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: 09 Jun 2017

Reviewer: Graeme Meintjes

Reviewer’s report:

The paper presents a pilot study of a novel diagnostic for HIV-associated TB: serum CFP-10 detection using antibody capture, trypsin digestion and MS identification. The sensitivity in patients with culture positive TB was 89.6%. The specificity reported was adequate and perhaps interfered with by TB cases that were not diagnosed as authors suggest. However, the major limitation is the small number of "non TB cases" in whom to estimate specificity (n=35). The findings with respect to sensitivity are impressive. Discovering new better diagnostics for HIV-TB is a global health priority.

The authors should follow the STARD guidelines and state that they were followed:


The abstract is lacking in some necessary detail. The reasons for so many individuals being excluded (g. missing samples) should be presented in Methods section. The Results section should provide more precise quantitative estimates of the performance of the test (eg. sensitivity and specificity with 95%CI).

Page 5 - AFB stands for acid fast bacilli.

Page 6 "or homology" repeated.

The Methods section of the manuscript needs to include section about Inclusion and Exclusion criteria for the main study (HTI) and this substudy.

The Methods need to clarify when serum sample was taken - was it immediately before TB treatment was started in those with TB? When in those without TB?

Insufficient detail about the parent HTI study, the clinical details for those with clinical TB and the characteristics in those with "non TB" are provided. Were the patients with "non TB" ill with other conditions, did they have TB symptoms, or were they healthy?

95% confidence intervals should be provided for the sensitivity and specificity estimations on page 10.
Page 10, second paragraph - the data should not only be presented as percentages but also give the actual numbers of participants positive as numerator with total TB cases as denominator, etc.

The sensitivity and specificity of iPRM using TB culture positivity as reference standard should be presented first and in the abstract as TB culture is regarded as the reference standard in diagnostic research albeit with limitations. Sensitivity and specificity of the culture/clinical composite category should then be presented after that. Although the diagnosis of clinical TB is likely correct in many patients, this is not a definitive diagnosis and some will be overdiagnosed using a clinical approach so this should not be the reference standard for primary analysis.

Page 15. What is meant by "pulmonary aspirates".

The discussion is well written. The authors should add a paragraph discussing how the findings and technology may have relevance (if at all) to settings like sub-Saharan Africa where HIV-associated TB is most common but lab infrastructure limited (esp MS platforms).

In Table 2, why are blank spaces left for specificity - it is possible to calculate specificity using positive culture as reference standard (but not negative culture).

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

No

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

No

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

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