Reviewer's report

Title: Predictors of persistently positive Mycobacterium-tuberculosis-specific interferon-gamma responses in the serial testing of health care workers

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Reviewer: Alamelu Raja

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This manuscript evaluates the performance of the IGRA QuantiFERON®-TB Gold In-Tube (QFT-GIT) in the serial testing of German health care workers (HCWs) in the absence of recent extensive exposure. The objective of the present study was to determine the frequency of IGRA conversions and reversions and to identify independent predictors of persistent IGRA positivity among serially tested German HCWs in the absence of recent extensive tuberculosis (TB) exposure.

The authors observed a strong overall agreement between baseline and follow-up QFT-GIT results that further improved in subjects with positive prior and recent TST results. Overall, the frequency of inconsistent QFT-GIT results was low. However, reversions occurred in about one third of initially IGRA-positive study subjects. Age, TST results, and the extent of baseline IFN-# responses independently predicted persistent QFT-GIT positivity over a median interval of 18 weeks.

General Comments:
Serial IGRA testing and calculating conversions and reversions have been reported before. As the authors themselves have quoted in references, this work has been done in other populations too.

Therefore the authors have to provide strong justification for their work and point out in what way their study is different and how it adds new knowledge in the field.

Moreover, the authors have to point out what is the significance of their results and how the results can be used in the field.

Major compulsory revisions:

1. Was this study approved by the Institutional Ethics Committee and informed consent taken?

2. It will be more meaningful if it is clearly stated in the “Introduction” why is serial testing needed and in what way is predicting persistent positivity useful.

3. IGRA was repeated at different time points in different centres and in different subjects. No elaborate data has been shown on this aspect. What effect did it have on conversion/reversion?
4. Is this study planned to measure the within subject variability? If so, the data and discussion are not complete.

5. As the authors themselves have agreed, the small sample size is small and no major conclusions can be drawn.

6. The time interval between the past TST and baseline TST is also variable in the study subjects, median TST 3 months to 38yrs. It is a well known fact that TST will show booster effect if re-tested within 16wks (4 months) and the effect may prolong up to 1 yr also. Therefore the time interval between past and baseline TST must be stratified and analyzed to see its effect on present TST.

7. Results showed no breakdown to TB during the observational period. Usefulness of the technique for prediction of breakdown to disease is not discussed.