Author's response to reviews

Title: The role of Sequence Type (ST) 131 in adult community-onset non-ESBL-producing Escherichia coli bacteraemia

Authors:

Yi-Hui Wu (wuyihui@gmail.com)
Ming-Fang Cheng (mfcheng@vghks.gov.tw)
Chung-Hsu Lai (ed101746@edah.org.tw)
Hsi-Hsun Lin (ed100233@edah.org.tw)
Chih-Hsin Hung (chhung@isu.edu.tw)
Jiun-Ling Wang (jiunlingwang@gmail.com)

Version: 4 Date: 10 October 2014

Author's response to reviews: see over
Dear Editor:
We are pleased to re-submit our manuscript entitled: “The role of Sequence Type (ST) 131 in adult community-onset non-ESBL-producing Escherichia coli bacteraemia “, for consideration as BMC Infectious Disease original article. A point-by-point description of the changes according to the reviewer’s opinion are shown as the following:

And about the isolates and medical record collection, we add the sentence in the Material and method: The study was done retrospectively and included patients older than 16 years old with at least one positive blood culture of ESBL-negative E. coli who were admitted to the E-Da Hospital during a one-year period

“Because the study was done via medical chart reviewing retrospectively and the pathogens were collected from the stock of the infectious isolates from the laboratory.”

The IRB waived informed consent requirements due to the research involves no more than minimal risk to the subjects and the waiver will not affect adversely the rights and welfare of the patients.

Response to reviewer:

Reviewer: Jorge Blanco
Reviewer's report:
This manuscript included new and interesting results. The manuscript is useful in its field. Furthermore, the topic is of potential interest to readers of BMC Infectious Diseases.
Major Compulsory Revisions: Some results in the results section are not the same as shown in Table 1. Please check and correct. Example: The day 30 mortality: ST131 18.2% vs non-ST131 12.5% P= 0.709 in results/ ST131 12.5% vs non-ST131 15% P=1.00 in Table 1. Another example: New ESBLEC infection in the following 2 years: ST131 18.2% vs 2.5% p < 0.05 in results/ ST131 20% vs non-ST131 2.5% P=0.038 in Table 1.

Answers:
Thanks for your comments. Some numbers in the result section were type-error. The numbers in the Table were correct. We have changed as the following:
P3. The Day 30 mortality rate was similar in the clonal group O25b/ST131 and non-clonal group O25b/ST131 (12.5% vs. 15 %, p=1.00),
P3. Patients infected with the clonal group O25b/ST131 were more likely to have
ESBL *E. coli* infection in the following two years than patients infected with the non-ST131 group (20% vs. 2.5% *p*<0.05)

Background

1. What is the first choice of antimicrobial therapy for complicated UTI or bloodstream infection?

   **Answers:**

   The first choice of antimicrobial therapy for complicated UTI or bloodstream infection in Taiwan are ceftriaxone, ciprofloxacin or levofloxacin. We have had this sentence in Introduction “In our institution, we often used 3rd generation cephalosporin such as ceftriaxone or fluoroquinolone such as levofloxacin or ciprofloxacin as 1st line empirical antibiotics for community-onset complicated UTI or gram negative bacillary bacteremia.”

Microbiological studies

2. You did not precise how you determined O25b positive *E. coli*. Please insert the reference 2 after “all O25b positive *E. coli*”.

   **Answers:**

   O25 positive *E. coli* isolates were determined by the PCR method described by Clermont et al. We have added this sentence on Page 2.

Results

3. The title of the result part is missing

   **Answers:**

   We have added the title.

4. You present many interesting results but you should organize the paragraph better because it is hard to read.

   **Answers:**

   We have divided the result into 3 paragraphs.

5. It could be interesting to give more details on the discordant antimicrobials. Which antibiotic was it?

   **Answers:**

   Nine cases (15%) received discordant antimicrobials before susceptibility data were available included levofloxacin (n=4), cephazolin (n=2), ceftriaxone (n=1), cefuroxime (n=1) and amoxicillin/clavunate (n=1). We have added this sentence in the Result Part (P2)
6. percentage for clonal group ST131 of the day 30 mortality are different in the text and in table 1 (18.2 % vs 15 % ???). Please correct it.

Answers:
Some numbers in the result section were type-error. The numbers in the Table were correct. We have changed.
P3. The Day 30 mortality rate was similar in the clonal group O25b/ST131 and non-clonal group O25b/ST131 (12.5% vs. 15 %, p=1.00),

patients infected with the clonal group O25b/ST131 were more likely to have ESBL E. coli infection in the following two years than patients infected with the non-ST131 group (20% vs. 2.5% p<0.05)

7. You say that “patients infected with the clonal group O25b/ST131 were more likely to have ESBL E. coli infection in the following two years than patients infected with the non-ST131 group (18.2% vs 2.5 % p<0.05).

