Reviewer’s report

Title: Factors associated with delayed treatment of tuberculosis in hospitalized patients: a retrospective cohort study.

Version: 2 Date: 8 January 2012

Reviewer: John Ayisi

Reviewer’s report:

1. Is the question posed by the authors well defined? No. The authors have to justify why they have not presented data on facility specific factors associated with delay. They need to clearly define delay and just imply

2. Are the methods appropriate and well described? Yes

3. Are the data sound? No. There is no denominator. Did all the suspects test TB positive? Was there a difference in delay with regard to TB test done etc…

4. Does the manuscript adhere to the relevant standards for reporting and data deposition? Yes, but have to present complete data as suggested in major revisions below

5. Are the discussion and conclusions well balanced and adequately supported by the data? No. The discussion is very weak as suggested in the major revisions e.g. no data is supporting their conclusions and statements they make

6. Are limitations of the work clearly stated? No. why was data on healthy facility not presented?

7. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished? Yes. They appear do have a limited understanding of statistics and need to read more on this subject to able to address the issues I have raised

8. Do the title and abstract accurately convey what has been found? Title is ok. Abstract has problems indicated below

9. Is the writing acceptable? Only if issues raised have been fully addressed.

- Major Compulsory Revisions

Abstract:

Results;

1. I thought at day 6 (the median), 50% of the cases should have been diagnosed. The authors report 33.2%, and in addition their values 33.2% and 45.6% do not add to 100%. What is the explanation for missing data (21.2%)

2. Line 11. What is the definition of diagnostic delay? If it is >6 days that should be stated.
3. Line 11, regarding main factors associated with delay, did the authors address the effect of HIV status, if so what was it?

4. Conclusion, last sentence. The authors need to allude to what facility specific factors contributed to delay otherwise why was the study done among hospitalized patients?

Introduction:

3rd paragraph, after last sentence, the authors have to include provider/facility factors that can cause delay otherwise why was study done on hospitalized patients only?

Methods:

1. 2nd paragraph. Line 2, ---- during the period of three years, kindly specify the period e.g. January 2001-December 2003

2. 2nd paragraph. Line 14, sentence ending with location [11]. It looks an incomplete sentence

3. 3rd paragraph. Line 12, ---- after discharge. What is the discharge policy in Brazil/study hospital? Was it e.g., after the intensive phase of treatment?

4. 5th paragraph. Line 7, ---- p# 0.05 is too conservative for inclusion in a multivariate analysis. It's usually 0.10 or even 0.20. Same line after univariate analysis, add -- or those known to have clinical significance.

Results:

1. 1st paragraph. Line 1, what was the denominator of your three hundred and five, since you were dealing with TB suspects, did they all have TB?

2. Note that apart from current smokers your table 1 has no results on the behavioural factors.

3. 2nd paragraph. Line 1, highlight the significant findings first, and mention the ones not significant

4. 2nd paragraph. Line 1, the variable age had p=0.079, this can't be ignored as not significant

5. 3rd paragraph line 2, data is misleading as 89 (53.6%) refers to #6days and not 24h

6. 3rd paragraph line 2, sentence starting There was no significant----, should be re-written as: Even though patients diagnosed #6days were more likely to be febrile 111 (66.9%) vs 79 (56.8%), the difference was not significant p=0.072

7. 4th paragraph lines 6 and 7. All patients with ---- extra-pulmonary TB. Add (data not shown)

8. 5th paragraph line 2. Re-write as in 6 above. HIV sero-positivity was more common in group 1 than group 2, though this difference did not reach statistical significance (p=0.059)
9. 5th paragraph line 3, comment on the fact that chronic renal failure numbers were too small

10. 5th paragraph last sentence starting with Age > 60 years----. This information is obvious and since it adds no value to the study in question I would suggest it be entirely deleted.

11. 6th paragraph line 5, ---- adjusted by age and sex. This makes no sense. The purpose of a multivariate analysis is to determine for independent explainable variables for the study question as all variables in the model adjust for each other. So those that remain significant have been adjusted for all variables that were in the model.

