Author’s response to reviews

Title: Social and environmental conditions related to Mycobacterium leprae infection in children and adolescents from three leprosy endemic regions of Colombia

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Author’s response to reviews:

Re: BMC Infectious Diseases - INFD-D-18-01835

Social and environmental conditions related with Mycobacterium leprae infection in children and adolescents in Colombia

Dear

Dr. Kevin Escandón-Vargas, MD MSc
Associate Editor - BMC Infectious Diseases

Please find attached a revised manuscript entitled "Social and environmental conditions related with Mycobacterium leprae infection in children and adolescents in Colombia" (INFD-D-18-01835). We have revised the submission based upon the suggestions of the reviewers and hope these improvements will allow for publication in BMC Infectious Diseases. As requested we have addressed these points directly in a point-by-point response as well as by indicating them in revised Tracked Changes file.

We greatly appreciate your consideration.

Dr Nora Cardona-Castro
Editor Comments:

In addition to reviewers' comments below, please:

1) Check author submission guidelines (https://bmcinfectdis.biomedcentral.com/submission-guidelines/preparing-your-manuscript/research-article) and check some other journal articles to adhere to formatting and style, (e.g., https://bmcinfectdis.biomedcentral.com/track/pdf/10.1186/s12879-018-3372-6


Corrections include but might not be limited to:

- Rename Introduction to Background (in both abstract and text).

This change has been made in both places.

- Objectives should not be a subheading in Abstract.

The Objectives subheading has been removed.

- Ethics approval and consent to participate should be in the Declarations section. –

This section has been added at the end of the “Materials and Methods” and relevant forms are attached

- Check style of in-text reference numbers [#], not parentheses. I recommend you to use the journal citation style in an appropriate reference manager to simplify the task.

This change has been made.

- Check style of ref 2.


- List of Abbreviations is missing.

An Abbreviations section has been added.

2) Carefully check https://bmcinfectdis.biomedcentral.com/submission-guidelines/preparing-your-manuscript for figures and tables. For instance, no color or shading should be used in tables. Improve quality and resolution of images. Check types, size and resolution requirements.

Shading has been removed from each Table
3) Next time you send this manuscript, please include the tables in the manuscript. Following author guidelines, "tables should not be embedded as figures or spreadsheet files, but should be formatted using ‘Table object’ function in your word processing program". A page with only the table legends is not needed.

Tables have been inserted into the text file as instructed.

4) There are several language issues including phrasing and grammatical typos throughout the manuscript (page 3 lines 15-16, page lines 14-15, etc). Ensure that a native English-speaking person or professional copyedits the paper.

The use of English has been reviewed throughout and adjusted where necessary.

TITLE

5) Change "related with" to "related to".

This change has been made.

6) Specify where in Colombia, as it stands one expects a large number of patients, a wide representativeness.

We now specify in the Background that sample collection occurred in the higher risk regions of Colombia, with expansion in the “Materials and Methods: Study and sample description” to detail the “three geographical regions Uraba-Antioquia-Chocoano (UACHR) (n=18 children), from the Caribbean Region (CR) (n= 43), and; from the Andean Region (AR) (n=21)”.

ABSTRACT

7) Write out anti-NDO-LID (it's first mention).

This detail has been added.

8) Change "transverse" to "cross-sectional".
This change has been made.

9) Lines 20-24. Delete "composed". Delete "selected". Delete "that were".
These changes have been made.

10) Change "qualitative-quantitative variables" to "quantitative variables". Those tests you refer to (t test, u test) are used for numeric variables, there is no qualitative data there but the fact is that the variables are compared in groups (defined by a qualitative variable; i.e., sex, city, etc).
This correction has been made.

11) Correct: Student t-test.
This correction has been made.

12) Correct: Mann-Whitney U test.
This correction has been made.

13) Change "taking into account the distribution of these variables" to "depending on the distribution".
This correction has been made.

14) Few words and same meaning beat the alternative. Please apply these synthesis advice throughout the manuscript, as well as every other correction if applicable.
The text has been edited throughout.

15) Line 39 "meat; over". There is a verb missing in here.
This has been corrected.
BACKGROUND

16) Change "failings" to "failures".
This has been revised to “failings”.

17) Line 50: write out first, then abbreviate.
This has been corrected.

Serologic is now used exclusively.

19) Last sentence: place it in M&M.
This change has been made.

M&M

20) Line 30: it is not clear how many and which sites were "," ";" ?
This has been clarified in the revised text.

21) Line 56: correct according to my comment 10).
This correction has been made.

22) Elaborate on who (selection criteria), when (time period) and where (place/sites); sample calculation, blood sample testing, processing.
Additional details have been added throughout the Materials and Methods section.
RESULTS AND DISCUSSION

23) Do not use decimals for percentage values. Instead, round accordingly. There is no warranted precision using decimals in this study given that the sample is very small (<100).

The suggested change has been made throughout.

24) Shorten the results section.

Results section has been shortened.

25) Use "sex" instead of "gender". Males (men) and females (women) are values of sex.

This change has been made.

26) Page 15 Line 39: credence or evidence?

This has been corrected to evidence.

27) Discuss the limitations of your study.

Limitations of the study have been added and are explicitly mentioned near the end of the first paragraph of the Discussion section.


This has been corrected.

