Reviewer's report

Title: Diagnosis of tuberculosis in an Indian population by an indirect ELISA protocol based on detection of Antigen 85 complex: a prospective cohort study

Version: Date: 12 February 2007

Reviewer: Marcus B Conde

Reviewer's report:

General
The MS addresses the problem of TB diagnosis in an Indian population evaluating an indirect ELISA protocol based on detection of Antigen 85 complex. The immunological method for TB diagnosis is attractive because it could be relatively rapid and simple. Challenges for development of effective immunological test include avoid cross-reactivity with BCG or mycobacteria other than M. tuberculosis, to perform consistently in genetically and immunologically diverse populations and the need to discriminate active TB from latent TB infection. The MS presents findings important to those with closely related research interests. However, the are some methodological concerns.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

1. Detailed information regarding the healthy volunteers´ evaluation should be given. Were they asymptomatic and with normal chest X ray? TST results?
2. The gold standard for TB diagnosis is culture positive and authors enrolled only 24 patients with TB diagnosis confirmed. One hundred and four patients of the TB group were cases with clinical diagnosis an instead microbiologic diagnosis. I understand this is an important group to be evaluated in a serologic test because they represent the group of patients without microbiologic diagnosis (not able to provide sputum, AFB negative in the sputum, etc). However, the diagnosis criteria for the group with clinical diagnosis must be very clearly explained and pointed in the MS (example: ...patients with improvement in clinical and radiographic abnormalities after three months of standard anti-tuberculosis treatment in the absence of therapy directed against other pathogens and absence of an alternative diagnosis were diagnosed as a case of active TB, etc, etc). Furthermore, in the actual MS I am not sure if this group should be kept because the very small number of asymptomatic controls. The N of asymptomatic control must be similar to the N of TB group. Methodologically, a study with 24 cases of TB (confirmed) and 68 controls (20 asymptomatic and 49 non-TB cases) makes more sense to me than a study with 128 TB cases and 69 controls (mainly when 104 of TB cases had no bacteriological diagnosis). I think the authors must seriously considered exclude these TB cases clinically diagnosed of the MS and work with a total sample size of 92 cases (24+68).
3. TB cases may be stratified according with AFB status
4. It was not clear to me how the normal value of the test was calculated and this must be clearly stated in the MS. Normally, authors use a ROC curve or use the mean of healthy control plus two SD.
5. Sensitivity and specificity of the test with the CI 95% should be presented in a table (maybe on table 1). I think results of table 2 can be presented in the text and this table excluded. Figure 1 could be excluded too.

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

First paragraph: I am not sure if culture for TB is frequently negative as stated. It is negative in about 20% of patients who provide sputum and have TB.
Second paragraph of the background: TST is not the only way to determine asymptomatic infection. Please, mention ELISPOT, etc.
Discretionary Revisions (which the author can choose to ignore)
Information regarding the BCG vaccination (and re-vaccination if any) policy in India should be provided.

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Discretionary Revisions (which the author can choose to ignore)
What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

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

Quality of written English: Acceptable

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' below