**Author’s response to reviews**

**Title:** Functional constipation in infancy and early childhood: Epidemiology, Risk Factors, and Healthcare Consultation

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**Version:** 1  **Date:** 04 May 2019

**Author’s response to reviews:**

*The answers are also added as a separate word document*

Comments from the second revision:

(Comments and answers from the first revision are added at the end of this document.)

Comment 15:

Editor Comments:

1) Under the heading “Ethics approval and consent to participate” in the Declarations please include the reference number for the ethical approval.

Answer:

The Sri Lankan college of Pediatricians gave approval for the study. The reference number was SLCP/ERC/2014/12.
BMC Pediatrics operates a policy of open peer review, which means that you will be able to see the names of the reviewers who provided the reports via the online peer review system. We encourage you to also view the reports there, via the action links on the left-hand side of the page, to see the names of the reviewers.

Reviewer 1: Ana Rita Goes:

Reviewer reports:
Ana Rita Goes (Reviewer 1): The authors made a clear effort to answer to the presented concerns. I keep some concerns/suggestions regarding the present paper:

Comment 16:
INTRO: "The authors are invited to present the arguments underlying the risk factors explored." The authors made a good job establishing the rational for the risk factors explored, which almost dismisses the need to justify the participants age groups in the methods. If they include in the intro all the risks being considered for each age group, that information will no longer be necessary at the methods.

Answer:
We thank the reviewer for this suggestion and transferred this information from the methods to the introduction.

Comment 17 (related to comment 7):
METHODS - Measures: "Please clarify how the assessment of psychosocial risk factors was done. You have included several sensitive variables and the way you collected these data may interfere with the results." The authors made a clarification in the answers file, but there is still no information about this within the methods section. I suggest they add some information on this subject (the specific variables collected) when describing the data collection tool.

Answer:
We added this information to the method section. (Please see line 161-165.)
Comment 18:

In addition, the structure of the questionnaire presented in additional file 1 is not totally consistent with the description at the methods.

Answer:

The method section is now consistent with the questionnaire. (Line 142-166.)

Comment 19 (related to comment 8):

METHODS - Measures: "Please clarify what was understood as "toilet training" as a behavioral intervention" My concern did not intend to question toilet training as a therapeutic intervention. Instead, I was only wondering how did the authors conclude that the child received that intervention because it seemed unlikely to me that the parents could distinguish general counseling on toilet training from a real behavioral intervention. In my opinion, considering the questions from the questionnaire, the authors should name it only as advice/counseling on toilet training - it seems to me that there is not enough information to name it behavioral intervention.

Answer

We agree with the reviewer that there is not enough information to name it behavioral intervention. Consequently we changed the wording as suggested by the reviewer into non-pharmacological intervention.

Comment 20:

METHODS - Measures - ADDITIONAL COMMENT: I also suggest that information on the kind of interventions explored through the questionnaire be added in the description of the data collection tool.

Answer:

We added this information to the manuscript (line 155-157).
Comment 21:

RESULTS - ADDITIONAL COMMENT: Suggest the authors make a revision on the tables (1, 2, 3) absolute and relative frequencies because there seems to be several mistakes.

Answer:

We thank the reviewer for the comment. Table 2 has been recalculated. The numbers in table 1 and 3 seem correct.

Comment 22:

RESULTS - ADDITIONAL COMMENT: Considering the kind of questions included in the questionnaire, it seems abusive to me to call behavior modification to interventions that may have been restricted to information giving regarding toilet training.

Answer:

We agree with the reviewer.

Reviewer 2: Soraia Tahan


Theme: relevant, considering few studies in the literature in this age group.

Title: suitable to the proposal.

Background: suitable.

Casuistic: the study has a sample size adequate.
Comment 23:

Methods:

The description of the nutritional assessment was not clear. Which curves were used?

"All children born in Sri Lanka receive a Child Health Development Record (CHDR), which is regularly filled by trained nurses. One section of the CHDR is devoted to growth monitoring and gives an idea about the growth of the child by serial recording of the weigh. The child is classified as having overweight (>2SD), normal weight or being underweight (<2SD). Mothers were helped by the research assistants to select the appropriate answer regarding the growth of the child."

Answer:

We used the different curves (growth patterns) to find an association between constipation and growth. A reference was added. Please see method section, line 143-159.

