Author's response to reviews

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

Authors:

Chandrashekhar T Sreeramareddy (chandrashekharats@yahoo.com)
Kishore V Panduru (pandu_vki@yahoo.com)
Sharat C Verma (verma_sharat@yahoo.com)
Hari S Joshi (drjoshiharish@rediffmail.com)
Michael N Bates (m_bates@berkeley.edu)

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Author's response to reviews: see over
Reviewer’s report
Title: Comparison of pulmonary and extrapulmonary tuberculosis in nepal- a hospital-based retrospective case-series analysis
Version: 1 Date: 27 August 2007
Reviewer: Philip Hill
Reviewer's report:

Dear Philip Hill

Thank you for reviewing our manuscript. We greatly appreciate your constructive criticism. We have read your comments and revised many 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

General
1. Is the question posed by the authors new and well defined? Not particularly new, except new for their setting. What is missing is a proper description of the clinical aspects of these cases. This is primarily a clinical case review and the authors have made it into a statistical comparison of PTB and EPTB. They should fill in the missing clinical details and make their statistical comparison less prominent.

The topic of EPTB in Nepal is new because no such studies have been reported from Nepal or similar developing country. The title “….case series analysis” has mis-lead to such a conclusion. The aims of the study were to report about EPTB and identify risk factors for EPTB. We disagree that our study is a case review. In the revision according to the second reviewer we have made some modifications. Otherwise the study objective remains the same in the revised manuscript. We did not intend to collect information about clinical details so we apologize for our inability to provide clinical details.

From the title and the abstract of the manuscript the concept of case-series analysis has been removed to avoid misleading conclusions.

2. Are the methods appropriate and well described, and are sufficient details provided to replicate the work? The methods are reasonable considering the aims. How does the total number of these hospital attendees related to the number at the local government DOTs clinics over the time period and the ratio of EPTB and PTB?
This point has been discussed in the section of discussion. More over the hospital attendees may not be representative of the community. EPTB is diagnosed mostly in Tertiary setting whereas PTB in the peripheral centres.

There should be much more detail about the clinical side: E.g. How many had x-ray-what were the main x-ray findings overall? E.g. Number of zones with disease on x-rays, bilateral vs. unilateral changes, cavitation etc, what proportion were malnourished, what were the smear results (eg what proportion had a full 3 smears, what proportion were only 1 smear pos plus xray?), what were the outcomes of treatment? And compliance-what is known about compliance. How were the diagnoses actually made in the EPTB? This would give a more balanced paper and also more insight into the completeness of the records.

As discussed with the first point this is not a clinical case review. Therefore above-mentioned points and also outcomes, compliance, diagnosis of EPTB are not relevant in the context of aim of the study.

3. Are the data sound and well controlled?
The main comparison relies on PTB vs. EPTB. One concern is how representative of all EPTB in this population are these patients. Hence some attempt to compare to the National programme numbers in this area is worth documenting.

The issue of representativeness of study sample is discussed under limitations and also other sources of bias. Attempt to National programme data on numbers were attempted but national programes report as either categories of treatment under DOTS or smear-positive/smear negatives. The reports don’t speak about PTB. EPTB. Hence, our apologies for inability to provide and compare our numbers with national data.

One could argue that this comparison has too many potential sources of bias to be the main analysis in a paper. This is of more concern, since it is not possible to adjust by HIV status. While many of those HIV tested were positive, it is likely not to reflect the overall HIV positivity, as HIV testing was clinically driven. Therefore this issue is of concern, but considering the overall rates of HIV in TB in Nepal, it is not a major issue. It would be sensible to do an analysis on HIV negative only, not necessarily as the main analysis, but to be able to say the results held up in these individuals.
Other sources of bias discussed in limitations as it was hospital-based retrospective analysis. A separate section in discussion is related to TB/HIV as it was commented by second reviewer as well. Small number of known HIV status (tested) precluded us to do a separate analysis on HIV negative only.

There is a concern about age with respect to the diagnosis in children. While the figures present some data relating age to diagnosis, it isn’t clear within age groups what proportions are due to EPTB or PTB. Similarly, while the median age is presented for each, there should be some age groupings. And it should be clear, if hilar adenopathy is being considered pulmonary TB in children, what proportion of children have this as the sole cause of their diagnosis?

In the revised paper we have a break down of the age groups instead of median ages. This gives proportions of PTB and EPTB. Yes a small number of children hilar adenopathy, positive Mantoux, AFB from gastric lavage, failure to thrive were used for diagnosing TB. We are unable to give the numbers since it is out of context of this paper.

It appears quite remarkable that the records were so complete—were there no incomplete records/lost records?

We apologize for not giving the details of incomplete/lost records. This issue was raised by other reviewer also and we have given the number of missing/lost/incomplete records in results sections.

It should be clear how the diagnosis of diabetes was made, and a comment on how this may or may not reflect the actual number with diabetes.

In the context and aim and methodology it will be difficult and not relevant to the present study to discuss about diagnosis of Diabetes because our study was a retrospective data analysis. Known case under treatment for diabetes was considered for analysis from the case file.

I am not certain that the 38 concurrent PTB and EPTB should have been part of this analysis. It would seem more sensible to compare EPTB only with PTB only. At least a separate analysis excluding the 38 should be considered and referred to in the discussion.
We agree with this point. A separate analysis excluding concurrent PTB and EPTB was made and did not change our results. Therefore, the issue was not discussed any further in the paper.

4. Does the manuscript adhere to the relevant standards for reporting and data deposition?
Yes

5. Are the discussion and conclusions well balanced and adequately supported by the data?
In the main the discussion is good. Other additional issues noted above.

6. Do the title and abstract accurately convey what has been found?
Yes, but will need to be modified along with modifications in relation to above.

7. Is the writing acceptable?
Yes, I think the authors are writing at a good level.