Reviewer’s report

Title: Rapid diagnosis of new and relapse tuberculosis by quantification of a circulating antigen in HIV-infected adults in the Greater Houston Metropolitan area

Version: 0 Date: 31 May 2017

Reviewer: Alberto García-Basteiro

Reviewer’s report:

Thank you very much for allowing me to review the manuscript entitled: "Rapid diagnosis of new and recurrent tuberculosis by quantification of circulating antigen in HIV infected adults in the greater Houston Metropolitan area: a retrospective cohort study". Despite the small sample size and the used of old archived samples, the results of the study seem to be tantalizing and encourage further research and studies evaluating this novel serum based antigen assay.

Below some comments:

Abstract

Line 19: I suggest to change "issues" by "limitations" or similar. I suggest to modify the abstract accordingly after reviewing the comments to the paper.

Methods:

In my opinion, this is not a retrospective cohort study. It has a retrospective nature, but the specific design implies a follow up period, which in your study did not happen (since you are testing samples at the time of the clinical and lab investigation of the patient.) I suggest to remove "retrospective cohort" from the title of the article.

Did non TB patients have any type of follow up? I think this information is important. If they developed TB disease a few months after the sample collection, how was this captured? I assume you had this information, but it is not clear in the methods section.

Recurrent TB is not a currently used term by WHO definitions. Could you reclassify those patients into the new definitions? In addition, can you clarify (the subgroups of the non TB cases? From table 1 I assume the cured TB patients were included among non TB cases (to study overall specificity-table 2-), but this needs to be more clearly explained in the methods section. In table one. Perhaps another top heading of the table could be (TB cases and non TB cases). However, the columns of table one have different dimensions (ie. among Tb cases, you stratify by culture confirmation, but among non TB cases, by past cured episode, which is slightly confusing). P values are also not very informative given the subgroups analysed.
Although I have read a previous study of the group, I do not know the details of iPRM. How well does iPRM differentiate TB disease from LTB infection? Given the antigen detected, this should not be a problem, but some info on the previous studies where iPRM was tested should briefly be included in methods.

In the statistical analysis, I would love to see what was the main endpoint. In the results section, you perform many subgroup analysis, but the main endpoints (the main group used in your denominators of sensitivity and specificity should stand out clearly).

Results

In table 2, I suggest to include the sample size of TB cases and TB non cases in a clear heading. This are the denominators for sensitivity and specificity, so this should be very clear for the reader.

Discussion

The discussion is clear and the main limitations clearly stated. Nothing is mentioned about missclassification of TB among those clinically diagnosed (this could even be an argument favouring the assay -lower sensitivity among culture negative TB).

Have you thought about the potential use for treatment monitoring in early stages of TB treatment? This should be an exciting field to explore.

The readers will be looking forward to knowing more about feasibility studies, costs of the study, turnaround times, among others. Perhaps you can briefly discuss some of these elements and the next steps in the evaluation of this new assay.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Unable to assess

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes
Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

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