Author’s response to reviews

Title: Nasal and perirectal colonization of vancomycin sensitive and resistant enterococci in patients of paediatrics ICU (PICU) of tertiary health care facilities

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Author’s response to reviews: see over
The BMC Infectious Diseases Editorial Team

Enclosed, please find the revised version of our manuscript entitled "Nasal and perirectal colonization of vancomycin sensitive and resistant enterococci in patients of paediatrics ICU (PICU) of tertiary health care facilities". In your letter, you encouraged us to revise our manuscript and address the issues raised by the reviewers who suggested more precision for our data. The reviewers also suggested to modifying our results and discussion.

We have carefully revised the manuscript according to the reviewer’s queries and a point-by-point reply to their comments is provided below.

We hope that the changes we have made in the new version of the manuscript have addressed all of the points raised by the reviewers, and that the manuscript is now acceptable for publication in BMC Infectious Diseases.

We are very grateful to the reviewers for the time they spent reviewing the manuscript and to Editorial Team for reconsidering this work for publication in BMC Infectious Diseases.

Yours faithfully,

Muhammad ArfatYameen

Point-by-point response to reviewer’s comments:

Reviewer: Maja Weisser

Reviewer's report: (Major Compulsory Revisions)

1. The study aim should be better defined: was the aim to describe local epidemiology?

Answer:

- The aim of study has been explain in detail in the background section. Now it is looking much improved and thanks for your guideline.

2. Parameters of inclusion are lacking:

   - time period of inclusion of patients ? (year, month?)
   - were patients included consecutively?
   - were patients admitted from home, from other units or from other hospitals?
   - when was the exact time point of sampling (at admission)?

Answer:

- Lacking parameters has been included in the methods section.
3. English spelling is poor with many orthographic mistakes. Please consider sending the manuscript for language review.

Answer:

- Proof reading has been done and the quality of English has been improved wherever required.

4. From the BAA plate: how were colonies selected, at random? Knowing that patients are usually colonized with different enterococcal strains this is a relevant point and should be addressed.

Answer:

- The colonies which show specific identification characteristics like pinpoint colonies and colonies with black zone around, were selected for further processing.

5. Unclarities in the result section should be addressed:

- What stands the p-value for in the first 2 paragraphs of the result section
- Results for resistance should be shown separately for E. faecium and E. faecalis, as these are two quite different species.
- The authors write in the result section, that resistance patterns were similar in rectal and nasal Swabs. In the abstract, they note that there were differences. I suggest, that a statistical analysis only in patients who had a detection of the same enterococcus species in nasaland rectal swabshould be done, if numbers allow to do so.

Answer:

- P value represents the result of Chi-Square test and has been added in the result section.
- Results have been modified according to your guidelines and Table 3 has been amended for showing the resistant pattern of E. faecalis and E. faecium of the nasal and perirectal area separately.
- Resistant pattern is edited again according to the changes made in the Table 3. Statistical analysis not possible becausesuch patients are few in the number. There are 03 patients with E. faecalis and 05 patients with E. faecium in both nasal and perirectal area. If you think it should be further modified then please let me know.

6. In the last paragraph of the result section entitled “Association between clinical diagnosis and enterococcal colonization” pneumonia is presented as a factor associated with
enterococcal colonization, which is an interesting finding. Nevertheless, authors should show baseline characteristics in a table and declare, which factors they analysed for a potential association with enterococcal colonization. Also here, a separate analysis for E. faecium and E. faecalis would be useful.

Answer:

- Important risk factors studied have been added in the background, result and discussion section and table 5 consisting of analysis of risk factors and strains of enterococci has been added in the manuscript.

7. In the discussion, the findings should not be repeated but discussed with respect to published literature and novelties found in this study.

Answer:

- Sir I have removed the repetition in the discussion section and more relevant previous studies have been added.

**Minor compulsory revisions**

**Abstract**

1. Separate Methods and Results paragraph
   - Methods have been separated from results in the abstract.

2. Many spelling errors, please correct (e.g. `'pathogen` instead of `'pathogne`, `Rawalpindi`, `PCR` instead of `PRC`, …)
   - Spelling errors has been removed from the manuscript.

