Author's response to reviews

Title: Risk factors for multi-drug resistant Acinetobacter baumannii bacteremia in patients with colonization in the intensive care unit

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Author's response to reviews: see over
Dear Saad Nseir

RE: MS. No. 1044398363730395

Title: Risk factors for multi-drug resistant *Acinetobacter baumannii* bacteremia in patients with colonization in the intensive care unit

Thank you very much for reviewing our manuscript. We appreciate your advice about the revision and are very pleased to inform you that we are ready to resubmit our second revised manuscript taking into account your comments. All significant changes have been written in red colored text. Thank you again for your kind review and we await your feedback and acceptance.

Sincerely yours,

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The authors provided a revised version of their manuscript. I still have several major concerns regarding this manuscript.

1. In the revised manuscript, authors stated that the study was performed during an outbreak period. Although this might explain the very high rate of AB bacteremia, this statement is confusing and merits further comment. I am not sure that risk factors for AB bacteremia during an outbreak period could be generalized to ICUs without outbreak related to this bacterium. Further, how comes that this outbreak was present during a 2-year period? What was the source, and what were the actions taken to try to stop it? Moreover, authors should clearly state in the abstract that the study was performed during an outbreak of AB.

Reply : We agree with the reviewer that risk factors for AB bacteremia during an outbreak period in this study could not be generalized to ICUs without outbreak. Therefore, we have stated this limitation in the manuscript (page 16, line 12). The source of MDR AB was from the index patients with pneumonia transferred from other tertiary hospital. We assumed that environmental contamination was occurred during the weaning period. When the outbreak of AB was recognized, the infection control committee held a meeting to evaluate the situation and recommended infection control measures as followings : hand washing, maximal barrier precautions for the operator performing invasive procedures (hand washing, wearing a cap, mask, sterile gown and gloves) and for the patient (covered from head to toe with a sterile drape with a small opening for the site of insertion) during invasive procedure, removal of invasive devices as soon as possible, use of closed suction catheter for prevention of environmental contamination. After these efforts have been encouraged and monitored, overall number of MDR AB bacteremia has been decreasing although the number seems to fluctuate from month to month. As the reviewer suggested, we have added this study was performed during an outbreak of AB in the abstract (page 2, line 11).

2. It remains unclear, at least to me, how patients were included. What were inclusion criteria, and when screening for AB was performed to detect ICU-acquired AB colonization? Authors stated that screening for AB was performed on ICU admission, that no screening was performed during ICU stay, and that microbiologic examination was performed when infection was suspected. Therefore, how colonization related to AB was identified? According to methods described by the authors only infection related to AB could have been diagnosed. Inclusion criteria should be clarified, and a figure with study profile should be provided.

Reply : First screening cultures were performed at the time of ICU admission then additional culture were performed every 4 to 5 days and when the infection signs existed. Inclusion criteria are the patients who were isolated with MDR AB without evidence of infection in ICU. If the MDR AB was isolated when the infection signs existed, we considered it as infection with MDR AB and excluded these patients in this study. Moreover, the patients who were already isolated with MDR AB before admitted to ICU or stayed in ICU less than 48 hours were excluded as well. As the reviewer suggested, we have made a figure to clarify the study population (page 7, line 1), and added more information about the additional cultures (page 6, line 12). Moreover, to avoid confusion, we have changed from “colonized” to “isolated” (page 6, line 20).

3. Authors should add a comment on how invasive procedures could simply reflect a higher
severity, and may not be a risk factor per-se.

Reply: There is no objective evidence that more invasive procedures could reflect a higher severity of the disease as the reviewer suggested. Therefore, we have deleted the phrases about this statement as below.

……even with a short duration of stay, patients with a high severity of disease requiring acute care and those maintaining mechanical ventilation and receiving invasive procedures developed bacteremia more frequently…… (page 15, line 16)

4. Authors stated that trans-tracheal aspirate was performed at ICU admission and during ICU stay to diagnose infection. Trans-tracheal aspirate is an invasive procedure and is not currently recommended. Do they mean endotracheal aspirate?

Reply: We are sorry to make you confused with the name of aspirate. As the reviewer pointed out, we meant the endotracheal aspirate. We have corrected all the trans-tracheal aspirate to endotracheal aspirate (page 6, line 11 and page 7, line 2).

5. Definition of colonization should be given.

Reply: We have added the definition of colonization in the Methods (Page 7, line 15).

6. Statistical methods: authors should state that distribution of continuous variables was tested, and that normally and non normally distributed variables are presented as mean ± Sd, and median (interquartile range), respectively.

Reply: We have revised the method of statistical analyses (page 9, line 11), and corrected the data in Table 2 (page 27) as the reviewer suggested.

7. Page 14, line 15: the paragraph on tracheostomy is out of the scope of the article and should be deleted.

Reply: We have deleted the sentences as the reviewer suggested.

8. Table 1: OR for APACHE II: per point?, OR for duration of MV: per day?

Reply: The reviewer probably meant Table 2 instead of Table 1. We have corrected the row headings in Table 2 (page 27) to give more precise information.

9. Table 5: percentage of patients with antimicrobial treatment should be provided in the two groups.

Reply: In Table 5 (page 33), the left column shows the number (percentage) of prior exposure antibiotics and the right column shows the duration of exposure in the two groups. We are sorry to make the reviewer confused about the table due to combining these data in one table. We have corrected the column and row headings in Table 5 (page 33) to give more precise information.