Author's response to reviews

Title: Clinical characteristics and risk factors for enterococcal infections in Nagasaki, Japan: a retrospective case-control study

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Author's response to reviews: see over
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Dear Sir/Madam (Editor in Chief of BMC Infectious Diseases),

Thank you for handling the reviews of our manuscript, “Clinical characteristics and risk factors of enterococcal infections in Nagasaki, Japan: a retrospective case-case control study”.

We have dealt with the reviewer’s comments and submitted the revised text. The revised word or sentences are enhanced by red color.

We believe that the findings of the current study are relevant to the scope of your journal and will be of interest to its readership.

This manuscript has not been published or presented elsewhere in part or in entirety, and is not under consideration by another journal. All the authors have approved the manuscript and agree with submission to your esteemed journal. There are no conflicts of interest to declare.

Thank you for your consideration. I look forward to hearing from you.

Sincerely,

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Response to Reviewer’s comments

Reviewer #2:

MAJOR COMMENTS

The article focuses on an argument which is relevant for the BMC Infectious Diseases journal and also specifically for nosocomial infections. The English language and writing level is sufficient.
The authors carried out a case-control study to describe clinical characteristics and risk factors for enterococcal infections in a teaching hospital in Japan.
The main finding was that abdominal surgery, structural abnormalities of the urinary tract and use of in situ devices are the most significant risk factors for enterococcal infection.
The study adds useful regional epidemiological information (Japan), and the findings are important to those with related research interests.

Background

1) Page 6, line 80: include one more specific reference (Orsi GB, Ciorba V. Vancomycin-resistant enterococci healthcare infections. Ann Ig 2013; 25 (6): 485-492);

Response: We added the reference according to reviewer’s suggestion (Page 5, line 77) and described the sentences about the added reference in discussion.

→ In addition, the resistance to anti-MRSA drugs, especially the increasing prevalence of vancomycin-resistant enterococci (VRE) present in nosocomial infections, has become a major problem in the United States and Europe [5]. (Page 13, Line 228-231)

Results

2) Page 10, lines 134-138: the phrase is not very clear, … “there were 583 Enterococcus spp case isolates…These corresponded to 181 infected patients …; moreover, 390 cases were colonized”. 181 infected patients + 390 colonized should be 571, please explain;

Response: We added the explanation as bellows in materials and methods according to the reviewer’s suggestion.

A total of 571 cases positive for Enterococcus spp. and 583 isolates were analyzed included twelve duplicated cases (the patients enterococci re-isolated over 3 months after first isolation or multiple enterococci isolation from a patient). (Page 6-7, line 97-99).

Discussion

3) Overall the Discussion looks a bit too long for the reader and needs to be shortened.

Response: We shortened the discussion according to the reviewer’s suggestion.

4) References cited in the Discussion do not appear in order. After reference number (7) in page 8 in the discussion page 13 line 204 appears reference (20), please check. Also reference (18) appears after reference (20).

Response: We checked and renumbered the references according to the reviewer’s suggestion.

References

5) There are seven references (11, 19, 21, 22, 23, 24, 36) I could not find in the manuscript text. If they have been eliminated during corrections please cancel them. Also renumber appropriately all references as described in the “Instruction for Authors”;
Response: We deleted six references, and renumbered according to the reviewer’s suggestion.

Minor essential revisions
1) Page 6, lines 86-87: “This study aimed to describe epidemiology, clinical characteristics and risk factors for enterococcal infections” please correct;  
Response: We revised the word according to reviewer’s suggestion (Page 5, line 85-87).

2) Page 7, line 94: “….an 862-bed tertiary care and teaching hospital…” please correct;  
Response: We revised the word according to reviewer’s suggestion. (Page 6, line 93).

3) Page 10, lines 145-148: data already reported in the Table 1 should not be repeated in the text. You might briefly underline something you consider important. Please cancel all repeated data;  
Response: We revised the sentences according to reviewer’s suggestion. (Page 9, line 150-152).

4) Page 13, line 210: “….from 2010 to 2011 …” or “…during 2010-2011….“ please correct;  
Response: We revised the word according to reviewer’s suggestion. (Page 13, line 215).

