Author's response to reviews

Title: Factors associated with anti-phenolic glycolipid-I seropositivity among the household contacts of leprosy cases

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Author's response to reviews: see over
Dear Editor,

We thank the reviewers for their positive assessment of our study and their helpful comments. We have made the changes suggested by the reviewers and highlighted these changes in the revised submission. Our responses to specific comments are provided below.

With kind regards,

The authors.

Referee 1 - reviewer's report

Major comments:
None noted

Minor comments:
1. The use of positive serology as a screen to preferentially identify those at risk of leprosy (52 to provide 5 with signs, versus 392 total examined to identify 11 with signs) is somewhat underplayed despite possibly being the major finding of the manuscript.
   Authors' answer: We thank the reviewer for this note. We have now presented this result as suggested and have discussed this finding in the results and discussion sections, page 7 (lines 173 to 176) and page 10 (lines 238 to 242), respectively.

2. Table 2 - sleep in same room category does not total 100%
   Authors' answer: The table has been revised, and the correct percentage of “sleep in the same bedroom” is 85.9%. However, as suggested by referee 2, we have changed the presentation of the tables, and the anti-PGL-I-negative column has been excluded.

3. Table 3 - clinical form should be translated to the English version of the R-J Scale
   Authors' answer: Unfortunately, we do not have enough clinical information about the leprosy cases in the SINAN database and patient charts to perform a conversion from the Madrid classification to the Ridley-Jopling Scale.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests: I declare that I have no competing interests
Referee 2 - reviewer's report

Detailed comments based on the guide to reviewers:

1. Is the question posed original, important and well defined?
The question posed is original, identifying contacts/early stage of leprosy, by
evaluating specific antibody production using the ML flow test in the
north-eastern municipalities of the state of Minas Gerais, Brazil. The study is well
defined and important globally especially for countries where leprosy is still
prevalent.

2. Is the data sound and well defined?
The data is sound. The seropositivity of household contacts has been evaluated
for association of socio-demographic characteristics, BCG, signs of leprosy and
consanguinity using appropriate statistical tools. Seropositivity of the contacts is
also studied in relation to the type of leprosy in the index case.

3. Is the interpretation (discussion and conclusion) well balanced and supported
by the data?
Major compulsory revision
The results are presented well, however the authors use the term Seropositivity
“rate” which is not clearly defined and may not be necessary and can just be
stated as ‘seropositivity’ between lines 165 – 224.
Authors' answer: We thank the reviewer for this note. We removed the term
“rate” as suggested and used just “seropositivity” between lines 165 and 229 as
well as in the abstract, discussion and conclusions sections.

The discussion and conclusions are based on the data of the study and is well
balanced.

4. Are the methods appropriate and well described, and are sufficient details
provided to allow others to evaluate and/or replicate the work?
Minor essential revision
The methods are well described, however, the anti – PGL, ML flow test can be
briefly described as it is the key test against which all the variables were
evaluated.
Authors' answer: A description of ML Flow test has been inserted into the
methods section (page 5, lines from 103 to 116).

In lines 121 & 122 the type of antibodies of anti- PGL1 detected should be
specified, whether it is IgG, IgM or IgA. This may have implications in the
differences observed in contacts of newly diagnosed versus contacts of old index
cases.
Authors' answer: A description of the immunoglobulin class detected in the
ML Flow test has been inserted in the description of the test mentioned above.
Studies evaluating the antibody reactivity to PGL-I present in the sera of patients
with leprosy have shown that the average IgG and IgM reactivities were higher in
the lepromatous pole in relation to the group and tuberculoid leprosy, and there is
a predominance of IgM in relation to IgG. The absence of cell-cell signaling between T cells and B and T cell deficiency, required for isotype switching, have been previously identified and may be responsible for the lack of a substantial change in isotype (Cho SN, Yanagihara DL, Hunter SW, Gelber RH, Brennan, 1983; Levis WR, Meeker HC, Schuller-Levis GB, Gillis TP, Marino LJ Jr, Zabriskie J, 1986; Koster FT, Scollard DM, Umland ET, Fishbein DB, Hanly WC, Brennan PJ, Nelson KE, 1987). Therefore, we do not believe that the immunoglobulin class has influenced the results related to contacts of newly diagnosed versus contacts of old index cases. Furthermore, the contacts living in an endemic region of leprosy are frequently exposed to *Mycobacterium leprae*.

5. What are the strengths and weaknesses of the methods?
The key test is the lateral flow test, which is now being researched in various populations and in other studies. The study is well designed and is a part of another ongoing major study of household contacts. Hence the primary & the secondary data derived are clear and well defined including the clinical diagnosis of index case. Additionally comparing the seropositivity of anti PGL in the contacts with the seropositivity of the index case would have given more direct implications and strengthened the study. (Discretionary Revision)

**Authors’ answer:** Unfortunately, we could not compare the seropositivity of anti-PGL-I in the contacts with the seropositivity of the index case because the ML Flow test was not used for the leprosy cases.

6. Can the writing, organization, tables and figures be improved?
Minor essential revision
The tables are well presented. The material & methods as well as the table could have defined the signs suggestive of leprosy, which the authors considered. The variables presented in tables are clear. In tables 1, 2 and 3 the total number of subjects in each variable can be presented in a column and the PGL seronegativity data (PGL negative %) column can be excluded.

**Authors' answer:** A description of the signs suggestive of leprosy has been inserted in the methods section (pages 5-6, lines from 123 to 131) and the tables have been reorganized as suggested.

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7. When revisions are requested. Define the term ‘rate’ or the authors could exclude the word. 
Authors’ answer: Changes have been made as described above.

8. Are there any ethical or competing interests issues you would like to raise? The studies have been cleared by the ethical committee as mentioned in “Methods” lines – 156-163. Issues of conflict of interest not found.

9. Confidentiality: Any manuscript sent for peer review is a confidential document and should remain so until it is formally published.
   In agreement

11. Are the included additional files (supplementary materials) appropriate? Not applicable

   **Level of interest:** An article of importance in its field

   **Quality of written English:** Needs some language corrections before being published

   **Statistical review:** No, the manuscript does not need to be seen by a statistician.

   **Declaration of competing interests:** 
   'I declare that I have no competing interests'