Reviewer's report

Title: Prevalence and drug resistance profile of Mycobacterium tuberculosis isolated from pulmonary tuberculosis patients in East Gojam Zone, North-West Ethiopia

Version: 2
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Reviewer: David W Dowdy

Reviewer's report:

This manuscript describes an analysis of drug resistance from a sample of patients with pulmonary TB in northwest Ethiopia. The analysis itself is straightforward and performed reasonably, and the manuscript is structured well, but in its current form, I have two major concerns.

Major compulsory revisions

1. Sample size: The total number of isolates tested for drug resistance is 89. This seems too small to draw precise inference about the prevalence of drug-resistant TB in this population. Ideally, the authors would expand their sample size. At a minimum, they should avoid providing results (for example, to the 0.1 place) that suggest more precision than they have, and should provide confidence intervals to demonstrate the range of potential variability.

2. Loss of samples: I find it hard to believe that 31 cultures did not provide sufficient growth for phenotypic testing - certainly all that would be required is to subculture those isolates and grow them for a longer period of time. The authors should present some data to suggest that the 31 cultures lost did not come from patients who were somehow different from those remaining in the sample (for example, if they were from a particular hospital, that might be concerning). But I would like to see - even if only in a response to reviewers - a better justification for having lost over 25% of all samples prior to DST.

Minor essential revisions

3. line 29: replace "rate" with "prevalence" or "proportion".

4. It is notable that these isolates were collected nearly 4 years ago, and the prevalence of drug resistance may have changed since that time. It is probably worth noting this in the Discussion.

5. line 175/176: "difference didn't reach statistical significant" should be re-phrased, and a p-value or CI provided. (In general, while the quality of English in this manuscript was acceptable, there were a few other minor grammatical errors in the text - it would be good for the authors to re-review closely.) It would also be good to couch these results in the setting of the small sample size, as above.
6. line 207: Given that only 89 patients had HIV status available, how did the authors classify the rest? This seems at odds with Tables 1 and 3, where 124 patients are classified as either HIV positive or negative (none "unknown").

7. line 211: with a 95% CI of 0.84-8.81, I would be very surprised that the corresponding p-value is 0.93. Again, any associations with drug-resistant TB need to be couched in language that describes the low power (resulting from the small sample size) in this analysis.

8. line 216: check your p-value (0.22, with a CI that does not include 1).

9. line 220: I would only make this statement if the confidence intervals for prevalence of resistance in this study do not overlap with those in the previous studies. I'm not sure there is the precision necessary to make this statement.

10. The limitations paragraph needs to be expanded, to include at a minimum the small sample size and the possibility that this sample may not be representative of the underlying population (as it only includes patients being treated in hospitals).

11. Table 3 should show the adjusted results in a separate column, not just the univariate results.

Discretionary revisions

12. I'm not sure how much the GenoType MTBDRplus results add to this analysis. I would consider removing them.

13. The text contains a lot of results that are simply recaps of what is already present in the Tables. Consider using the text to summarize those results, not simply re-state them.

14. lines 232-307: I don't think it's necessary to compare the results here to so many other published studies of drug resistance. As per the most recent Global TB Report, every high-burden country has an estimated prevalence of DR-TB, even if they are not all published. By contrast, it would be nice to have a little more in the Discussion about directions for future research and implications of these findings for public health practice.

Level of interest: An article of limited interest

Quality of written English: Needs some language corrections before being published

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