Author’s response to reviews

Title: Maternal socio-demographic and psychological predictors for risk of developmental delays among young children in Mongolia

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Author’s response to reviews:

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RE: BPED-D-17-00033, Maternal socio-demographic and psychological predictors for risk of developmental delays among young children in Mongolia
Dear Dr. Santosh,

Thank you for sending us the comments from the reviewers, and for giving us the opportunity to revise our manuscript. Please find attached the revised version of the above titled manuscript and our response to the reviewers.

We have responded to the reviewers’ comments below and highlighted our changes in the revised manuscript in gray.

Thank you for your consideration of our revised manuscript. We look forward to hearing from you in due course.

Sincerely,

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RESPONSE TO THE REVIEWERS

Manuscript ID BPED-D-17-00033

Sincerest thanks for reviewers’ comments on our manuscript. We have modified the paper in response to the extensive and insightful reviewer comments.

RESPONSE TO REVIEWER Dr. Antony Simon Opwora

1. Comment: Methods - Exposure and outcome - 3rd paragraph:

It appears that information on jaundice was collected for siblings at baseline and also the transcutaneous bilirubin level was measured in the index child for the first six days. At follow-up however, information on the history of jaundice is obtained through a questionnaire administered
to the mother. It is not clear whether this information at follow up is specific to the index child or any child in the family. The mother could recall presence of jaundice in any of her children.

Response: Transcutaneous bilirubin was measured in all children at 6 – 144 hours postpartum. In our model, we used this variable as hyperbilirubinemia. At follow-up, all the questions relating to child health conditions were specific to the index child. We clarified this in paragraph 3 of exposure and outcome as follows.

“The questionnaire was divided into two parts and assessed maternal characteristics in terms of socioeconomic status and health (health behavior, history of neonatal jaundice, breastfeeding practices, and disease history) specific to the index child.”

2. Comment: Also, if this information is obtained a year or 2 later, there is a risk that the mother may not remember. Furthermore, the importance of this question in the maternal questionnaire is doubtful as it could be obtained more reliably from the baseline data (and therefore avoids recall bias). Kindly clarify this information.

Response: We agree that the history of jaundice collected later would be subject to recall bias as compared to the baseline data, and it was not necessary because we had data on measured transcutaneous bilirubin level from the baseline survey. Moreover, other health conditions in the children may also have been subject to recall. Thus we added following point in paragraph 5 of the discussion section.

“Third, the health condition of the children, including history of jaundice was obtained 1-2 years after birth thus introducing the possibility of recall bias.”

3. Comment: Methods - Exposure and outcome - 4th paragraph:

Was the information on asset ownership collected at baseline or at follow-up? Was there any accounting for the possibility in change of economic status between baseline and follow-up? This information, though not perceived by the child could affect their risk for developmental delay.

Response: We have tried to reflect the most recent economic status of the family in our analysis. Therefore, information on economic status was collected at follow-up. We added this in the paragraph.

“Economic status was assessed using data on asset ownership and household characteristics at follow-up and a wealth index was constructed from the data using principal components analysis [1].”
It is true that children may not know that economic status of their household has changed, but it can affect developmental delay. We also agree with the point that economic status change between baseline and follow-up should be taken into account. However, as baseline data did not include this information, we have acknowledged this as a study limitation in the Discussion section.

“First, factors that change with family situation such as home environment, changing economic status, cognitive stimulation in the home, and family structure change could not be included in our study.”

4. Comment: Methods - Statistical analysis - 2nd paragraph:

The authors state that they compared the characteristics of the children enrolled in the follow-up study to those of the "rest of the cohort". I find this comparison disturbing because first, it implies the "rest of the cohort" was under study for data presented in this paper. Secondly, if comparison is to be made, the study will need to change its name and methodology to incorporate the comparative aspect. However, no data was collected at follow-up for the "rest of the cohort" to make that comparison meaningful. Authors need to either cut out this part of the information or incorporate new data to justify the mention of this in the methods. The authors are nevertheless advised that there is a possibility of mentioning this information in the discussion section to prove or make a point about the strength (or weakness) of the study.

Response: Your point is well taken, and we have removed the analysis comparing the baseline characteristics of the study participants to the rest of the cohort.

We have also revised the Results section accordingly.

As advised we added this point in Discussion section along with strength of study as follows.

