Reviewer's report

Title: The Enigma of Extrapulmonary Tuberculosis in Ethiopia: no single driving Factor but possible Roles for Zoonotic Transmission of Mycobacterium tuberculosis and a Complex Interplay of Host and Pathogen Genotypes

Version: 1 Date: 21 November 2014

Reviewer: Eric Walter Pefura-Yone

Reviewer's report:

This study attempts to identify factors that may explain the high incidence of extra-pulmonary tuberculosis in Ethiopia. This is an interesting topic but the approach used in the paper does not allow easily understand of the results. Several major revisions seem necessary.

Major Compulsory Revisions

Title
1. The title does not reflect the content of the manuscript.

Abstract
The result and conclusions section of abstract should be rewritten according to the below comments.

Background
1. The introduction is too long and does not pose the question straightforward.
2. There is no need to state the signs of TBLN. The sentence containing this statement is not well written
3. I don’t understand the relationship between consumption of raw milk (with M. bovis contamination) and cervical TBLN.
4. Please, it is not possible to conclude that there is no relationship between extra-pulmonary TB and M. bovis infection based on the fact that only 1% of TB patients had M. bovis infection (line 150-line 154).
5. Why metadata and not data?

Methods
There are major methodological problems in the manuscript.
1. The one major problem is that there is no information about HIV status of patient with pulmonary TB. Extra-pulmonary TB is more frequent in patient with HIV infection.
2. The diagnosis of TBLN should not only be based on fine needle aspiration but also on lymph node biopsy.
3. The paragraph concerning sites of study could be shortened because you have already published some results related to the current study.
4. You stated that: “you included volunteer patients”. The risk of selection bias is high. Why you didn’t use a random sampling method?
5. Please, you should summarize the key clinical data collected in the test.
6. Once again, the collection of specimens section is too long.
7. What were the conditions to include or exclude an independent variable in the logistic regression models?
8. Please, specify the significance threshold.
9. How did you create the binary variable for lineages?
10. Please, why did you restrict multivariable adjustment only for sex and site? You should also include all variables that appear to be significant in univariable analysis in multivariable regression models. This is very important to adjust all significant variables (for example raw milk consumption and contact with animals) before drawing a conclusion about independent associated factors. It is possible that patients who are often in contact with the animals are also those who also consume more often raw milk.

Results
1. Please, sample collection should be replaced by sample collected.
2. I think that the results section should start by study population and sample collected. You should give the descriptive statistics of the participants and information on sample collected in this paragraph.
3. There is no need to explain the reason why you chose different health centers to conduct this study. This is a results section and not the discussion section. Please, you should consider remove the explanation in the result section.
4. Parts of the results section are about the relation between clinical features and positivity of culture. This will be removed because it is not in line with the objectives of the study. The aim of the study is to compare patients with pulmonary TB to those with TBLN in order to fine risk factors of TBLN.
5. Please, in the subheading “demographics”, please, just give the fact. Explanation and interpretation should be stated in discussion section.
6. In the result section, there is no need to cite previous published data.
7. Please, concerning lineage analysis, you should compare PTB to TBLN and not describe the characteristics of patient with a specific lineage.

Discussion
1. Please, you should summarize the main results of the study early in discussion section.
2. The discussion is too long and not reflected the results of the study. Many paragraphs are hypotheses.
3. The limitations of the study are not acknowledged. For example: selection bias, lack of HIV test in pulmonary TB patients.
Conclusions
The conclusions are not supported by the results.

Minor Essential Revisions

Figures and Tables
1. Please, all the abbreviations in tables should be explained (TB, AFB for example).
2. p-values indication should not be placed in the title of table 2.
3. What is rel% (Table 2).
4. In figure 2, is it percentage?

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

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

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