivering today, for example the increased prevalence and degree of obesity, higher proportion of women delivering by caesarean section now.

Response: We agree with the reviewers view and have discussed this further in the discussion section. This part of the discussion now reads as:

"Our data represents the obstetric population of Brisbane in the early 1980's, this may not be representative of today’s obstetric population. In contemporary obstetric populations in industrialised countries including Australia, United Kingdom and the United States of America, short hospital stay (e.g. <48 hours after birth) are recommended for healthy term newborns[1], considerably shorter than the average stay of 4 days in our study population. As expected the prevalence of overweight and obesity for the current obstetric population has increased two to three folds during the last three decades. During the same period cesarean section delivery has increased in the same hospital two to three folds (it was 10.4% in MUSP and now 27%[2]). Despite marked differences in mean length of postnatal hospital stay, prevalence of overweight/obesity and cesarean section delivery in our population compared to contemporary populations, the association of maternal pre-pregnancy BMI with length of stay in hospital and cesarean delivery are similar in MUSP to that of other contemporary
populations[2, 3] suggesting that the association may still be relevant. For instance, when we compared the association of pre-pregnancy obesity with length of hospital stay and cesarean delivery with the recent study by Callaway et al [2] who used obstetric data from 11252 women for the period 1998-2002 from the same hospital in Brisbane, the direction and magnitude of the associations reported are essentially the same in both studies. This suggests that our findings are likely to have relevance for today’s obstetric population.”

2. The authors use the IOM categories throughout, but make no discussion of the derivation of these categories and the criteria used by the IOM to define weight gain as excessive.

Response: We have presented the derivation of the IOM categories in web-based table 1. However, we did not discuss the details of the derivation process and criteria as the IOM have many published articles describing this in detail. However, we have now refereed the recent IOM[4] discussion on their derivation and implications of choosing cut-off.

3. I would like to see a clear power analysis in the methods section; I am concerned that some of the differences that the authors report in their results compared with previous studies may be due to limited study power.

Response: We agree with reviewer that the differences of the prematurity by pre-pregnancy BMI categories are inconsistent with some studies and consistent with others. Recent meta analysis[5] concluded that although the overall risk of preterm birth was similar in overweight and obese women and women of normal weight, the risk of induced preterm birth was increased in overweight and obese women (relative risk 1.30, 95% confidence interval
They also found that after adjusting for publication bias, the risk of preterm birth appeared significantly higher in overweight and obese women (RR 1.24, 1.13 to 1.37). In our study, for a sample size of 6632 and 4% prevalence of prematurity and RR of prematurity among overweight and obese women 1.24 (same as the meta analysis) with 0.05 level of significance, we have 75% power. We did not include this power calculation in the method section because the manuscript is already long (word count ~4000). However, if the editor(s) recommend to add this we are happy to do so.

4. Can the authors discuss the clinical and public health significance of an average increased length of stay of 0.09 days?

Response: For each 100 gm increase of gestational weight gain maternal stay in the hospital increased 0.09 days i.e. mothers will stay 2.2 hours longer in the hospital, which is equivalent to one day longer stay in hospital for every one kg increase of gestational weight gain. Increasing studies suggesting that excess gestational weight gain has a negative impact on both mother and offspring health. From clinical and public health policy perspective, it is imperative to argue that staying one day longer in the hospital increases the health care cost considerably. We have discussed this in the discussion section in the revised manuscript.

5. The first line of the discussion lists a greater risk of pregnancy complications, caesarean delivery and length of stay as significant. However, they demonstrate that after adjusting for the former two factors, length of stay is no longer significant, and I feel this should be clarified in this sentence.
Response: In the revised manuscript we have separately described the results for exposures GWG and pre-pregnancy obesity and further clarified the first line of the discussion.

Minor essential revisions

1. The background section of the abstract is actually the study aims and should be renamed.
Response: We have edited this in the revised manuscript.

2. Some correction of the English is required, for example the first paragraph on page 13.
Response: We have edited the whole manuscript including the first paragraph on page 13 of the original submission.

3. Page 16 consists of one very long paragraph. It would be helpful to break this up.
Response: In the revised manuscript we have divided this long paragraph into three separate paragraphs.

4. Discussion page 16. Might placenta praevia, accrete and previous cesarean delivery be other complications which might result in increased length of stay which the authors did not consider?
Response: We agree with the reviewers view and have considered this in the revised manuscript.

5. Web-table 2 lists classical caesarean section as the mode of delivery for more than 10% of women. Should this read lower segment caesarean section?
Response: In the revised manuscript we changed this to lower segment caesarean delivery.

6. Web-table 3: Is length of stay normally distributed? Are medians and ranges or IQR more appropriate?

Response: The distribution of length of hospital stay followed an approximately normal distribution (results available from author on request). We have stated this in the method section (under statistical analysis).

7. Table 1 and 2 are made unnecessarily complex by the presentation of data on more than one model. Can the authors limit to the fully adjusted model?

Response: We have revised the presentation of the tables 1 and 2. Instead of mentioning multiple models, we have now simplified this by mentioning Age adjusted and fully adjusted associations.

