Reviewer’s report

Title: Exploring telomere length in mother-newborn pairs in relation to exposure to multiple toxic metals and potential modifying effects of nutritional factors

Version: 0 Date: 12 Nov 2018

Reviewer: Pam Factor-Litvak

Reviewer’s report:

This is an interesting analysis in a small birth cohort in rural Argentina. The authors collected maternal blood/urine, placentae, and cord blood samples in varying degrees and measured relative telomere length (rTL), a variety of nutritional factors and a variety of toxic metals. They then evaluated the associations between these 'exposures' and rTL in each media. I have several comments pertaining to the methods used, and the interpretation of the results.

1. The authors need to discuss the merits of rTL compared to actual TL measured in base pairs using Southern Blot analysis, as there is substantial controversy regarding the reliability of rTL measures. More detail is required on the laboratory QA/QC methods for the rTL measures, especially compared to other established laboratories.

2. I was not sure of the point of the paper. Was it exploratory, to evaluate a multitude of exposures or to evaluate specific hypotheses or to evaluate perhaps mediation of the toxic metal to rTL association by nutritional factors? The authors need to lay out specific hypotheses or indicate that the analysis is exploratory prior to describing the results.

3. Expanding upon comment 2, the authors make quite a number of comparisons. If the point of the study is to explore associations then these need to be adjusted either with a False Discovery Rate or with a Bonferroni correction. If there are specific hypotheses then it is fine to evaluate at p < .05, but please indicate as such.

4. I was concerned that no differences were found between boys and girls for rTL (in cord blood). This is established in the literature (see, e.g. Factor-Litvak, et al). Can the authors give a possible reason why this was not found?

5. Maternal rTL is a strong predictor of child rTL in cord blood and perhaps should be evaluated as a possible covariate in the models.

6. I am also concerned about the very small sample size of the study, and the possibility of selection issues regarding exposure levels.

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.

No

Are the conclusions drawn adequately supported by the data shown?
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No

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