5) Page 13, line 211: “….indicating this complication incidence is high at 42% …” please correct;  
Response: We revised the sentence according to reviewer’s suggestion. (Page 13, line 215-216).

Reviewer #3:
Kajihara et al performed a retrospective case-case control study to determine the clinical characteristics and risk factors associated with enterococcal infections in Nagasaki, Japan.

Major:
1. Tables 1 & 2: Please provide chi square analysis between E. faecalis and E. faecium variables to determine if the differences are statistically significant or not and add P values to the text.  
Response: We added the statistics of Bonferroni post-hoc test and mentioned in materials and methods, revised the sentences according to the reviewer’s suggestion.

   —“In intra-peritoneal infections after liver transplantation, the number of E. faecium infections was significantly more than that of E. faecalis infections (p < 0.001). On the other hand, In urinary tract infections, the number of E. faecalis infections was significantly more than that of E. faecium infections (p = 0.016). (Page 8-9, Line139-143).

   —“Compared with E. faecalis, bone marrow and stem cell transplantation were significantly common in E. faecium infections (p = 0.027). (Page 9, Line156-157)
We determine the results of chi square analysis between E. faecalis and E. faecium in Table 2.

2. Line 127: Please explain how colonization vs infection were determined.
   **Response:** We were defined as infections a patient with clinical symptoms (temperature > 37.5°C and organ-specific symptoms), laboratory data (white blood cell count > 9100/mm³ and C-reactive protein > 0.17 mg/dL; standard criteria of our hospital), and bacteriological tests (monomicrobial culture or the same organisms isolated from two organs). And we were defined as colonization a patient with Enterococci positive culture, without no clinical symptoms and laboratory data. (Page 6, line 102-111).

3. Was there a link between colonization and the risk of acquiring infection?
   **Response:** We added the following sentences in Introduction according to reviewer’s suggestion.
   —"Previous reports have shown pharyngeal or intestinal colonization of enterococci were the risk factors for enterococcal bacteremia which is associated to increase the mortality particularly in the immunocompromised patients (Page 5, Line 79-82)."

4. Please common on the lack of VRE isolated from this study. What is the VRE prevalence rate at the institution?
   **Response:** In this study no VRE was isolated at our hospital during 2010-2011. In Japan the rate of VRE is very low (reference number 12,20).

Minor:
1. Line 42: Should be: …patients with Enterococcus spp infection…
   **Response:** We revised the word according to reviewer’s suggestion. (Page 3, line 39).”

2. Line 87: Remove “as” from the sentence.
   **Response:** We revised the sentence according to the reviewer’s suggestion. (Page 5, line 85-87).

3. Line 122 under Statistical Analysis: There should be at least a count of 10 in any category to determine statistical significance and not the use of 5 as described.
   **Response:** Thank you for your suggestion however we consider the statistical analysis made by using the SPSS with expected count < 5 is common (e.g.: Launes C, et al. Clin Microbiol Infect. 2013). If there are another statistical problems for our results, please don’t hesitate to contact us and give us your suggestion.

4. Line 137: Please rephrase the sentence. …; moreover, 390 patients were colonized with Enterococci.
   **Response:** We revised the word according to reviewer’s suggestion. (Page 8, line 139-141).

5. Line 139: Insert “and” between abscess discharge and blood.
   **Response:** We revised the word according to reviewer’s suggestion. (Page 9, line 145).
6. Lines 146-148: Rearrange comorbidities from the most common to the least common in the sentence.  
**Response:** We revised the sentences according to reviewer’s suggestion. (Page 9, line 150-152).

7. Please combine tables 3-5.  
**Response:** We combined Table 3-5 and renamed table 3 according to reviewer’s suggestion.

8. Line 208-212: The sentence needs to be reworded especially the ending.  
**Response:** We added the sentence according to reviewer’s suggestion.  
→There was significant relationship between liver transplantations and infections with E. faecium compared to E. faecalis. (Page 16, line 276-277).

9. VanA and VanB need to be corrected in the manuscript. There is no space between Van and the determinant.  
**Response:** We revised the word according to reviewer’s suggestion. (Page 13-14, line 230-231).