Author's response to reviews

Title: A risk factor analysis of healthcare-associated fungal infections in an intensive care unit: a retrospective cohort study.

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Author's response to reviews: see over
Dear Editor,

We have made some changes in the revised manuscript entitled “A risk factor analysis of healthcare-associated fungal infections in an intensive care unit: a retrospective cohort study” No.6350974047086425; and upload it through the website. The newly added contents are covered with yellow shadow. We add a new author “Liang-yu Chen” as the fifth author. He is one of our team colleagues and helped with data analysis and tabulation. A point by point response to the concerns of the reviewers is listed on the following pages.

Thank you very much for the kindest help.

Best regards.

Su-pen Yang.
For Reviewer BITAM Idir,

Thank you very much for the comments. We have made some changes in the revised manuscript. The newly added contents are covered with yellow shadow. A point by point response is listed as the followings:

1. The authors identify the species of Candida, while there is no specialist in mycology among the co authors even in the acknowledgments.

   **Response:** Thank you for the reminding. We have addressed this in the acknowledgements that “We thank Wan-May Lin in the Department of Clinical Mycology Laboratory, Taipei Veterans General Hospital, for identification of the fungi during the study period.” (page 21)

2. Page 4: give the fungal species isolated and identified in the results

   **Response:** Thank you for the reminding. We have added the fungal species isolated and identified along with their rates in the results of the text (page 13) and abstract (page 4).

3. give the species of fungus isolated in the abstract

   **Response:** Thank you for the reminding. We have added the fungal species isolated and identified along with their rates in the results of abstract. (page 4)

4. Reference 9 is not complete

   **Response:** The citation of reference 9 and 22 (articles from the journal of BMC Infectious Diseases) are according to the website of BMC Infectious Diseases; eg. *BMC Infect Dis 2009, 1:115.* refers to article 115 (not pages) from Volume 1 in 2009 of the journal.

Thank you very much for the kindest help.

Best regards.

Su-pen Yang
For Reviewer Emmanuel Roilides,

Thank you very much for the comments. We have made some changes in the revised manuscript. The newly added contents are covered with yellow shadow. A point by point response is listed as the followings:

1. Although the authors refer to health-care associated infections, the risk factors they quote mainly refer to BSIs- however in the manuscript they do not even mention the rate of various infections (RTI, UTI, BSI, surgical site etc) in their patients. It would also be useful that the risk factor analysis is according to the type of infection. Moreover, the authors do not define criteria used for respiratory tract infections, as Candida infection of the respiratory tract is known to be difficult to prove. Similarly, they should define “sputum cultures" - how they were taken and in which patients (ventilated or not).

   **Response:**
   
   #1. We have revised figure 1, which now shows trend for various infections (UTI, BSI, pneumonia, SSI and other sites). We change “RSI” to “pneumonia” because all the cases of RSIs were nosocomial pneumonia cases. The rates of various infections are added in the results of the text. (page 12,14).
   
   #2. We analyze risk factors according to the type of infections; the results are shown in the revised table 2 and in the results of the text. (page 15)
   
   #3. We have added definitions of nosocomial infections for UTI, BSI, pneumonia and SSI in the methods of the text. (page 8,9,10)

2. There are some queries as to the data of the 11 patients the authors mention explicitly: in the third patient with two episodes of UTI, what was the time interval in between and in the fourth patient the 2 episodes of CVC tip and BSI 1 week later isn't it more likely to represent the same BSI?

   **Response:** Thank you for the reminding. In the third patient with two episodes of UTI, the time interval in between was 5 days. The urine culture was once sterilized between the 2 episodes. And indeed, in the fourth patient, the 2 episodes of CVC tip and BSI 1 week later should be treated as 1 episode of central line-associated BSI. However, there were no fungi identified in the environments of the fourth patient. That means yeasts were identified in the environments from the 3 patients with 2 episodes of fungal HAI; and not in the other 8 patients with single episode of fungal
3. Finally, as the authors have collected environment samples from patients with HAIs it would be useful to do so in the environment of patients without HAIs to see whether there were any differences.

   **Response:** Indeed. But alas, we did not collect fungal cultures from the environment of patients without HAIs. We have added this as limitation of our study in the discussion. (page 19)

4. Two other comments regarding their results are that it appears that the rise in HAIs is parallel to the rise of UTIs while BSIs increase to a much lesser extent and at the same time there is a rise mainly in C. albicans. How do they comment on that?

   **Response:** Thank you for the reminding. We have put this part “it appears that the rise in HAIs is parallel to the rise of UTIs while BSIs increase to a much lesser extent” into the results of the text (page 12) if you would agree. *Candida albicans* accounted for 63% of all the *Candida* species that cause fungal HAI during the study period; and the rise in *Candida albicans* in figure 2 (page 30) seems to be parallel to the rise of BSI in figure 1 (page 29). (page 13) We have described the secular trend of nosocomial candidemia in our hospital during 2000-2008 in a study published earlier, *C. albicans* accounted for 62% of candidemia hospital-wide.[1]

5. The authors state that " along this trend, these infections occurred more often in the non-neutropenic, critically ill patients than the traditional hosts..." apparently they mean more often than in the past, but this should be rephrased

   **Response:** Thank you for the correction. We have rephrased it on page 6.

   “Along with this trend, these infections occurred more often in the non-neutropenic, critically ill patients than in those patients who were neutropenic or had received organ transplantation in the past.” As English is not our mother tongue, we would be happy to have our manuscript edited and polished by the company recommended by the website of BMC Infectious Diseases as necessary.

Thank you very much for the kindest help.

Best regards.
Su-pen Yang

References