Comment 24:

The authors did not describe which methodology they used to evaluate about stressful life events such as physical and psychological violence in children and mother. These questions are very complex to evaluate and accurate diagnosis. There were used any standardized questionnaires?

Answer:

Several studies conducted in Sri Lanka previously assessed the association between functional gastrointestinal disorders and abuse in teenagers.

We used a standard questionnaire in these studies. The questions are rephrased directly from the questionnaire used for those studies.
Following references were added to the method section (line 163):


Comment 25:

What is the basis for choosing these social indicators? (Income meets essential; Family has loans; Relationship between parents; Change place of residence).

Answer:

This is described in the introduction. (Line 100-104.)
Comment 26:
Results: interesting and well described.
Answer:
Thank you.

Comment 27:
Discussion:
I suggest adding the article cited below* in your literature and discussion. The authors evaluated the prevalence of constipation in children who attended day care centers in Korea and found a prevalence of 8.5%. This index is very close to the prevalence of constipation found in your research, although in the Koreans study other risk factors were evaluated.


Answer:
We thank the reviewer for the reference. We added this article to our discussion.

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First revision:

Reviewer comments and answers
Reviewer reports:

Comment 1
Ana Rita Goes (Reviewer 1): In this manuscript, the authors examined functional constipation in Sri Lanka. The paper focus a highly relevant issue, considering the multidimensional impact of this disorder.
Answer
Thank you
My comments and concerns are presented below:

Comment 2
GENERAL: I suggest a revision of the English and also of some terms (e.g., pp 11, ln 199: the term correlated probably should be replaced by associated)
Answer
The manuscript was edited by an expert in English, who is one of the joint editors of the Sri Lanka Journal of Child Health and section editor of the Ceylon Medical Journal and the mistakes were corrected. The specific error pointed out by the reviewer was also corrected.

Comment 3
INTRO: The authors are invited to present the arguments underlying the risk factors explored.
Answer
We agree with the reviewer and added a paragraph to the introduction on risk factors.

Comment 4
METHODS - Participants: Toddlerhood is usually understood as the period form 12 to 36 months.
Answer
We thank the reviewer for pointing out our mistake. It was corrected in the revised manuscript.

Comment 5
METHODS - Participants: The authors are urged to justify the participants age groups, considering that during the selected period children should complete toilet training and functional constipation may develop a different presentation, including soiling.
Answer
A justification was added to the method section for selecting specific age groups.
Comment 6

METHODS - Questionnaire: Please clarify how parents filled out "a question to identify the growth pattern of the child" (Pp 9, ln 30-31). Considering parents' health literacy levels, was it feasible to ask them to select a growth curve?

Answer

We would again like to thank the reviewer for pointing out this important issue. We agree with the reviewer that parents only have a vague idea about interpretation of the growth chart. Once the parent of the child completed the questionnaire, the researchers collected the questionnaire and the child health development record of the child, checked the growth pattern, selected the appropriate answer and helped the mother/father to enter that answer into the questionnaire. A few sentences were added briefly describing this point. (line 143-149)

Comment 7

METHODS - Measures: Please clarify how the assessment of psychosocial risk factors. You have included several sensitive variables and the way you collected these data may interfere with the results.

Answer

Our data collection tool included several stressful life events that could be faced by families. They include, exposure of mother or child to physical or psychological abuse, economic strains faced by the families and change in residence. We fully agree with the reviewer that some of these questions are sensitive questions. However, none of the parents refused to answer the questionnaire. The questions were phrased in very simple language so that there could be no confusion with regards to understanding. However, as any other questionnaire based study, we had to depend on parents to divulge the information. A statement on this was included in the section of limitations.
Comment 8

METHODS - Measures: Please clarify what was understood as "toilet training" as a behavioral intervention

Answer

Toilet training is one of the cornerstones of therapy in young children with FC. It is extremely difficult to achieve a sustainable therapeutic efficacy of any drug without toilet training. It is a well-recognised mode of behavioral interventions in the ESPGHAN and NASPGHAN guideline released by experts on constipation [1].

We have changed the word ‘behavioral intervention’ into non-pharmacological modification.


Comment 9

METHODS - Statistics: It is not clear how was the regression performed.

