Reviewer's report

Title: Multiplex PCR technique could be an alternative approach for early detection of leprosy among close contacts - a pilot study from India

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Reviewer: Tom Gillis

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Major compulsory revisions:

1. The authors have addressed my question raised about the reason for multiplex PCR. They also state that the M. leprae-specificity issue was not confirmed by DNA sequencing. While not an imperative, it would strengthen their findings. Particularly, with regard to the very high rate of positivity in the paucibacillary group of patients.

2. The discussion was improved by bringing in other literature regarding levels of positivity of their assay. It was still not clear as to the actual BI of the PB group and would be informative (Table 1) if they would include the percent positive by PCR in the BI negative group within the PB group.

3. The revised manuscript improved on the description of anatomical sites being sampled for various patient/contact groups.

4. The manuscript makes clear that no PCR-negative contacts developed leprosy within the two year window of follow up. Of course, this is the crux of the issue when putting forth a test like PCR as an alternative diagnostic tool to clinical diagnosis with histopath or SSS testing for “early diagnosis.” A study of this kind must determine the predictive value of a test in a reasonable timeframe and two years in leprosy is insufficient. The manuscript continues to state (page 5, line 9 and 2nd page of discussion, line18) the notion that they are examining the M-PCR tool as an alternative for early diagnosis of leprosy. There is absolutely no mention of the timeframe for the patients tested in terms of when they acquired their disease. Indeed, the 2 contacts that developed leprosy can be considered early infections as they showed no signs of disease at first survey only a PCR+ nasal swab. But again to determine the value of this kind of test the follow-up of the other PCR-positive and negative contacts must be sufficiently long enough for a proper evaluation. So, while we get a sense of the preliminary nature of the data, the discussion, abstract and summary imply a much stronger case than the data support. More needs to be done to rectify this in the language of the manuscript.

5. The authors have changed the language to reflect that finding a PCR-positive nasal swab from a contact does not mean they are infected with M. leprae. This is the kind of language modification that I’m referring to in #4

Finally, the authors refer to the results in Table 1 and 2 as measures of
sensitivity. While that is accurate, in order to get a sense of utility of the test one needs to know the specificity of the test (test reactivity with true negatives). Both aspects are critical when attempting to get a sense of the value of applying a test as they have suggested. I remain unconvinced that the authors have sufficiently addressed concerns of the review to put forward the manuscript for publication.

**Level of interest:** An article of limited interest

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

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

'I declare that I have no competing interests'