12. 6th paragraph line 7, ---- The statement starting The following variables ----- should read-- The following variables remained significant in the final ----

13. Since this study was facility based, the results would be incomplete without the authors mentioning provider/facility based factors that could have contributed to delayed diagnosis

14. Table 1. Under demographic characteristics, Age >60 years is missing data on totals column. Replace (-) with data

15. Table 1. Footnote, Data are presented as mean ±SD, clearly clarify that continuous variables (age) are presented as mean ±SD, and not blanked as currently presented

Discussion:

1. The last sentence of your results (6th paragraph lines 8 and 9) contradicts your discussion (1st paragraph line 4) as diabetes and chronic renal failure were not significant in your final model

2. 2nd paragraph line 2, ---- The statement starting—we found unacceptable time delay ---- is totally misleading as the authors do not provide other comparative data from Brazil and/or other similar settings elsewhere to justify their statement. In addition, information in line 10 confirms that their findings agree with other studies referenced [14-18].

3. Again depending on diagnostic method used (e.g. culture), your observed delay may be acceptable

4. 2nd paragraph line 7, does 2-87 days refer to patient or facility delay?

5. 2nd paragraph, line 10, sentence starting. Another warning ----, does not make sense

6. 2nd paragraph, line 10, your findings of 45.6% and 30% from Canada (line 12) contradicts your information as cited by Ward and others [12], as presented in line 4, sentence of Ward and others [12] ----

7. Were the 30% in Canada duet to pulmonary or extra-pulmonary?

8. 2nd paragraph line 14, --- diagnosis was probably ----. Why use probably and yet you have results??
9. 2nd paragraph lines 18 starting with In the multivariate analysis --- up to line 22, authors are repeating what they have already stated in lines 15-17

10. 2nd paragraph line 23. In reference [18], what were health system factors in Rwandese study and can current study replicate them? The authors need to look at health system delay also as their study was facility-based as I have already stated earlier.

11. 3rd paragraph line 3, reference [9], were participants hospitalized as is the case of the current study. Again delay in diagnosis among hospitalized cases cannot be due to age. I had stated this even in my earlier review

12. The whole paragraph 3 talks a lot about age as though this was the main aim of this study and yet it was not!!!!

13. 3rd paragraph last line (line 10) ending ---- which was not evaluated in the present study. This is the weakest part of your study as you must explain why you did not assess facility related factors contributing to diagnostic delay, otherwise why target hospitalized patients?

14. 5th paragraph line 6, ---- thought symptoms would go away has nothing with causing delay of diagnosis once a patient has been hospitalized/admitted as is the case with the study under review.

15. 6th paragraph lines 1-2, there is no group diagnosed less than 24h as per your results

16. 6th paragraph line 5, --- In the same way----default----. This sentence is poorly constructed as default of treatment and night sweat are not related to be in the same paragraph

17. 8th paragraph HIV makes people more sick and you may be required to check for effect modification in your analysis

18. 9th paragraph, Diabetes and chronic renal failure were only in the univariate analysis, and not multivariate analysis and thus one cant rule out confounding, as these variables were not in the final model

19. 11th paragraph 1st sentence is misleading as you have not provided any data on health system factors causing diagnostic delay

20. 11th paragraph line 4, you have not provided any evince to show that TB awareness was low among clinicians

21. 11th paragraph line 8, recall bias may not be an issue among newly diagnosed patients

22. 11th paragraph line 10, sources of delay need to be addressed by study looking at both patient and facility/provider related factors

23. 12th paragraph line 2 ---- setting is long---. This is not true as studies you have cited show that your observation is consistent with other studies (4-12.5 days [ref. 14-18])

24. There may have been no really delay in this study depending on methods used to diagnose extra pulmonary TB, as it is hard to diagnose it, thus could methodology of TB have been the issue?
- Minor Essential Revisions

The author can be trusted to make these. For example, missing labels on figures, the wrong use of a term, spelling mistakes.

Introduction
Line 7, what does 2010 stand for in inhabitants/year/2010?

Methods:
1. 2nd paragraph. Line 13, --- tests according with--, should be ---- tests according to--- [11]
2. 2nd paragraph, line 15, --- our hospital has all ---, should be our study hospital has all –
3. 2nd paragraph, line 20, --- the word reported to be replaced by confirmed

Results:
1. 3rd paragraph line 1, --- patients whit, should be – patients with ---

Discussion:
1. 2nd paragraph, line 4, the sentence starting, Ward [12] suggests ----should read: Ward and others [12] suggest -----
2. 7th paragraph line 2, sentence starting: In fact---, should read: A similar study has also shown that radiographic changes-----

- Discretionary Revisions

These are recommendations for improvement which the author can choose to ignore. For example clarifications, data that would be useful but not essential.

Please note that both the comments entered here and answers to the questions below constitute the report, bearing your name, that will be forwarded to the authors and published on the site if the article is accepted.

Based on your assessment of the validity of the manuscript, what do you advise should be the next step?

- Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions