Author’s response to reviews

Title: Fecal carriage and molecular epidemiology of carbapenem-resistant Enterobacteriaceae from outpatient children in Shanghai

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Author’s response to reviews:

Dear Prof. Maria Hodges and Prof. Cecilia Devoto,

Thank you for your letter. We have acknowledged your and the reviewer’s comments and constructive suggestions, which are valuable for improving the quality of our manuscript. Based on your helpful comments and request, we have revised the manuscript raised by the reviewers, and the amendments are made in the revised manuscript. Then some explanations regarding the revisions of our manuscript are as follows.

Paul Lephart (Reviewer 2): Unfortunately, there seems to have been issues in interpreting the English grammar and usage changes I suggested in my previous review which utilized text strikethrough to indicate words that should be removed, as many of my fixes were not implemented properly at all. I have included examples below with parentheticals added as the strikethrough font is not displaying:

Answer: Thank you for your kind advice. We have tried our best to revised this manuscript for the English grammar and also ask a native people to help us. And changes have been made in revised manuscript and in the below. We hope that the revised version of the manuscript will meet the standard of you.
Page 3, line 29: Epidemiological information including patient demographics, prior hospitalization, and previous receipt of antibiotic therapy, and invasive operation during hospitalization was obtained from the medical records of each patient.

Answer: Thank you for your kind advice. Changes have been made in the revised versions (Page 3, line 30; Page 4, Line 1).

Page 6, line 3: By analyzing the patient data, The CRE strains were isolated from 32 individual children (19 male and 13 female) whose mean age was 1.3±1.5 years (rang: 1m-5y).

Answer: Thank you for your kind advice. Changes have been made in the revised versions (Page 6, line 4).

Page 6, line 14: The results of the antimicrobial susceptibility testing of the 32 CRE strains were are shown in Table 1.

Answer: Thank you for your kind advice. Changes have been made in the revised versions (Page 6, line 15).

Page 6, line 17: Tigecycline remained retained excellent activity…. 

Answer: Thank you for your kind advice. Changes have been made in the revised versions (Page 6, line 18).

Page 7, line 18: To the best of our knowledge, knowing about Investigation of the fecal carriage prevalence of CRE among outpatients from the community setting can help us to better understand the origin of CRE isolates responsible for outbreak events and contribute to control CRE dissemination.

Answer: Thank you for your kind advice. Changes have been made in the revised versions (Page 7, line 19-20).
* Page 7, line 25: ….which (add "may") may also explain also make an explanations of (delete "also make an explanations of ") the occurrence in community-onset cases

Answer: Thank you for your kind advice. Changes have been made in the revised versions (Page 8, line 1).

* Page 8, line 2: Last but only (delete "only", replace with "not") not least, CRE strains could spread via physical contact with other people and have the propensity to acquire genetic materials mostly in the form of plasmids and transposons, through horizontal gene transfer

Answer: Thank you for your kind advice. Changes have been made in the revised versions (Page 8, line 6-9).

* Page 8, line 10: The major resistant (delete "resistant", replace with "resistance") resistance mechanism of CRE is…

Answer: Thank you for your kind advice. Changes have been made in the revised versions (Page 8, line 14).

* Page 8, line 14: NDM-1 and its minor variants, as (delete "as", replace with "a") a class B carbapenemase first clinically isolated from a patient at a hospital in New Delhi, India, have (delete "have", replace with "has since") has since been identified all over the world and always (delete "always", replace with "only") only detected in E.coli and K.pneumoniae

Answer: Thank you for your kind advice. Changes have been made in the revised versions (Page 8, line 18-20).

* Page 8, line 20: As is known to all, (delete "as is known to all") NDM-1 producing K.pneumoniae are highly resistant pathogens with no effective beta-lactams, including recent ones such as ceftolozane tazobactam (delete "tazobactam", replace with "tazobactam") tazobactam and ceftazidime avibactam and the only one that works are (delete "are", replace with "is") is aztreonam

Answer: Thank you for your kind advice. Changes have been made in the revised versions (Page 8, line 24-27).
Page 9, line 1: Several STs were are clearly related to specific bacteria, which were prevalence and are prevalent all over the world.

Answer: Thank you for your kind advice. Changes have been made in the revised versions (Page 9, line 6-7).

Page 9, line 12: Deeply and Importantly, children with CRE strains in fecal samples are considered as a high risk group, which can spread CRE by intimate contact and travel.

Answer: Thank you for your kind advice. Changes have been made in the revised versions (Page 9, line 17-18).

Page 9, line 13: The origin of CRE isolates in these children remains unknown and it is the main drawback limitation that we don't know if the source of the described CRE carriage in these children is not the result of an adult transmission in the community or in the hospital.

Answer: Thank you for your kind advice. Changes have been made in the revised versions (Page 9, line 20-21).

Page 9, line 16: Also we know that children are at high risk for are at high risk for multi-drug organism carriage and further studies should be carried out to figure out evaluate the phenomenon of the original source of CRE strains.

Answer: Thank you for your kind advice. Changes have been made in the revised versions (Page 9, line 24-26).

In response to the lack of significance between the min, max and mean times of hospitalization for the CRE and non-CRE groups with recent hospital exposure; withholding this information because it does not fit with your presumption that recent hospital exposure is a risk factor is not appropriate in my opinion and should be included in the presented data. This could be included in your discussion (page 7, line 30) importantly showing that despite previous studies showing an increased risk of CRE carriage with hospital exposure, your study did not show the same. This interesting data presents itself for inclusion again in the final paragraph of your discussion when
you state that the main limitation of this study is that you do not know the source of the CRE carriage, particularly because you show that it is not tightly linked to hospital exposure alone! Including this data also lends support to your final statement that children with hospital exposure should perhaps be screened for CRE at discharge, as this data would help to definitively establish where acquisition of CRE is truly occurring: hospital exposure or community exposure…or perhaps acquisition occurs in both environments but exposure to antibiotics is the true key to acquisition, not simply hospital exposure alone!

Answer: Thank you for your kind advice. We agree that point mentioned above that despite the previous studies showed an increased risk of CRE carriage with hospital exposure, there is no significance between the min, max and mean times of hospitalization for the CRE and non-CRE groups with recent hospital exposure in this study. But exposure to antimicrobial agents in hospital setting might increase the risk of colonization. Changes have been made in the revised versions (Page 8, line 2-5).

Concerning about the origin of CRE isolates, screening for CRE at discharge may provide an explanation for this hypothesis. We also agree that point mentioned above and changes have been made in the revised versions (Page 9, Line 22-24; and Page 10, Line 2-3).

We hope that the revised version of the manuscript will meet the publication standard of BMC Infectious Diseases. We are looking forward to hearing from you soon.

Thank you and all the reviewers for the helpful advice.

Best wishes,

Sincerely yours,

Hong Zhang.

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