**Introduction**

3. Spelling errors: e.g. ‘isolation’, ‘persistantly’, ‘methicillin resistant’
   - Spelling errors has been removed from the manuscript.

**Methods**

4. Microbiological workup is described very detailed for an epidemiological paper and could be shortened with citation of the literature. In particular no new laboratory methods are presented.
   - Methodology paragraph has been reduced by giving the relevant citation

**Results**

5. Refer to Table 2 in the first paragraph.
6. Statistical analysis. I suggest to delete the title of this paragraph and to show clinical patient data here. Is the indicated duration of patient stay during the whole hospitalization or before swab?

- Paragraph title “Statistical analysis” has been changed according to the suggestion. The duration of stay of patient in the hospital mentioned in the manuscript is before collection of samples.

Discussion

7. Please comment on possible explanations of the discrepancy of resistance testing between rectal swab and nasal swab, are these due to small numbers or is the hypothesis, that patients are colonized with different E. faecium and E. faecalis strains in the nose/gut? Do different enterococci colonize preferentially different sites?

- The discussion section has been amended according to the changes made in table 3.

8. Please discuss potential bias due to low sensitivity of rectal/nose swab cultures

- As data is arranged according to the suggestions given in Q. No. 5 E. faecium is more resistant than E. faecalis which is obvious.

9. If you postulate that simultaneous colonization with enterococci and staph aureus might be a reason for emergence of VISA, please show data (own or from literature) and discuss, what your study adds in this respect.

- Reference from previous study has been added in the background section. The present study highlights the enhanced possibility of transfer of vancomycin resistance gene due to nasal colonization of resistant strains of enterococci.

Level of interest: An article of limited interest.

Quality of written English: Not suitable for publication unless extensively edited

General comment about the quality of the English:

- The quality of English has been improved, wherever required and should be in good shape for publication.

Statistical review: No, the manuscript does not need to be seen by a statistician.
Point-by-point response to reviewer’s comments:

Reviewer: Bin Cao

Reviewer's report: (Major Compulsory Revisions)

1. Background:
   • The significance of the study was not clearly introduced.
   • Whether VRE nosocomial infections have caused severe disease burden in the hospital?
   • Have they experienced VRE or VSE outbreak in PICU in this hospital?
   • As they have isolated VRE and VSE in this PICU, what will they do next, such as isolation of colonized patients, hand hygiene?

Answer:
   • The significance of the study has been added in the background section.
   • Previously, there was no scientific study report available for this infection spreading in the vicinity. There is no outbreak of enterococci reported, but the study was conducted as a precautionary measures.
   • With this study, another study was conducted for co-colonization and co-existence of both organisms that is still in progress.
   • For hand hygiene, hand scrub solutions were installed in PICU to control the transfer of organisms to patients.

2. Methods: At the beginning, the authors should describe this was a prospective microbiological surveillance study. The authors should report how they choose the patients in PICU for collection of swabs, what are the inclusion and exclusion criteria of the study?

Answer:
   • Parameters and the criteria of selection have been added in the light of your kind suggestions.

3. Discussion: The most interesting finding of the study is the difference of VRE and VSE colonization between rural and urban area. But the authors did not discuss fully about it. The authors found patients with pneumonia and miscellaneous group were more likely to be colonized with VRE or VSE. But also the authors did not discuss in this part.

Answer:
• Sir, the particular parameters have been discussed with the relevant references in the particular section.

4. Statistics: The comparison of VRE and VSE isolation ratio between rural and urban area should be described in statistic methods part.

Answer:
• Now it has been described well.

**Minor compulsory revisions**

1. misspelling: Abstract part 1: pathogne should be pathogen
   • Spelling errors has been removed from the manuscript.

2. MIC determination method: disc diffusion method and agar dilution method was described in abstract, but not in Methods part.
   • Now it has been added. Thank you

3. Figures 1-3 did not give more information than text. They can be removed from the paper.
   • Figures have been removed.

4. Table 4 was not reported cleared and should be re-written.
   • It has been done now.

Level of interest: An article of limited interest.

Quality of written English: Not suitable for publication unless extensively edited

The quality of English has been improved, wherever required and should be in good shape for publication.

Statistical review: Yes, and I have assessed the statistics in my report.