Author's response to reviews

Title: Maternal obesity and fetal deaths: results from the Brazilian cross-sectional demographic health survey, 2006

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Author's response to reviews: see over
Dear Dr. Camille Raynes-Greenow,

We are writing regarding the comments and modifications made in the manuscript entitled “Maternal obesity and fetal deaths: results from the Brazilian demographic health survey, 2006” (MS: 318184954946843). First of all, thank you for reviewing our paper. We proceeded with the modifications suggested in order to allow it suitable for publication and the comments on each suggestion and modification made follows below (the responses to the editor comments are in red and bold).

The first modification made was on behalf of the following comment:

1 – The method is well described; however it is difficult to interpret the significance of the results as it is not possible to determine the temporal relationship between BMI and perinatal outcome. This is touched on in the limitations, but I feel that it is a more profound flaw in the methodology and that the conclusion ‘obesity is associated with an increased risk of spontaneous abortion… ’ is not truly justified based on these data – more discussion is required here.

We acknowledge the comment made by the reviewer and agree with the lack of a clear statement in the text regarding the necessity of interpreting our results with cautious, since in this study it is possible that some women could gain weight after the outcome occurrence. Unfortunately pre-pregnancy weight is not available in the DHS dataset. In fact, the use of longitudinal data would be the ideal to investigate these relationships. Even though, this kind of data with representativeness and external generalizability is scarce in low and middle income nations.
This potential methodological flaw is a common aspect in cross-sectional studies. Because we do not have the exact date for the abortion and stillbirth’s occurrence we examined, in additional analysis of the same dataset, if women BM1 changes between the birth index and collection date survey differ in women with live and deceased infants. This analysis shows the BM1 value as a function of time since delivery. After regression analysis we observed weight lost among women whose child died (–0.07 for BM1 and –0.26 for WC for each month elapsed since birth date, p<0.05) and no significant gain or lost among women whose children survived. This shows that the time elapsed between the index birth and survey is not clinically important. This indirectly shows that the participants could not change their BM1 after the occurrence of the outcome, which in this particularly study was children’s death.

Similar argument was used in a paper published with similar hypothesis which also analyzed DHS data, but from a pooled sample of sub-Saharan African countries. The authors tried to overcome this limitation by analyzing if changes in BM1 after birth differed between women who lost their babies and those who did not (Creswell et al., 2012 – Reference number 14).

We believe this could also be evidence towards the consistency of our results. In order to address this topic we have two new paragraph in the discussion section:

As previously reported, longitudinal data on this matter with nationally representative data are scarce, especially in low- and middle-income countries (26).

We recognize that women could gain weight for some reasons other than multiple pregnancies, and this lack of temporal information indicates that our results should be interpreted carefully. Another way to overcome this limitation could be to evaluate whether changes in BM1 after birth differed between women who lost their babies and those who did not (14); however, because of the lack of exact data of the outcome (abortion or stillbirth), we could not perform this evaluation.
The second modification made was in accordance with the following comment:

2. An association between obesity and fetal death has been well established in the literature (although it is acknowledged that this has predominantly been in high-income countries), and therefore for this paper to be of more interest to the reader a point of difference from previous papers needs to be identified. For instance, why were there different findings in relation to the two measures of obesity described (waist circumference and BMI) and the association with early and late fetal deaths.

We agree and we have pointed out this difference more clearly in the text at the end of the last paragraph in the section “Results in the context of other studies”. New text as follows:

These studies corroborate our results, although we found WC to be related more to the occurrence of stillbirths than to BMI.

We also tried to address this difference in the section “Biological plausibility and implications”. Although a clear and well-established explanation is still lacking, there are some evidence that lead us to speculate if the triggers of abdominal obesity and global obesity are different, which could be the reason BMI is more related to abortion and WC to stillbirth, when altered. We believe further investigation is needed in order to better understand the mechanisms involved in these relationships. We have added a phrase and a new paragraph in the discussion section to address this point raised by the reviewer:

This link may be directly related to obesity or to obesity-associated conditions, such as gestational diabetes and hypertensive disorders.

The differential association of the two measures of obesity (BMI and WC) with early and late fetal deaths, respectively, is uncertain. This uncertainty might arise because WC is a more proximate measure of fat accumulation in the abdominal region, indicating a more deleterious form of obesity, a condition that is highly associated with inflammation, insulin resistance and the future development of diabetes (36). Although very speculative, these events may have different triggers.
and stillbirths are more closely related to a pre-diabetes condition while abortions are more closely related to the direct effects of obesity on reproductive function.

Regarding the other comments denoted minor issues:

1. Minor issues re definition: marital status included single, married, widowed and divorced—how were cohabitating couples who were not married classified?

   The cohabitating couples was considered married and are already classified as married in the analysis we have performed. We tried to better address this in the methods section.

2. The meaning of the second half of the first paragraph under Prevalence of abortion and stillbirths is unclear.

   We agree and we fixed the sentence. There were some words missing and exceeding turning it difficult to understand. We rewrote the sentence and we believe it is more reasonable and clear now.

3. Second paragraph of biological plausibility and limitations—the public health implications are mentioned, however an analysis of the literature in how (or how difficult) this can be achieved would add depth to the paper.

   We have added two new paragraph in the discussion section to address this point raised by the reviewer:

   In Brazil, non-communicable diseases have become the most important health problem. Brazil’s Unified Health System (SUS) provides primary health care based on Family Health Programme teams. Improvements in access to integral care towards the prevention of chronic diseases have been observed since its implementation and continuous expansion. Specific programs,
such as smoking cessation, diabetes screening, and the distribution of low cost, generic and even free medications, have already been implemented. Despite these advances, critical aspects of the chronic care model of this program still remain, such as pressure for the incorporation of high complexity care rather than making good use of cost-effective technologies, and the absence of legislative and regulatory norms. Other health professionals, such as nutritionists, physical educators, psychologists, and psychiatrists, should support primary health care teams (37). This initiative could promote physical activity and dietary modifications as a strategy to improve weight control and to avoid postpartum weight retention, consequently preventing maternal obesity.

We would like to inform that all text added or modified in the original manuscript evaluated is highlighted in yellow and two new references were introduced. All authors agree with the points discussed and the new version of the manuscript.

Sincerely yours,

Gustavo Velázquez Meléndez