Reviewer’s report

Title: Determinants of multi drug resistant tuberculosis in patients who took first line tuberculosis treatment in Addis Ababa: a case control study.

Version: 2 Date: 11 April 2013

Reviewer: Anil Pooran

Reviewer’s report:

The authors have conducted a case controlled study to determine the factors that are associated with the development of MDR-TB in Addis Ababa, Ethiopia. The study is of sound design with a sufficiently large cohort to draw statistical conclusions. However, the conclusions that non adherence to treatment and treatment with Category II regimens were strongly associated with MDR-TB progression is somewhat apparent and has been shown to be the case in many other African and non African settings. Nonetheless, it does provide some merit to the current literature. The major drawback of the manuscript is the often poor sentence construction and numerous grammatical errors which often make some of the authors’ reporting and arguments unclear and circular.

Major Compulsory Revisions

1. There are a large number of grammatical errors and problems with sentence construction that needs to be addressed. This reviewer has pointed out some of the more apparent errors in the minor essential revisions section.

2. In the 4th paragraph of ‘Background’, the authors mention the limited availability of tests to detect MDR-TB then give stats on lab capacity for performing smear and culture but do not mention DST. MDR-TB cannot be detected by smear and/or culture alone and there must be some method of drug sensitivity testing that need to be performed i.e. what method was used to detect drug resistance (culture DST, Hain, Gene Xpert?), and what was the lab capacity of doing MDR-TB detection. It is important to state these facts.

3. In the ‘eligibility of study participants paragraph’, the definition of the study participant groups is confusing and needs to be better defined. Were these MDR-TB patients diagnosed by DST and by what method was used? Were they drug sensitive TB patients who took first line drugs for more than a month but did not respond to treatment? How long have these patients been on first line therapy before being diagnosed as MDR-TB? Similarly, is the control group comprised of TB patients who were recruited after successful completion of treatment? Also, it would be helpful if the TB screening tool mentioned was included in an online supplement.

4. Were the results from the multivariate logistic regression analysis included in the results? In yes then please make the reporting of the outcome of this particular analysis a bit clearer.
5. In the second paragraph of the discussion, the authors suggest that being a male patient was associated with MDR-TB development as they do not adhere to treatment as well as females. Perhaps the authors can do an association of being male and defaulting from treatment to emphasize and provide evidence for this point. At the very least, the authors can report on the number of defaulters/non adherers that were male.

6. In the third paragraph of the discussion, the authors state that a 2 to 7 month duration of first line anti TB treatment was associated with MDR-TB development. A 6 month course of anti TB treatment is generally considered a full course for treating drug sensitive TB, at least using category I regimen. For this particular group, i.e. patients treated for 2-7 months, it would be helpful to report the median length of first line treatment in these individuals.

7. In paragraph 8 of the discussion, the authors state that smear negative or EPTB is difficult to diagnose and may explain the association of smear positive TB with MDR-TB development. Do the authors mean that due to lack of laboratory infrastructure to diagnose smear negative or EPTB, there may cases of MDR-TB that are not being diagnosed and, as a result, explain the association of MDR-TB with smear positivity? If so then the authors need to explain their reasoning with a bit more clarity.

8. The incidence of adverse drug reactions in HIV+ MDR-TB patient on HAART usually tends to be higher than HIV- MDR-TB patients due to the increased number of possible interactions with the addition of ARVs to the MDR treatment regimen. It would be informative if the authors can do additional analyses to determine if HIV positivity had an association with higher incidence of ADRs, or treatment default.

9. In table 1, state the median weight of the cases and controls. In table 3, what were the most common drug side effects? Also what was the median duration of the first course of anti-TB treatment?

Minor Essential Revisions

10. Paragraph 1 of background - Change ‘most potent’ to ‘first line’
11. paragraph 1 of background – Isoniazid spelt incorrectly
12. paragraph 3 of background – the last sentence of this paragraph is too wordy and a bit confusing – please reword
13. paragraph 4 of background - there is no need to put the incidence of laboratories doing smear and culture in brackets
14. Results section - While it may be correct to spell out numbers at the beginning of a sentence, it would be easier to read if these were stated as numerical values
15. paragraph 7 of discussion – the last sentence of this paragraph beginning ‘This may be related to one of the reasons that…….’ is too wordy and a bit confusing – please rewrite
16. paragraph 8 of discussion – change ‘Being’ to ‘having’ at the beginning of this paragraph. Also change ‘had’ to ‘was associated with' in this sentence
17. Paragraph 9 of discussion – In sentence 4 of this paragraph, change ‘less susceptible’ to ‘susceptible’

18. Last paragraph of discussion – the strength of the study are somewhat unclear, particularly the first strength listed – please reword

Discretionary Revisions

19. Perhaps the authors would list the drugs in Category I and II in the text or in table 2

20. It would be informative if the authors include the TB screening tool and the study questionnaire used in an online supplement.

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

Quality of written English: Not suitable for publication unless extensively edited

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