Reviewer's report

Title: T-cell-based diagnosis of tuberculosis infection in children in Lithuania: a country of high incidence despite high bacille Calmette-Guerin vaccination coverage

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Reviewer: Satoshi Mitarai

Reviewer's report:

Major comments;

The authors evaluated the clinical usefulness of T SPOT TB test for the diagnosis of latent tuberculosis (TB) infection among children under high TB prevalent and BCG vaccinated setting. As the authors describe, it is very important to diagnose latent TB accurately to prevent the development and further dissemination of TB. It is clear that any ex vivo test must avoid the affection of BCG vaccination to diagnose TB infection accurately. It means that the test result should correlate with the risk of TB infection. The methodology/design employed in this study may be appropriate, however, the results obtained indicate no clear difference between the groups of high and low risk for TB infection. It means the T SPOT TB test is not useful to differentiate the recent TB infection, which could be the major target of chemoprophylaxis, under the current setting. If the authors would conclude that the T SPOT TB is useful to diagnose latent TB infection, the difference between risks ought to be demonstrated. If the test is positive for many individuals among low risk group, how we can utilise it for decision making for chemoprophylaxis. It may be an issue of policy for chemoprophylaxis. If all the IGRA positive individuals who do not have active TB receive anti-TB chemoprophylaxis whether the infection is new or old, it may be useful to eliminate the false-positives by TST. This point should be discussed to clarify the point of discussion.

The authors describe that three children were infected by MDR-TB. Is it practical to implement INH prophylaxis under such high TB resistant setting?

Minor comments;

Page 3, line 12

Which category is indicated as the incidence of drug resistance among new TB cases? Is it any resistance to first line anti-TB drugs, or any designated drug?

Page 3, line 15

Although the authors describe that TST has poor specificity and sensitivity, TST normally has high sensitivity despite of low specificity, especially among BCG vaccinated population.

Page 3, line 20 and others
Interferon-gamma is normally abbreviated to “IFN-#”. In the manuscript, “INF-#” is also seen. Please unify the term.

Page 4, line 7
I am not convinced of the definition of “children”. A man of 17 years-old could be categorised into child?

Page 4, line 17
Please describe the definition of “TB-sick” in detail. Does it mean smear positive patient? If so, what was the average positivity of the group? It must be surely important for the readers to recognise the risk of TB infection.

Page 5, line 7
The spell of pyrazinamid must be pyrazinamide.

Page 6, line 7
“Student’s test” must be “Student’s T test”.

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

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**
I declare that I have no competing interests.