Reviewer's report

Title: Association between interpregnancy interval and birth weight: what is the role of maternal polyunsaturated fatty acid status?

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Reviewer: Rebecca Merrill

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Review of Manuscript submitted to BMC Pregnancy and Childbirth:

“Association between interpregnancy interval and birth weight: what is the role of maternal polyunsaturated fatty acid status?”

This article explores the association between maternal long-chain polyunsaturated fatty acid (LCPUFA) concentration in early pregnancy, interpregnancy interval (IPI), and pregnancy outcome (birth weight and small for gestational age (SGA)) in a Dutch cohort. The study objectives and the extant data used for the described analyses are well defined. Based on the analytic methods applied, the authors found no strong support for a relationship between a) LCPUFA concentration and IPI nor b) IPI and birth outcome adjusted for LCPUFA status.

Major Compulsory Revisions

1. The calculation of when in gestation the first prenatal care visit occurred is confusing. Could the authors please elaborate on how gestational age was calculated from ultrasound (line 34, page 4)? If the calculation was largely based on an ultrasound early in pregnancy then describe why gestational age at the first prenatal visit was back calculated from the date of birth and gestation at birth. As IPI and SGA are based on gestational age calculations, clarifying the estimation method employed is highly relevant.

2. This reviewer feels that the regression techniques applied could be strengthened to reflect the U shaped association between LCPUFA status and the main outcomes. The authors describe which quintile coefficients were significantly different when compared to the reference LCPUFA quintile but did not fully describe whether other coefficients were different from other quintiles or if there were trends, such as U shaped trends, in the relationship between quintile status and the outcomes. Additionally, the methods descriptions in lines 13 to 16, page 6, are unclear.

3. Which characteristics were found to be significant confounders and which were retained in the final models? Could this information be included in the tables as well as the text when relevant?

4. Based on the analyses presented, this reviewer feels that the comment that there is “no evidence for any important role for maternal EPA, DHA, DGLA or AA concentrations in the association…”, as mentioned in the abstract and similarly
mentioned in lines 1 thru 4 page 10 and lines 28 through 31 page 10, takes the interpretation of the described analysis and associated limitations too far. This reviewer suggests limiting the broadness of the implications and interpretations to reflect the nature of the described study.

Minor Essential Revisions

1. Are the CVs available for the fatty acid analyses? It would be helpful to include that information in the methods section if possible.

2. In the Methods section, line 19, page 5, pre-pregnancy BMI was listed as a co-variable and was later mentioned to be collected by questionnaire. Since BMI may be associated with LCPUFA status and pregnancy outcomes, and thus a confounder, could the authors please elaborate and mention in the text whether this characteristic was included in the regression analyses as well as mentioning the limitations associated with collecting BMI information by recall?

3. Co-variables
a. It was mentioned that smoking and alcohol use were classified as yes/no based on self-report. Since self-report can result in under-reporting and categorizing these exposures as only yes or no is associated with limitations in terms of exploring the effect these may have on the outcomes, could the authors describe these limitations in the Comments section?

b. The authors did not include information on factors such as supplement use in pregnancy or previous pregnancy history, among other factors, which may influence the relationships of interest and may influence LCPUFA status. Were these variables not available? Could the authors elaborate on these limitations in the manuscript?

4. In lines 29 to 31 page 9 the authors mention that “Our results, however, indicate that fatty acid status as measured during pregnancy is not different for women with either short or intermediate interpregnancy intervals.” Where were these data presented in the manuscript? Could a table or figure be included that illustrates LCPUFA status by IPI?

5. In lines 8 and 9, page 10, the authors mention “…the relatively high exclusion rate affected the amount of events in the short interpregnancy interval group..”. Perhaps this aspect of the included vs excluded sample could be mentioned / elaborated in the results section?

6. Table 3:
   a. Could the authors include in the footnote what the SGA “%” column represents. Is this the % of women in the quintile who delivered an SGA infant?
   b. Please correct the interpretation of odds ratio as described in the footnote.

7. Table 4:
   a. What does the “%” column describe for each FA? Please include a definition in the footnotes.
   b. It may be helpful to include the selected quintile for each FA in the column header.
c. Were any confounders included in the final models? Please include adjustment information in the footnotes.

8. Table 5:
   a. When adjusting for LCPUFA status, was only 1 quintile for each FA, the same quintile selected for table 4, included? If so, please elaborate in the footnotes.

Discretionary Revisions

1. Figure 1 could be enhanced by adding in percentages and including a little more information on exclusions.
2. Did the authors investigate the influence of total fatty acid concentration on the associations between IPI and birthweight and SGA?

Minor issues not for publication

1. The writing is strong but could benefit from review by a native English speaker. A few examples are:
   a. Line 5 of the abstract should read “in the association between IPI and birthweight.”
   b. Line 29 of the Introduction, page 2, should read “…and are involved…”
2. The subheadings “Main variables” and “Co-variables” could be changed to more descriptive text such as “Birth outcomes” and “Potential confounders.”
3. Please define acronyms when first used including in the abstract (LCPUFA, ABCD cohort, SGA, etc)
4. The sentence starting with “Characteristics of the included…” in line 13 to 15 page 7 seems out of place.
5. For table 3, it is assumed that 1659 women are included for each Fatty acid and that there are equal numbers of women in each quintile. Therefore the “n” column may not be necessary.

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests