Reviewer’s report

Title: Mediating Role of Arsenic in the Relationship between Diet and Pregnancy Outcomes: Prospective Birth Cohort in Bangladesh

Version: 0 Date: 22 Oct 2018

Reviewer: Anne Bozack

Reviewer's report:

Comments to the authors

This study contributes to epidemiological research regarding the health effects of prenatal As exposure. Building upon previous research identifying positive associations between GA, GWG, and BW and carbohydrate intake, but negative associations with protein, fat, and fiber, this study investigates As as a mediator. The study has the strengths of a large sample size with biomarker and nutritional data. The manuscript could be improved with clarifications in the results and discussion section. Additional sensitivity analyses may provide information about the contribution of micronutrients, if data are available. Grammatical errors should be corrected throughout the manuscript.

Introduction

- Lines 109-11: These references (33-36) do not all include analyses of interactions between arsenic and folate status - please confirm references cited here.
- Lines 114-116: Are there data on As concentrations in these foods? If so, this information should be included.

Methods

- Lines 150-151: Please confirm if the water samples were collected postpartum.
- Lines 162-163: Please describe if health care workers were trained in administering FFQs. Please describe if FFQs were designed to ask about specific time intervals (e.g., month 1, month 2, etc.).
- Lines 169-172: Include p-values for correlations. It is not clear that these correlations were determined previously in FFQ validation - this would be clearer if this sentence were moved to the beginning of the paragraph.
Lines 207-208: Was the correlation between maternal education and income assessed? It may not be necessary to include both of these potential confounders in the model. How were education and income categorized? If categorized as listed in Table 1, it may be more appropriate to combine <25 USD and 25-36 USD due to the small N in the <25 USD category.

Results
- Lines 259-260: Table 3 should be referred to in the first sentence of this paragraph.
- Lines 261-262: Table 4 should be referred to in this sentence.
- Lines 323: What effect size was used for power calculations?
- Were any sensitivity analyses performed controlling for micronutrient intake known to influence As methylation capacity and birth outcomes (e.g., folate and other one-carbon metabolism micronutrients)?
- Were any sensitivity analyses performed controlling for water As as a confounder? Water As may be associated with both toenail As and birth outcomes, acting as a confounder, rather than an effect modifier (as tested for in stratified analyses).

Discussion
- The mean energy intake of 3,049 kcal/day seems high particularly for this region (Table 2). Are there data on potential differential bias in FFQ reporting relative to other confounders (e.g., income, education)? The authors should report if this overestimation is biased by As exposure, birth outcomes, or any confounders.
- Lines 358-360: If the FFQ gathered information on the relative consumption of rice and other grains, please report this data. The association between carbohydrate consumption and birth outcomes is puzzling, and data regarding replacement of rice with other grains would help to explain this observation.
- Were changes in energy and macronutrient intake throughout pregnancy captured by the FFW, or assumed to be constant? If so, the implications of this assumption should be discussed.

Tables and Figures
- Table 1: Want does the subscript 1 refer to within the table? Please report descriptive statistics for energy and macronutrient intake.
- Table 2: Effects significant at 0.05 should be indicated with an asterisk. As written, it is not clear if effects with CIs with lower or upper bounds of 0.0 are significant.
- Table S1: The number 1 should be superscript in the table legend.
- Tables S2-7: P<0.05 should be indicated.
- Figures S1-3: The legend should specify that the numbers in parentheses are SEs.

Level of interest

Please indicate how interesting you found the manuscript:

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Quality of written English

Please indicate the quality of language in the manuscript:

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