Author's response to reviews

Title:A Retrospective Review of a Tertiary Hospital's Isolation and De-isolation Policy for Suspected Pulmonary Tuberculosis

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Author's response to reviews: see over
To:
The Editor
BMC Infectious Disease

Dear Editor,

We are pleased to enclose a revised copy of our manuscript titled ‘A Retrospective Review of a Tertiary Hospital’s Isolation and De-isolation Policy for Suspected Pulmonary Tuberculosis.’

We thank the reviewers for their detailed review of the manuscript and have addressed their comments below.

Reviewer 1

Introduction

1. 2nd Paragraph 1st Sentence: “Protocols for isolation…. disease”. Add reference to this statement.

   Authors’ reply: We have added in the relevant reference.

2. 3rd paragraph: Who is “suspected for pulmonary TB” in your setting?

   Authors’ reply: We have defined in the Introduction, Paragraph 3, Page 6, the type of patient who would be suspected of having pulmonary TB in our institution.

3. The research question/objectives mentioned at the end of the introduction is vague and broad. It says “We performed this retrospective study to evaluate our existing hospital protocol for isolation and de-isolation of suspected pulmonary TB cases”. This must be made more specific.

   Author’s reply: We acknowledge that our objectives were not clearly defined in the original manuscript. We have amended the Introduction, Paragraph 4, Page 6 to state ‘The main objective of this retrospective study was to evaluate the timeliness to de-isolation of patients with smear negative respiratory samples. In particular we wanted to assess the excess time smear-negative patients spent in our isolation facility.’

Methods

4. Methods. The methods section is written haphazardly. It will be easy to read and understand if the methods are organised into various subsections such as setting, study design (rationale for choosing this study design in comparison to other study designs), study population (inclusion and exclusion criteria), selection of study participants including sampling and sample size calculations (if applicable), study period, study variables (and its sources), study investigators, ethics approval, data
management (data validation) and analysis plan (including what was done when the data was missing).

**Authors’ reply:** We agree that the methods section could have been written in a more systematic manner and have re-organized the Methods section in the style the reviewer has suggested.

5. Describe what tests that are performed and in what sequence they are done for ruling out pulmonary TB as soon as the patient is admitted to the isolation ward? Are all tests mentioned in the first paragraph of the methods section done simultaneously or is there an algorithm? If an algorithm is available, then this may be provided in the form of a figure. This should also give information on what is done for patients whose sputum samples are positive or negative for *Mycobacterium Tuberculosis*. Are new WHO endorsed tests such as cartridge based Nucleic acid amplification tests (eg Xpert MTB-rif), which is fast, highly sensitive used in this setting or not?

**Authors’ reply:** We have amended the manuscript accordingly to describe the tests which are done and the sequence in which they are performed to rule out pulmonary TB (Methods, Study Population, Paragraph 2, Page 7). We have also described what is done for patients whose respiratory samples are positive or negative for *Mycobacterium Tuberculosis* (Methods, Study Population, Paragraph 2, Page 8).

At the time the study was conducted in 2010, our institution had not started using the new nucleic acid amplification tests such as Gene Xpert MTB rif. We have clarified the specific PCR assay which was used by our microbiology lab at the time (Methods, Study Population, Paragraph 2, Page 8).

6. The reviewer does not understand that out of 201 patients why only 121 patients’ data were analysed? This is perhaps linked to the study objectives or research question which at present is not clear and vague.

**Authors’ reply:** We acknowledge that our study objectives were not clearly defined in the original manuscript and have amended them accordingly (please see our reply to Reviewer’s Point 3). The 121 patients were analysed as they returned only smear negative respiratory samples and this was the population we were interested in studying to assess their timeliness to de-isolation. The remaining 81 patients had smear positive samples and thus were excluded. We have included a consort diagram (Figure 1.) to better illustrate this.

Results
7. General comment: The tables should stand alone and the percentages should add up to 100% (if they don’t add up, then some explanation has to be provided).

**Authors’ reply:** We thank the reviewers for spotting these errors and have amended the tables accordingly. We have also shifted the tables to the end of the manuscript as per BMC’s requirements for manuscript formatting.

Demographics
8. Demographics
  8.a. Age- only median is given; give range as well
Authors’ reply: We have added in the age range of the study participants.

8.b. Table 1:
8.b.i. The title of the table is incomplete, does not provide information on the total number of study participants.
Authors’ reply: We have amended the title of Table 1 to include the total number of study participants.

8.b.ii. Some percentages are confusing; for example: residency n(%) = 27 (22.3%) what does this mean and what happens to the other 77.7%?
Authors’ reply: We thank the reviewer for spotting this error. It was due to misalignment of the table and we have amended Table 1 accordingly.

8.b.iii. Percentages under type of housing adds up to 101.1%, under occupation adds up to 103.8%?
Authors’ reply: We thank the reviewer for spotting this error and have amended Table 1 accordingly.

8. c. The information provided in the narrative and tables don’t match. For example 9.1% don’t live in a fixed abode as per the table whereas in the text it is mentioned as 10%.
Authors’ reply: We thank the reviewer for spotting these errors and have amended the text accordingly so that the information matches that which is provided in the tables.

9. The median duration of symptoms was two weeks (mean: 46 days, range: 1-365). What symptoms are they referring to? Is it all symptoms or a few symptoms and how good is the data collected here?
Authors’ reply: In this case we are referring to the median duration that patients were symptomatic for any of the following: cough, fever, anorexia, loss of weight, dyspnea and hemoptysis. We have amended the manuscript to state this clearly (Results, Clinical and Radiological data, Paragraph 3, Page 10).

10. How have the costs been arrived at? What components does it contain? Is it only isolation bed charges or does it also include charges for human resource and other aspects? It appears that the calculation of costs is very superficial and does not carry much meaning.
Authors’ Reply: Our cost calculation only includes the cost of isolation bed charges. We acknowledge that this is a very superficial calculation and that this is one of the limitations of our retrospective study. We have included this in the discussion section.

11. The discussion and conclusion section is well written and addresses all the major issues. It may be require certain modifications based on the suggestions above.
**Authors’ reply:** We thank the reviewer for his positive comments and have modified our discussion section accordingly.

**Reviewer 2**

1. Only small number of patients (24) was enrolled in the premature de-isolated group and was not randomized.

   **Authors’ reply:** The design of our study is a retrospective analysis of patients who were isolated for suspected pulmonary TB and who were subsequently smear negative. In such a retrospective study it would not be possible to randomize patients.

2. The incidence of positive TB culture between the group who follow the hospital guideline and control (who not follow guideline) was not tested.

   **Authors’ reply:** We acknowledge that this data was missing and have added it in to the Results section of the manuscript (Management & Diagnosis, Paragraph 6, Page 12)

3. The data is not consistent. In the result “page 13” stated “Of the 24 patients who were de-isolated prematurely, three patients were subsequently diagnosed with pulmonary TB after their specimens returned culture positive for M tuberculosis.” However, the abstract stated that “non (sic) of those patients had proved to be culture positive” which is contradictory to their own statement in result.

   **Authors’ reply:** We thank the author for spotting this erroneous statement in the results section of our abstract and have removed it accordingly.

Once again we thank both reviewers for their constructive comments and we hope we have addressed their concerns satisfactorily. We look forward to a favourable reply from the Editorial team.

Yours Faithfully,

Dr Shirin Kalimuddin