Reviewer’s report

Title: Comparison of the QuantiFERON(R)-TB Gold In-Tube and the tuberculin skin test in a prospective study in Warao Amerindian pediatric tuberculosis contacts

Version: 1 Date: 4 February 2014

Reviewer: Suzanne Anderson

Reviewer’s report:

General comments on manuscript:

This is an interesting study completed in a S American population about which there is relatively little information in the literature, despite the reportedly very high rates of childhood TB. The most important finding (though not surprising) is the fact that children exposed to a SSP/Cx proven TB case really do need IPT and this data should be fed back to the Venezuelan national Tb programme.

I have a few general comments:

1. The title is not very specific – what are the authors comparing with the TST and QFG? Suitability for detecting infection, detection of disease, progression to disease, comparison with CXR findings? All of these factors are incorporated into the analysis and yet the title gives no indication of this.

2. Likewise the abstract needs to state more clearly what the aims and objectives were. Otherwise it looks as tho’ this was a cohort used for another study and in whom someone thought it was a good idea to screen all childhood TB contacts with a TST and QFT and CXR without really thinking about how were going to analyse the data. Currently this has the feel very much of a post-hoc analysis.

3. Many features are evaluated in this manuscript making for a very long paper with many inconclusive findings. Could this not have made two papers with a separate one for the comparison of CXR lesions with QFT-IT results? It would certainly make the paper more succinct. Alternatively, the QFT and TST do not really add anything new to the already very extensive literature on this area of paediatric TB diagnostics and could potentially be left out all together, whereas the CXR vs QFT analysis is relatively novel.

Discretionary Revisions

1. The introduction is well written but overlong, repetitive in parts and would benefit from being more concise

Methods:

1. Repetitive and overlong. Would benefit from shortening though needs some further clarification on specifics as detailed below.
3. Was the cohort actually prospectively screened for HIV as part of this study? It's not entirely clear from the methods. It would be good to know what the HIV prevalence is estimated to be in this population.

4. It would be clearer to give detailed description of F/U timepoints and illustrate all of this with results of recruitment and classification in a consort style flow diagram. Figure 1 is not clear and should be revised.

5. Where was the QFG-IT assay completed – on site or transported to a lab elsewhere? If transported elsewhere what was the time delay before getting into an incubator?

6. I wonder why the authors didn’t use SSP Tb cases (culture confirmed) for screening contacts since this might have increased their yield of secondary paediatric cases.

7. It's surprising that the mean age of secondary cases in the initial (T0) screen was relatively high given that one would expect the highest rates to be in young children. No discussion of this finding is included in the discussion. Similarly the large gender difference is surprising in this pre-pubertal age group but may simply reflect the fact that the numbers are too small to draw any meaningful conclusions.

8. A table summarizing key findings eg median/mean age, gender diffs, nutritional status, % TST positive by age, as well as breakdown of Tb cases by age would have been easier to view rather than reading in text.

9. Eleven children were diagnosed with TB but details of the site of TB is only given for 9! What was the site of the two Cx proven cases?

10. Why exclude indeterminate IGRA results when calculating sensitivity and specificity? Does this not result in an over estimate of the sensitivity?

11. How were the TSTs read? Needs documenting.

Results Section:

1. Progression to active TB during F/U- what was the diagnostic certainty and the site of disease – PTB or EPTB? it would be helpful if this was detailed.

2. The change in TST and QFT results from neg to positive with time may relate to on-going TB transmission within the community. Without knowing if there were further adult SSP TB cases within the households included in the study it is difficult to draw any conclusions about these findings.

3. TST and QFT-GiT results during F/U:
In the final sentence re QFT recruitment responses, there seem to be quite a lot of negative responses. While this is obviously due to high IFNg levels in the negative control tube it does make it difficult to interpret the data (range -7.6 to 0.17).
4. Overall there appears to be a lot of data but relatively small numbers at follow-up. I am therefore concerned that the very inconclusive findings re conversions and reversions relates to the fact that this study is underpowered to show any significant and meaningful trends.

Level of interest: An article of limited interest

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