“To the best of our knowledge, this is the first study conducted in Mongolia assessing maternal socio-demographic and psychological risk factors related to young child development in Mongolia. We also examined the influence of hyperbilirubinemia on child development using the first country-specific validated screening tool to assess child development. Although the study did not include all the children from the baseline study, our study population was shown to be representative when we compared the characteristic of the study population to the rest of the cohort that did not participate in this study.”

5. Comment: Results - 2nd paragraph:

Please refer to comment #3 above. The information needs to be edited accordingly. Additionally, reference is made to Table 1, which should also be edited accordingly.
Response: We have revised the information in the 2nd paragraph of the results section and table 1 accordingly.

6. Comment: Results - 3rd paragraph:

Please include the lower limit for the definition of "moderate hyperbilirubinemia".

Response: Moderate hyperbilirubinemia is defined as serum bilirubin concentration of 10-20 mg/dl [2], therefore the lower limit of moderate hyperbilirubinemia is 10 mg/dl. This is described in 4th paragraph of the Background section, when “moderate hyperbilirubinemia” appears for the first time in the manuscript.

Thank you for noticing our error in the results section. It should have been the greater than (>) sign instead of less than (<) sign. We have revised the results section as follows:

“Seven (4.7%) children in our study were born preterm, 95 (63.3%) were scored <7 for 1 minute Apgar score, and 105 (70%) had moderate hyperbilirubinemia (transcutaneous bilirubin level of >10mg/dl) at birth.”

7. Comment: Results - 5th paragraph:

Please clarify the direction and significance of age as a risk factor for developmental delay (i.e. is it maternal or child's age and was the association related to increasing or decreasing age?)

Response: This has been clarified as follows.

“Other predictors associated with risk for developmental delays were gender being female (AOR- 0.25; 95% CI [0.06-1.00]); and increasing maternal age (AOR- 1.12; 95%CI [0.98-1.27])”

8. Comment: Discussion - 3rd paragraph:

Please correct the typo in sentence 2.

Response: The typo has been revised accordingly as follows.

Notwithstanding, this finding is important given that child rearing practices could be affected by maternal depression [3].
9. Comment: Discussion - 3rd paragraph, last sentence:

It would be interesting to read about the authors' postulations about preventive interventions for maternal depression that "may enhance not only improvement in young child development, but also influence school achievement during adolescence."

Response: Following the reviewer’s comment, we have suggested the influence preventive interventions may have on child development and school achievements as discussed in paragraph 3 of the Discussion section as follows:

“For example, early parenting programs are reported to improve parental responses [4-6] and lead to increase in the abilities of depressed mothers to support their child’s executive functions which controls and regulates a child’s thoughts and behaviors [7, 8].”

10. Comment: Table 1

Please edit based on comment #3 above. Also, the Title label could be more specific, thus "Characteristics of child and mother at birth", and similarly for Table 2.

Response: Tables have been revised accordingly and titles of Table 1 and Table 2 were changed.

RESPONSE TO REVIEWER Dr. Judi Mesman

1. Comment: Most importantly, the sample size is too small for analyses on a problem that is not highly prevalent, with only 17 children in the sample at risk for developmental delay. Analyzing the characteristics of only 17 infants on so many variables can simply not yield enough robust and reliable information on risk factors for developmental delays.

Response: We thank the reviewer for the comments, as well as acknowledge that our sample size may have been small. However, the sample size used in this study was calculated based on robust methods from a previous study [9]. The calculation was performed using formula below:

\[ n = \frac{2SD^2(Z\alpha/2 + Z\beta)^2}{d^2} \]

where SD- standard deviation from previously published population based study[10],

\[ Z\alpha/2 = 1.96 \] from Z table at type 1 error of 5%,

\[ Z\beta = 0.842 \] from Z table at 80% power

d- effect size
Further, as described in the Statistical analysis section, sample size for this study was estimated assuming a MORBAS score standard deviation of 3.0 [10], significance level of $\alpha=0.05$ using two-sided test with power of 80% ($\beta=0.20$) and an effect size of $d=1.5$ [11]. Under these assumptions, a total sample size of $n=128$ was required to detect differences in the risk for developmental delay. Our final sample size was 150 children anticipating a 15% attrition rate. We have included the references supporting the methods used for arriving at the sample size in the corresponding parts of the manuscript.

Regarding our result for children at risk of developmental delay, we modeled our statistical analysis at baseline and follow-up. Details are explained in response to comment 3.

