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

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Reviewer: Wael elamin

Reviewer's report:

Summary:
The authors attempt to clarify factors that influence the rate of extrapulmonary TB in Ethiopia, a populous country with a high burden of TBLN. In previous work using molecular typing, the authors have shown a minimal role for M. bovis (Firdessa et al., 2013), despite it being endemic in Ethiopian Cattle. The authors also collected epidemiological, demographic and clinical data, from the previously mentioned study which is presented in this paper.

Their findings have excluded zoonotic transmission of M. bovis, HIV co-infection and lineage diversity as major factors in the increased incidence of TBLN in Ethiopia. These findings are in themselves useful to set a direction for further investigations and studies.

A) Major comments:

1. The article title suggests a complex interplay of host and pathogen genotypes; however, the manuscript provides no evidence to substantiate the statement. The authors have previously characterised the TB isolates for large sequence polymorphisms and spoligotyping, and SNP analysis (Firdessa et al., 2013), however the samples were stratified according to the geographical regions; with no further human population or genetic analysis. The conclusion of the abstract (line 116-117) stating “genetic features of the pathogen and/or the host population”; should also be revised or further evidence to support the statement provided in the manuscript.

B) Minor comments:

1. Line 128: “is the most frequent form”: please provide a reference.

2. Line 133-135: “Zoonotic transmission can occur through the aerosol route during close contact with animals leading to pulmonary disease”: Please provide a reference.

2. Line 136: “M. bovis is primarily transmitted through consumption of contaminated milk and is therefore often associated with TBLN”: Please consider removing the word therefore.

3. Line 148: it would seem likely: Consider using the word plausible rather than likely.
4. Line 258: (from where patients were recruited in this study) – I am not sure if the statement is necessary.

5. Lines 289-292: Was there any correlation with the volume of aspirate?

6. Lines 298-299: I could not comprehend the statement “Five HIV positive patients were confirmed with TBLN by culture”.

7. Lines 333-338: Please rewrite to make more comprehensible.

8. Lines 374-375: Please provide a reference for the sentence - In comparison; prevalence rates of 1-10% for bovine TB in Ethiopian zebu cattle grazing in pasture are relatively low.

9. Line 382: The authors state despite the fact these countries are endemic for bovine TB, however the reference 26 (Diguimbaye-Djaibé et al., 2006) is specific for Chad, with no reference for the other mentioned countries.

10. Line 481: Please provide a reference for Sudan and Somalia rates.

C) Discretionary revision

Discussion: Lines 488-495 – urbanisation is a recognised risk factor for TB infection and is not specific to Ethiopia; please refer to (Hargreaves et al., 2011) to support your argument.

References


Level of interest: An article of importance in its field

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