2 29553 Response to reviewers

Dear…

I would like to thank you and the reviewers for your valuable comments and suggestions. Please find below the responses to the reviewers comments as well as the changes that have been made in the revised document. The modifications are highlighted in red

Kind regards,

Binila Chacko

Reviewer 1:

1. I do believe that this work could be improved with a more strict approach and a modification of the conclusion section. In fact, in this section, you discuss mainly the impact of nosocomial infection on limited resources of developing countries. Therefore, you need to introduce this important data in your method section (or to re-write the discussion section).

   Response: In the introduction, the reasons for this study were clearly stated including the perception of poor survival and limited resources that would steal opportunities from the treatable. The conclusion reflects exactly the same thoughts.

   In the methods section, we have included a section on outcomes.

   Outcome data: The impact of infections on outcomes was explored. This included its effect on length of stay (ICU and hospital) and hospital mortality. We also assessed the impact of individual infections (VAP, UTI and BSI) on mortality.

2. **Specific comments:** Methods section. You stated: "adult patients were enrolled if the stayed beyond 24-H in the ICU." As you know: Infections which occur more than 48 Hours after admission are considered nosocomial. Therefore, it seems obvious that in such a study patients should stay at least 48 hours in ICU.

   Response: This study was part of a costing study that has been published in *Annals of American Thoracic Soc*iety (see Reference 11 in the main document). In that study, adult patients were enrolled if they stayed beyond 24 hours in the ICU. As has been correctly pointed out

by the reviewer, a nosocomial infection was diagnosed in this study only in those patients who stayed for at least 48 hours.

The following line has been added to the methods section:

A diagnosis of HAI was made only when a new infection occurred 48 hours after hospital admission.

3. **Results section.** Details on the excluded patients should be added in this text. All the readers are not expected to have easy access to medical literature and a simple table can summarize the number of excluded patients and reasons for exclusion.

   Response:
   Thank you for this suggestion. The following has been added to the initial section on baseline and demographic data.

   Patients excluded were those admitted under specialty units (n = 434), those who died or were discharged within 24 hours (n = 105), those who refused consent (n = 58), and those not recruited during weekends and public holidays (n = 503).

4. **Infection data**: If infection data was available in 496 patients, the three other should be exclude. This will not modified significantly your results, but you cannot introduce in a study patients with major data missing.

   Response: All the infections data calculations have been done only on 496 patients. (See Tables 1-3)

5. As far as I understand correctly your text, all the patients ventilated had invasive ventilation with a tracheal tube. It would be interesting to know how many patients had a central venous line (risk factor for blood stream infection) and how many had a bladder catheter (risk factor for urinary tract infection).

   Response: 86% of the cohort was intubated and all intubated patients had an indwelling urinary catheter.

6. It is interesting to learn that, in your experience, nosocomial infection do not increase mortality incidence, and do not increase cost per day (when length of stay double in infected patients, cost double also). Extra cost due to infection and increase in mortality incidence are observed in developed countries.

   Response: In this paper, we have clearly shown that the cost of stay doubles although the mortality was not increased in patients with HAI.

We have rephrased the statement "The cost of an infection acquired in the ICU was similar for VAP, BSI and UTI were almost similar (Table 3) when data was analyzed as median (IQR). " as "An infection acquired in the ICU was associated with doubling of overall cost. When VAP, BSI and UTI were analysed independently, the overall cost (median IQR) of each infection was almost similar (Table 3)"

7. As you stated in the introduction, it is "admitted" by the medical community that nosocomial infections are associated with poor survival, while in fact your results suggest that "treatment of nosocomial infections did not steal opportunities away from other potentially treatable patients waiting for an ICU bed." I think that these to facts should be highlighted and discussed.

   Response: As written in the conclusion, the results suggest that treatment of a nosocomial infection potentially steals opportunities from other patients as there is doubling of ICU length of stay of patients who develop HAI.

   Reviewer 2:
   I am not clear about the statistical validations. The work is novel and good.

   Response:
   Thank you for your review of the study. We have made an addition to the methods section on outcomes and to the stat

   Outcome data: The impact of infections on outcomes was explored. This included its effect on length of stay (ICU and hospital) and hospital mortality. We also assessed the impact of individual infections (VAP, UTI and BSI) on mortality.

   Statistical analysis:

   Outcome data was compared between the two groups of patients - with and without HAI.