8. Page 18 line 8 should “The relationship between prepregnancy obesity and increased length of hospital stay was fully mediated…”

Response: We have revised this following the reviewer’s comments.
Response to reviewer 2

1. The paper would benefit considerably by keeping a focus on the association between GWG and postnatal stay- given that there is already existing evidence showing a positive association between obesity and delivery outcomes. Indeed, the outcomes specified in the analyses could be potential confounders determining the length of post-natal stay.

Response: We agree with the reviewers comment that there is already existing evidence showing positive association between obesity and delivery outcomes. Pre-pregnancy obesity and delivery outcomes are not the main focus of our study. Our primary focus was gestational weight and its association with delivery outcomes and length of hospital stay. In the introduction we have clearly stated that "We hypothesise that the association between excessive weight gain and postnatal hospital stay will be mediated (and hence attenuate towards the null) by complications of pregnancy and caesarean section delivery". We have revised the introduction of the manuscript and clarified this further.

2. The analysis considered self-reported prepregnancy weight at baseline which might be subject to reporting bias- as women generally tend to underreport their weight even in clinical settings. This is major weakness of this study and should be discussed. Did the study measure women's weight at the time of first antenatal examination?

Response: Women's self-reported pre-pregnancy weight and measured weight at first clinical visit were highly correlated (r=0.95). This indicates that it is unlikely that
women’s pre-pregnancy self-reported weight produced considerable bias in the measurement. In epidemiological settings, measured pre-pregnancy BMI is rarely collected in any of the existing birth cohort studies. In the MUSP the first clinical visit occurred on average at 18 weeks of gestation with a range from 7 weeks to 40 weeks. Because of huge variation of the gestational age at entry into the study, use of the measured weight at entry would highly under estimate the total GWG and over estimate the BMI.

3. I could not follow the logic of estimating the mean difference in birth weight.

Mean difference of which groups? The results discussing the mean difference should be clarified and where appropriate the methodology should be discussed.

Response: These results are from the linear regression analyses. For instance, in the birth weight analysis- birth weight was the dependent (outcome) variable and IOM categories the independent (exposure) variable with adequate category as the reference group. In the linear regression analysis with a categorical exposure like IOM the estimated regression coefficients provide the mean difference of birth weight for IOM categories, typically setting '0' for the reference category which is adequate for this example. We have clarified this in the revised manuscript.

4. The difference in mean postnatal stay for different GWG classifications is not large, except for the obese category. The results are not significant (based on the 95% CIs across groups, as shown in Table 3). This is an important finding and should be made explicit in the paper.
Response: In the age adjusted model (table 3) only pre-pregnancy obese category was positively associated with the mean length of hospital stay (mean difference was 0.30 with 95%CI 0.10, 0.49). When we adjusted for the mediating factors of birth weight and method of delivery this association attenuated (model 4). However, in table 4, for the similar analyses but with IOM categories considered as the exposure, showed that the association remains statistically significant although effect size was small. In the revised manuscript we have further clarified this.

5. The finding that the odds of a preterm birth are lower for prepregnancy obesity and excess weight gain at delivery is bit tricky. Any further explanations?

Response: We agree with the reviewer that the relationship of obesity with prematurity is complicated than we thought. Please see our response to point 3 (reviewer 1) regarding the association of obesity and prematurity. In our study excess weight gain is protective to prematurity mainly because women with normal pre-pregnancy BMI gained more weight during pregnancy than obese women. Again we did not explain this result further in the revised manuscript because of word limitation. However, if the editor(s) suggest adding this, we are happy to do so.

6. Table 1 predicting the odds of delivery outcomes include IOM, prepregnancy BMI and GWG. However, GWG is the difference between prepregnancy BMI and IOM. If this is the case, then the statistical modeling should be revised, also taking into account of potential multicollinearity problems.
**Response:** GWG is the difference between pre-pregnancy weight and highest recorded weight during pregnancy. Please see the derivation of GWG in pages 7 and 8, in the method section. In table 1, IOM and pre-pregnancy BMI were not considered in the same statistical model as IOM categories are derived combining pre-pregnancy BMI and gestational weight gain. We have clarified this further in the revised manuscript.

7. The average days stayed in the hospital is 4.3 days- how did this vary between a normal vaginal and a caesarean section delivery?

**Response:** For normal vaginal delivery the mean length of hospital stay was 4.00 (SD 1.33) days, for caesarean delivery 6.21 (SD 1.58) days and for other types of delivery it was 4.80 (SD 1.55) days. We have now added this result in the revised manuscript.

8. Parity is an important variable missing in the list of confounders- why?

**Response:** We agree with reviewer that parity is a potential confounder in this study. We have added parity in the methodology and repeated the analyses including parity in the adjusted model. Inclusion of parity did not make considerable change in the magnitude of the association that we have presented in the manuscript. This result was not presented in the table but discussed in the method, result and discussion section.

9. Overall CS rate of 11.8% is not high. Has this changed recently? This should be discussed in the concluding section?
Response: We have now discussed this further in the revised manuscript (page 11, first paragraph).

10. Abstract: I could not follow the birth weight data reported in grams. It seems incorrect (birth weight of 206.45 grams?). It is probably the difference in birth weight.

Response: We have edited this in the revised manuscript.

11. Page 8: Explain the IOM categories in the text (reference 26)

Response: Please see our response to R1 point 2.

12. The language and grammar needs attention throughout the manuscript.

Response: While revising the manuscript we have corrected language and grammar throughout the manuscript.
References