First, the percentage 18.2 % is different in the text and in the table 1.
Second, this affirmation seems to be statistically proven but the number of patients is very low and moreover you didn’t compare the strains. You don’t give any informations on these strains. Are they of the same Sequence type 131 ? have they the same pulsotype ? you could do the pulsotype on these strains and compare it to the ST131 strains…
You should delete this sentence or give more data. This sentence is also in the abstract and should be deleted.

Answer:
We have change the sentence to “patients infected with the clonal group O25b/ST131 were more likely to have ESBL E. coli infection in the following two years than patients infected with the non-ST131 group (20% vs. 2.5% p<0.05) (data not shown). However, we don’t have the following ESBL E. coli isolates for further pulsotype study.” And we deleted the sentence in the Abstract.

Discussion
8. I don’t agree with the first sentence : “we have shown that O25-ST131 is the predominant clone in non-ESBL-producing E. coli bacteremia. It accounted for 5.9 % ...”
You tested 40 O25b negative clones and you found 12 ST95 (30%) and 6 ST69 (15%) … So you can’t say that ST131 is the predominant clone. Please change the sentence.

Answer:

We have changed to “we have shown that O25-ST131 is also the important clone in non-ESBL-producing E. coli bacteremia.

Table 3:

9. Why haven’t you included the antibiotic resistance of all O25b-ST131 negative strains in the table? As you compare differences between ST131 positive and ST131 negative strains, you lose information.

We have changed the Table 3 as the following and add a supplement table for all isolates.

Table 3. Percentage of antibiotic resistance in ST 131 clones and non ST131 clones in 60 cases of clinical study. (N=60)

<table>
<thead>
<tr>
<th>Resistance percentage (%)</th>
<th>O25b-ST131 N=20</th>
<th>Non O25b-ST131 N=40</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amox/Clavu</td>
<td>6(30)</td>
<td>12(30)</td>
<td>0.788</td>
</tr>
<tr>
<td>TMP/SMZ</td>
<td>14(70)</td>
<td>20(50)</td>
<td>0.141</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>7(35)</td>
<td>4(10)</td>
<td>0.018</td>
</tr>
<tr>
<td>Cefazolin</td>
<td>6(30)</td>
<td>5(12.5)</td>
<td>0.099</td>
</tr>
<tr>
<td>Cefmetazole</td>
<td>4(20)</td>
<td>1(2.5)</td>
<td>0.038</td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>2(10)</td>
<td>0(0)</td>
<td>0.107</td>
</tr>
<tr>
<td>Piperacillin</td>
<td>16(80)</td>
<td>26(65)</td>
<td>0.232</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>11(55)</td>
<td>6(15)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Note: Amox/Clavu denotes as Amoxicillin/Clavunic acid, TMP/SMZ denotes as Trimethoprim/sulfamethoxazole

No resistance of cefepime, imipenem, amikacin found in these two groups.

Supplement Table 1. Percentage of antibiotic resistance in ST 131 clones and non ST131 clones in all isolates. (N=371)
<table>
<thead>
<tr>
<th>Resistance percentage (%)</th>
<th>O25b-ST131 N=22</th>
<th>Non O25b-ST131 N=349</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amox/Clavu</td>
<td>7(31.8)</td>
<td>107(30.7)</td>
<td>1.000</td>
</tr>
<tr>
<td>TMP/SMZ</td>
<td>15(68.2)</td>
<td>148(42.4)</td>
<td>0.018</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>8(36.4)</td>
<td>41(11.7)</td>
<td>0.001</td>
</tr>
<tr>
<td>Cefazolin</td>
<td>6(27.3)</td>
<td>51(14.6)</td>
<td>0.110</td>
</tr>
<tr>
<td>Cefmetazole</td>
<td>4(18.2)</td>
<td>23(6.6)</td>
<td>0.042</td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>2(9.1)</td>
<td>15(4.3)</td>
<td>0.297</td>
</tr>
<tr>
<td>Piperacillin</td>
<td>18(81.8)</td>
<td>216(61.9)</td>
<td>0.06</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>13(59.1)</td>
<td>44(12.6)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Note: Amox/Clavu denotes as Amoxicillin/Clavunic acid, TMP/SMZ denotes as Trimethoprim/sulfamethoxazole
No resistance of cefepime, imipenem, amikacin found in these two groups.

Sincerely yours,
Wang Jiu-n-Ling