Answer

We thank the reviewer for this comment. Details were included in the statistics section of the methods. (line 197-204)

Comment 10

RESULTS: considering that the diagnostic of functional constipation may represent different clinical presentations, I would suggest the authors to present some descriptive data concerning children's bowel's habits and ROME III diagnostic criteria.

Answer

We agree with the reviewer and therefore we inserted another table to show the prevalence of diagnostic criteria we used to define functional constipation. However, description of bowel habits would be of out of the scope of this manuscript and will unnecessarily lengthen the article and dilute our message. Please find the additional data in the additionally added table 2 in the manuscript and below.
Table 2: Descriptive data of bowel habits of children with FC

<table>
<thead>
<tr>
<th>Diagnostic criteria of FC</th>
<th>FC n (%)</th>
<th>Controls n (%)</th>
<th>p-values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Two or fewer defecations per week</td>
<td>22 (25)</td>
<td>8 (0.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>At least one episode/week of incontinence after acquisition of toileting skills</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>-</td>
</tr>
<tr>
<td>History of excessive stool retention</td>
<td>28 (32)</td>
<td>7 (0.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>History of painful or hard bowel movements</td>
<td>84 (94)</td>
<td>204 (20)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>History of large diameter stools which may obstruct the toilet.</td>
<td>58 (66)</td>
<td>30 (34)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Comment 11

RESULTS: The higher prevalence in older children that were probably already toilet trained reinforces my concerns regarding the age groups and the need to analyze them in separate.

Answer

In this case we disagree with the reviewer, the number of patients with constipation in the different age groups is too small to draw firm conclusions.

Comment 12

RESULTS: Regarding the healthcare data, it would be interesting to have interventions considered by age groups and eventually splitting the children by toilet training status. Regarding children already toilet trained, it would be interesting to examine interventions considering the presence of soiling.

Answer

Only 47 children have sought healthcare for their symptoms. This is a very small number to be categorized as suggested by the reviewer. However, we included a separate table as the reviewer requested. The prevalence of soiling (fecal incontinence) was 0% in our cohort, therefore examining interventions considering soiling will not provide interesting data.
Table 5: Children suffering constipation clustered by age in months (n (%))

N (%) receiving treatment and the number toilet trained

<table>
<thead>
<tr>
<th>Age (months)</th>
<th>6.5 – 12</th>
<th>13 - 24</th>
<th>25 – 36</th>
<th>37 - 49</th>
</tr>
</thead>
<tbody>
<tr>
<td>Received treatment</td>
<td>18 (38)</td>
<td>10 (21)</td>
<td>6 (13)</td>
<td>13 (28)</td>
</tr>
<tr>
<td>Treatment – dietary</td>
<td>17</td>
<td>9</td>
<td>5</td>
<td>9</td>
</tr>
<tr>
<td>Treatment – behaviour</td>
<td>16</td>
<td>4</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>Treatment – drug</td>
<td>16</td>
<td>4</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>Toilet trained (amongst the ones receiving treatment)</td>
<td>7</td>
<td>4</td>
<td>5</td>
<td>7</td>
</tr>
</tbody>
</table>

Comment 13

DISCUSSION: Regarding the lack of association with psychosocial risk factors, the authors should consider the interference of methodological issues, such as the way by which those factors were assessed.

Answer

We do not think the methodological issues are the only reason for lack of association between stressors faced by children and constipation. In the discussion we clearly elaborated other possible factors related to this phenomenon.

1. Lack of full maturation of the brain-gut axis.

2. The possibility of necessity to have a time lag between exposure to stresses and develop abnormalities in the brain-gut axis strong enough to alter the bowel function leading to constipation.

3. Recall bias in studies involving adults/older children.

The only way to gather information close to the reality regarding stressors faced within the family is to question from a family member as children cannot comprehend the questionnaire. Therefore, we used some questions to gather information in our questionnaire and they were answered by mother/father/caregiver who attend to the clinic with the child. However, addressing the concerns raised by the reviewer, we added a sentence to the discussion raising these issues.
Comment 14

CONCLUSIONS: Considering my previous comment, in my opinion that result should not be emphasized within the study conclusions.

Answer

This comment is not very clear to us. One of the main objectives of our study was to identify potential risk factors for constipation in early childhood. Although we did not find significant associations between stressors and constipation in this age group, we firmly believe it is an important negative finding of our study. Therefore, if the reviewer agrees, we would very much like to keep the conclusions the same.