Author's response to reviews

Title: Comparison of pulmonary and extrapulmonary tuberculosis in Nepal- a hospital-based retrospective study

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Author's response to reviews: see over
Dear Dr. Veeranoot Nissapatorn,

Thank you for reviewing our manuscript. We greatly appreciate your constructive criticism. We have read your comments and revised most of the parts keeping in mind the second reviewers comments also.

Point-by-point replies to the issues raised by you are given below for your further consideration.

We look forward for your further concerns if any after this revision

Reviewer's report:
General
This manuscript is generally interesting in terms of epidemiology and related issues of TB (public health), particularly in an area where high burden of TB has been identified with limited published information.

Thank you. Yes, there is a lack of information particularly on EPTB from Nepal which is a high burden country.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

Introduction

This part should be more of a literature review (as shown here were recent studies) on TB and both subtypes (PTB and EPTB). However, the authors seem to be more focused on EPTB than PTB (according to the objectives), as very clearly shown in the 1st and 2nd paragraphs. I would recommend the authors to rewrite and readjust the contents with a clear cut paragraph. Some of these references should be more cited in the discussion.

The paragraphs have been readjusted according to the contents on TB in general and EPTB in particular into a clear cut paragraphs. The recent studies have been more frequently cited in discussion.

Avoid repeating the sentence, term or phrase such as vary according to, host-related factors, etc. - summarize and group as one
Third paragraph: line 7-9; Risk factors...are lacking - revise and combine It would be better to combine these two objectives as one sentence.

Repetitions have been modified and the sentence on aims has been combined into one sentence.

Materials and Methods:

Study setting: The authors can elaborate a bit more on general information in term of size of population and the incidence of TB (PTB and/or EPTB in this setting, etc.

The size of population has been included. But there is no information about TB (EPTB). There we apologize for our inability.

Line 5-7 - combine (both are referred to TB Dx)
Line 9, according to NTP guideline à any references.

Combined and reference for the NTP guidelines quoted.

Data collection:

All TB patients - How many?
Any inclusion criteria for this study
How long for the duration of the patients who was having these co-morbid diseases and use of immunosuppressive drugs.

The number of TB patients has been mentioned.

All patients included from TB register were included for this study. There were no other inclusion criteria.

Information on co-morbid conditions, use of immunosuppressive drugs just taken as yes/no. Duration was not available from most of the case files. So we could not provide the details.

Classification of PTB and EPTB patients
Page 7, line 3, ...pleura... - PTB
Page 8, line 4, ....pleura.. - EPTB
How did you differentiate these two conditions with the same organ involvement?
The sentence on the definition of PTB and EPTB has been modified to clarify the meaning.

Result

Table 1. From the text part, the subtopics were chronologically divided therefore it would be better if the authors make a similar pattern in the Table as well.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>PTB EPTB</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographic factors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Life style factors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinical profiles/factors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>History of contact - ?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Use of immunosuppressive drug - refer to Materials and Methods.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The table has been modified as suggested.

1. Demographic factors
The last 2 lines of paragraph at younger ages - be specific a bimodal pattern - clarify

Specific age and age peaks of bimodal pattern have been mentioned.

2. Life style factors
“ever smoked” - clarify (If any term that has not been used/mentioned in your previous text, give a kind of “definition” or “a short meaning” which is correlated with your data).

Clarified and a short working definition of the term is given within a bracket.

3. Clinical profiles
Line 7-11 - revise (it is not clear what the authors try to tell the readers related to TB/HIV in this study and I also see in the Discussion (page 13, line 1-4).
Note: I would suggest that the authors should write in detail (eg., percentage) of 1, 2 and 3.

The details about TB/HIV have been revised here as well as in discussion also.

The percentages of 1, 2 and 3 were given in the brackets.
Multivariate comparison
Line 3; lower age - younger age

Corrections made in the text.

Discussion:
I would suggest that the authors should group the titles for discussion by following the “Result” (there were too many paragraphs). It will make your discussion more interesting and easier to understand for the readers.

The titles were grouped for the main ideas in the discussion as suggested.

Page 13, 1st paragraph, line 1-6 (1-4 and 4-6) - ?
This paragraph, the authors should revise by comparing with other studies either similar or contrary and giving meaningful/supportive comments/observations or any hypothesis behind these results (It is very clear that line 4-6 just like repeating the result and hanging there with no meaning).

We agree with the suggestion. But we apologize for not revising.
The first paragraph was to mention the main results. The similar or contrasts to previous studies has been made in the main body of discussion. Even the hypothesis has been mentioned in the other sections of discussion.

2nd paragraph, Line 12, may be having been - ?
Line 12-13, erroneously diagnosed/over-diagnosis - misdiagnosis?.
Line 1-2, Earlier studies…13-15, However…. and line 4-6, Recent studies…. In Background)- revise (not keep repeating).

The suggested revision was made in the above mentioned lines.

Page 14, 1st paragraph, line 1…aimed to……EPTB - remove (it is better to present their results which may be similar or contradict with the present one and further discuss about “Why” or “Why not”).

Discussed as suggested.

Line 2-5 - revise (combine these two sentences… a bit confusing!).
Line 5-7 - revise (What did the authors try to tell? Is it the reason why the incidence of PTB was low, high or ?).

Sentences were combined and explained why incidence of TB was low in our setting.
2nd paragraph, line 1-4 - avoid repeating the word “gender differences” and “differential”. Line 1-3 - combine these two sentences and avoid repeating.

The sentences have been rephrased to avoid ‘gender differences’ and the sentences combined.


Discussion about the association was made.

Page 16-17, 2nd and 3rd paragraphs should be combined
3rd paragraph, line 3: in our study…..associated with TB - remove and the authors should highlight/suggest the importance of TB screening in these patients eg., highly suspicion, h/o contact TB, or etc in your setting. This will make this paragraph looks better than just only comparison.

Removed as suggested and highlighted the importance of screening in our setting.

Page 17, 1st paragraph, line 5-6 However……2001.02 [13] - remove and actually this paragraph is very useful for the authors to emphasize the significant role of TB in HIV/AIDS patients by suggesting TB screening in HIV patients even though the incidence oh HIV/AIDS is very low compare to other countries or further study should be highlighted particularly the association between TB (PTB or EPTB)/HIV because the incidence of HIV/AIDS is likely to increase in the future…Who knows?

The paragraph has been rearranged for clarity and screening the HIV/AIDS patient emphasized and further study was also indicated.

Reference:
The following references are recommended for correction (refer to original articles);
Ref 2: Tuberculosis-a global..- Tuberculosis: a global..
Ref 12: extra pulmonary - extrapulmonary
Ref 16: socioeconomic - socio-economic

The suggested changes were made in the reference list.