2. Comment: Another issue is the conception of the variables and models. The Introduction broadly mentions biological and psychosocial factors and then seemingly randomly discusses a few, whereas many other potentially relevant variables are left out. It is unclear why these risk factors were chosen out of the multitude of potential variables. There is no clear theoretical model guiding these choices, so that the reader is left with a list of predictors that could also have looked very different, but without knowing why. It would be important to provide a clear theoretical framework to remedy this.

Response: Given that our study was conducted in a developing country, the main conceptual framework is based on the framework proposed by Walker et al. Lancet. 2007 [12] series on child development risk factors in developing countries. As stated in this series, risk factors for child developmental delays can be divided into biological and psychosocial factors [12]. But the framework includes only modifiable risk factors which can be influenced through interventions or public policy. We added this into the Background as follows.

“Given that our study was conducted in a developing country, the main conceptual framework is based on the framework proposed by the Walker et al on child development risk factors in developing countries [12]. This framework includes only modifiable risk factors which can be influenced through interventions or public policy.”

Figure 1. Pathways from poverty to poor child development (The figure included in the response letter as a supplementary file)

Using this framework, we made effort to include the main factors from each of the domains. For socio-cultural risk factors, we included child gender and maternal education to reflect gender inequity and low maternal education. While among biological risks factors, we included variables representing prenatal and postnatal growth such as delivery mode, gestational age at birth, birthweight, apgar score, transcutaenous bilirubin level, season of birth and exclusive breastfeeding. Biological factors specific to the mother were parity, history of miscarriage, and disease during pregnancy. For psychosocial risks factors, we included environmental and
parenting factors such as family crowding, maternal work, single mother household and maternal depression symptoms. Impairment in child development was thereafter assessed in seven child developmental domains.

However, we agree that many other potentially relevant variables such as reduced access to services, nutrient deficiencies, environmental toxins, and maternal exposure to violence are not considered and acknowledge these as our study limitation. To address these changes in the manuscript, we have revised the Discussion section including the limitation stated above as follows:

“Second, other potentially relevant variables such as reduced access to services, nutrient deficiencies, environmental toxins, and maternal exposure to violence were not considered.”

3. Comment: If I understand correctly, the authors tested two cross-sectional models: one with baseline predictors in relation to baseline risk for developmental delays and one with follow-up predictors of follow-up risk for developmental delays. I would have expected to see longitudinal analyses.

Response: Thank you for addressing this important point. As noted in your previous comment 1, we collected many variables, but we have only 17 children with the outcome of interest. This situation made us to systematically model our analyses using two models: one with the baseline predictors in relation to risk of developmental delay at follow-up and the other with predictors collected at follow-up for risk of developmental delays at follow-up. Therefore, our longitudinal analysis result is shown in Table 3, which included risk factors from baseline and outcome at follow-up. Whereas, we agree that Table 4 shows the cross-sectional result only for predictors collected at follow-up.

4. Comment: A few other issues:

- The manuscript needs to be edited in terms of wording and grammar.

Response: Thank you for suggestion. A native English language speaker has edited the entire manuscript.

5. Comment: It is unclear how the sample drawn from the larger sample was selected.

Response: We have described the methods used for drawing the sample from the larger cohort under Statistical analysis in the Methods section as follows.
“We randomly selected mother/child dyads from the baseline sample of 1297 women. Telephone calls were made to randomly selected numbers. Of the 1297 eligible women, 344 women could not be reached on phone due to connection error. Additionally, phone numbers provided by 248 women were no longer in use and 53 women declined to participate in the study before we reached the desired sample size.”

6. Comment: P12: the covariates might be better framed as predictors, since they constitute substantive variables with complex relations to the outcome variable.

Response: This has been revised.

7. Comment: There are a lot of predictors for a relatively small sample size. Could looking at composites be better? Maybe more robust as predictors?

Response: We agree that there are many predictors for a relatively small sample size.

We made a composite score for wealth index. The wealth index was constructed from the data on asset ownership and household characteristics using principal components analysis and has been described under Exposure and outcome in the Methods section.

In addition, as we said earlier in the response to comment 3, we created two models to take all the predictors into account in systematic manner.

Thank you for the suggestion. All the explanatory variables in our study have now been referred to as predictors.

We thank all the reviewers for their insightful comments for improving the quality and content of our manuscript.

References