TABLES AND FIGURES

29) Table 1: We know the meaning of the abbreviations here, but the reader does not. Consider the relevance of this table and the need of a legend/footnote.

Footnotes have been added to aid the reader
30) Change "exposition" to "exposure".
This has been corrected.

31) Reduce the number of tables and figures. There is a redundant presentation of data (results text, figures and tables).
The number of Tables has been reduced from 10 to 5 and the number of Figures consolidated to from 7 to 3.

Reviewer reports:
Bruna Hinnah Borges (Reviewer 1):
The manuscript is very interesting specially by studying Mycobacterium leprae infection in children and adolescents, population most vulnerable.

But I think that it is needing to shorten specially the results. As for the method, the authors did not specify the selection criteria of the participants of the study and about data collection.

We thank the reviewer for these kind comments. As suggested we have shortened the text of the Results section, as well as providing clarity with regard to the selection criteria used (Materials and Methods: Study and sample description).

Joilda Nery (Reviewer 2):
- List of abbreviations: If abbreviations are used in the text they should be defined in the text at first use (for example acronyms of table 1), and a list of abbreviations should be provided.
This alteration has been made and a list of Abbreviations has been added.

- A review of English is necessary. There are terms that are not commonly used in scientific language.
The use of English has been reviewed throughout and adjusted where necessary. The text has been reduced without any removal of, or impact on, data interpretation.

**Abstract:**

- Please insert background information on why leprosy is a public health problem in Colombia (especially among children and adolescents) and the relationship of antigens indicating M. leprae infection with social and environmental conditions.

As suggested, we have added the details that 7-10% of cases in Colombia occur in children and that antibodies can indicate infection.

**Introduction:**

- Please insert more information on why leprosy is a public health problem in Colombia, presenting epidemiological data (especially among children and adolescents) and the relationship of antigens indicating M. leprae infection with social and environmental conditions.

Additional information pertaining to leprosy in Colombia has been added. We also note that “In patients, the magnitude of the antibody response correlates strongly with the level of infection”.

- Make it clear to the reader if there are studies that point out the association between PGL-I and social determinants of leprosy. Is PGL-I considered the gold standard?

We have clarified the text and highlight the transition from the gold standard PGL-I antigen to the use of synthetic conjugate NDO-LID.

- Lines 46 to 57 - this section has been displaced - contextualize with epidemiological data on leprosy in Colombia

We have re-arranged the Background section to provide greater clarity and have expanded the of epidemiological data.

- Page 4 (lines 17 to 21) - as it is written it seems that the study was carried out on children from all over Colombia; when in fact it was from a municipality? state? - rewrite making the goal more synthetic.
We have clarified the extent of the study subjects were from “the higher risk regions of Colombia”.

- The variables presented in lines 22-24 should be shifted to the methodology.
Details of the variables have been transferred to the Materials and Methods.

**Methods**

- Lines 32 to 41 - I recommend better detailing the process of obtaining the serum samples and patient information - I suggest creating a separate topic just by explaining this step that is as important as the serological evaluation

We have created a separate and distinct section entitled “Study and sample description”.

- Lines 32 to 41 - these children and adolescents and during which period? The sample calculation process was not properly explained

Samples were collected in 2015 and 2016, and this detail has been added within “Study and sample description”.

- If possible give more information on the criteria of choice of these regions; their representativeness in the country, socio-demographic data and burden of leprosy in these communities.

- What are the data sources? Make the whole process of data collection clearer

We have added the note that “The study population was derived from three geographical regions where the reporting of new leprosy cases is greater than other parts of Colombia: Uraba-Antioquia-Chocoano (UACHR; n=18 children), from the Caribbean Region (CR; n= 43), and from the Andean Region (AR; n=21).”

- If it is possible to cite a reference or insert in the supplementary material the data collection instrument

The data collection instrument was annexed in supplementary material.
- Lines 52 to 55 - If possible, I recommend that other socio-economic variables related to leprosy be included

We have removed reference to other variables collected in the questionnaires to allow focus to those particular to this study. As mentioned, the data are already quite dense and introducing further variables at this time would be require a large addition of text.

** Results

- Lines 26-39 - How many? what are the eligibility criteria? What is the study population? The highest proportion of participants were from which regions?

These details have been added within the Materials and Methods section.

- Lines 44-45 - inform on the methodology or insert reference regarding the socioeconomic categories established by the Colombian government

The socioeconomic categories established by the Colombian government are named status 1. Low-low, 2. Low, 3. Medium-low, 4. Medium, 5. Medium-high, 6. High. Status 1, 2 and 3 corresponding to low status that included the people of scarce resources [11]

- Page 9 - lines 13 and 51 - inform or refer to the methodology on this cohort

This has been corrected.

- Page 10 - line 24 - I consider inappropriate to infer risk since it is a cross-sectional study

This has been corrected.

- Reducing the number of tables and figures is essential. It has many tables that can be synthesized in 3 at the most. These regressions were adjusted by which variables?

The number of Tables has been reduced to 5. Figures has been reduced to 3.
- Table 1: Insert a footnote with the meaning of the acronyms of the clinical forms of the index cases. Is this table essential? The table is not self explanatory - it is not clear what the title and the first row of the table mean

This has been corrected.

- Improve figures resolution

Figure resolution has been improved.

- The session of results and discussion is too long and confusing for the reader. I recommend synthesizing highlighting the main findings

We have shortened both sections.