Author's response to reviews

Title: Emergence of Endemic Serogroup C Meningococcal Disease Associated with a High Mortality Rate in Hefei city, China

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Version: 4 Date: 16 April 2012

Author's response to reviews: see over
Dear Dr. Roselle Pangilinan,

Thank you very much for your letter and advice. We have revised the paper, and would like to re-submit it for your consideration. We have addressed the comments raised by the reviewers, and the amendments are highlighted in red in the revised manuscript. We also have correctly formatted our revised manuscript according to the journal style. The revised manuscript has been edited and proofread by a medical editing company in Hong Kong. We hope that the revision is acceptable, and I look forward to hearing from you soon.

With best wishes,

Yours sincerely,

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We would like to express our sincere thanks to the reviewers for the constructive and positive comments.

Replies to Reviewer 1

Needs some language corrections before being published
The revised manuscript has been edited and proofread by a medical editing company in Hong Kong.

Replies to Reviewer 2

Minor essential Revisions:

1. The numbers of the tables and figures do not coincide with the referrals in the text. Figure 1 is not even referred to in the text. Correction has been made in the revised manuscript and the missed figure 1 was added in the revised revised manuscript (page 8, line 153).

2. In results line 141 to 149, antibiotic susceptibility data is presented. The methods and breakpoints used were not given in the microbiology laboratory procedures. Think you for your comment and the methods of antibiotic susceptibility were added in the revised manuscript (page 5, line 102 to 108).

3. In the discussion from line 236 to 247 the authors speculate about capsular switching as a possibility for the emergence of serogroup C. There is no data presented from molecular tests to capsular switching. A discussion should discuss the results presented.

Several sentences have been added in the DISCUSSION (page 13, line 270 to 271) in the revised version to address this issue.
4. line 275 to 284 The Glasgow scoring system is mentioned and highly praised why was it not used with the clinical data available?

Actually, we first plan to use the Glasgow scoring system. However some of the factors (e.g., C-reactive protein and fibrinogen levels) were not routinely checked in our cases. Finally and regrettable, we give up to use the Glasgow scoring system for assessing the prognosis and mortality of meningococcal disease.

Replies to Reviewer 3

General:

1. The article lacks an abstract?

The article has an abstract.

2. The English is poor and needs to be revised throughout - spelling, grammar and general formatting.

The revised manuscript has been edited and proofread by a medical editing company in Hong Kong.

3. A mixture of different fonts were used in the tables and figure - looks like the
data were 'cut and paste' together.

Thank you very much for your finding. We indeed neglect this mistakes in our first draft, and we have adjusted the fonts of the tables and figure according to the journal.

Specific:

1. Page 1, line 7 - author affiliation is listed as 'Department of Center Laboratory'. Is this correct as it doesn't make sense?

   The affiliation is correct.

2. Page 3 - Methods - please indicate which area was sampled - only Hefei City? How many hospitals/clinics and during which years.

   All of the cases were sampled only in Hefei City. There are about 40 hospitals/clinics and only six hospitals have departments of infectious disease. Patients with meningococcal Disease were only admitted in one of above six hospitals.

3. Page 4, line 70 - 'as soon as possible' is quite vague - was it generally within several hours or several days?

   Actually, in our routine work, after a patient admission, the blood and/or CSF of the suspect N. meningitidis would be sampled before using antibiotics and those samples were sent to the bacteriology laboratory of Hefei CDC within several hours.
4. Page 4, lines 76-77 - please specify what methods were used for biochemical testing or cite appropriate reference. Which serogroups were detected by latex?

We cited an appropriate reference in the revised manuscript (page 5, line 98) and introduction. About the detection of serogroups by latex has been added (page 5, line 99 to 101).

5. Page 4, line 85 - which PCR method was used - please specify or cite relevant reference.

A appropriate reference was cited in the revised manuscript.

6. Page 5, line 102 - sentence is incomplete? ’….. assuming that the distribution of serogroups .....’ is what?

This sentence is redundant and has be deleted in our revised manuscript.

7. Page 6, line 114 - P<0.1 is not usually considered to be statistically significant. Is this correct or should it be P<0.01 or 0.05?

It should be P<0.05 and the mistake has be corrected in the revised manuscript (page 7, line 140).

8. Page 6, line 126 - Table 1 shows characteristics of meningococcal strains – not 'demographic characteristics of patients'.

Correction has been made in the revised manuscript (page 7, line 148 to 149).

The P value has been indicated in the revised manuscript (page 8, line 151).


The P value has been indicated in the revised manuscript (page 8, line 158).

11. Page 7, line 135-136 - incidence of serogroup C from 2008-2010 - please show individual incidences for the 3 years as 0.92-3.14 is quite varied and therefore confusing.

Modification has been made to show individual incidences of serogroup C from 2008-2010 in the revised manuscript (page 8, line 158 to 160).

12. Figure 1 - perhaps I missed it but this figure is not mentioned anywhere in the text?

Ideally, it should be referred to in the first paragraph on page 7.

The missed figure 1 was added in the revised manuscript (page 8, line 1153).

13. Page 7, line 141 - there were 845 cases in total and only 374 meningococcal strains? What happened to the remaining 471 - please clarify?

Actually, in our study, all of the cases were diagnosed by three methods and it was defined
in the Definitions.(page 6,line 110 to 115).

14. Page 7, line 142-145- penicillin nonsusceptibility is mentioned but no indication is given in the 'Methods' section as to how antimicrobial susceptibility testing was performed or which breakpoints were used?

Think you for your comment and the methods of antibiotic susceptibility were added in the revised manuscript(page 5,line 102 to 108).

15. Page 8 - age, sex and seasonal distribution - no age data are shown in Table2.

Please also clarify why numbers for serogroup A and C (lines 153-154) are different to those mentioned in Table 2.

Although no age data are shown in Table2, We indeed had showed the characteristic of age, sex and seasonal distribution in this section. What were showed in table 2 were the cases that had complete detailed clinical information available. So, The numbers in Table 2 are different to those. Mentioned in lines 175-176. and This was specially explained in page 10 line 202 to 203.

16. Page 9, lines 184-185 - this is shown in table 2 - not table 3 as indicated in the text?

Think you for your find and Correction has been made in the revised manuscript (page 10,line 204).
17. Table 2 - what is DIC and MOF? 'sequelas' should be 'sequelae'

The abbreviation of DIC and MOF was given a full name in page 11(line 216 to 218 )and Table2. The mistake about 'sequelas' had been corrected in the revised manuscript.(page 11,line 219 and Table2.).

18. Table 3 - the data should show characteristics/risk factors for serogroup A and C separately to assess whether there are any differences i.e. column showing mortality rate should be split into two - one showing data for serogroup A and the other for serogroup C.

Think you for your good advice. Firstly, we indeed split the death cases into two groups to study, but we found the obtained informations were vague and minor. So, we had taken the death cases as a whole to assess and found some valuable informations.

19. No mention is made of the reference by Zhou et al. published in Epidemiol. Infect. in Sept 2011 which describes epidemiological data from China over a 4-year period (2004-2007). Since this work appears to be an extension of that study and there is some degree of overlap, it should be mentioned either in the Introduction or Discussion.

The paper cannot be searched before we finished our study, so we did not made of the reference by Zhou et al. Actually, we had referenced a similar paper in our
Discussion. We also made the reference by Zhou et al in the revised manuscript (page 13, line 274).