Author's response to reviews

Title: Drug-resistance in Streptococcus pneumoniae isolates among Spanish middle aged and older adults with community-acquired pneumonia.

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Cover letter

Dear Editor,

Please find enclosed the revised version of our manuscript entitled “Drug-resistance in Streptococcus pneumoniae isolates among Spanish middle aged and older adults with community-acquired pneumonia” (reference:1408777051232562).

In the present revised version of our manuscript, as Reviewer 1 mentions, we have added information on treatment of patients, so associations between susceptibility and outcome can be made. Furthermore, we have also provided data to estimate susceptibility according to new pneumonia breakpoints for intravenous penicillin (January 2008), and we emphasize in the conclusion that “considering the new pneumonia breakpoints, in our study almost all isolates were susceptible to intravenous penicillin”. In addition, in the present revised manuscript we have made all the minor essential revisions suggested by Reviewer 2.

Point-by-point response to Reviewer’s comments and changes introduced in the revised manuscript are provided below.

Yours sincerely,

Angel Vila-Corcoles
(corresponding author)
POINT-BY-POINT AUTHOR’S RESPONSE TO THE REVIEWER’S COMMENTS.

Reviewer 1: Michael Jacobs

Reviewer 1 report: No information was provided on treatment of patients, so associations between susceptibility and outcome cannot be made. The conclusion that, in the study area, resistance to penicillin among Streptococcus pneumoniae remains high, but such resistance does not result in increased severity or mortality is likely due to the fact that patients were treated with active agents, such as penicillin (based on the new pneumonia breakpoints, almost all isolates were susceptible) or a third generation cephalosporin.

*Authors’ response:

To increase the interest of the manuscript, as the Reviewer requires, in the present revised manuscript we have added two new paragraphs (at the end of the Results section) including information on antimicrobial treatments used among the total 104 case patients and according to cases with intermediate and high-resistance to penicillin. Furthermore, in the present revised version of our manuscript, we have extensively described characteristics associated in deaths occurring among patients with penicillin-resistant strains.

Furthermore, as the reviewer also suggests, in the present revised manuscript we have also provided information to estimate resistance and susceptibility to penicillin among our pneumococcal pneumonia cases based on the new pneumonia breakpoints and we have included a new paragraph in the Discussion section commenting on this concern. Thus, in order to facilitate estimations on penicillin resistance according to new pneumonia breakpoints, we have added a new line in the Results section which provides the exact value of MIC among each penicillin-resistant strain.

In addition, as the Reviewer also suggests, we have re-written the conclusion that said “in the study area, resistance to penicillin among Streptococcus Pneumoniae remains high...” and currently we emphasize that “considering the new pneumonia breakpoints, in our study almost all isolates were susceptible to intravenous penicillin”.

Finally, as the Reviewer mentions, in the present revised Discussion section we have added a new paragraph that says "... the low case-fatality rate observed among patients with pneumonia due to penicillin resistant strains could likely be due to the fact that patients were treated with active agents, such as penicillin or third generation cephalosporin".

Reviewer’s report

Reviewer: Fernando Saldias

Reviewer’s report:

The objectives posed by the authors are well defined, methods and results are
appropriate and well described, the manuscript adhere to the relevant standards for reporting and data deposition, and the discussion and conclusions are well balanced and adequately supported by the data.

Minor essential revisions

The manuscript has some imprecisions and mistakes in their draft that the authors should correct:

1. Page 5, paragraph 7: Penicillin-resistance in contemporary isolates was 21.2% (14/66).
   Author’s response: As it can be seen in the Results section and in tables 1, 2 and 3 there were 27 penicillin-resistant strains (15 penicillin-resistant strains in early isolates and 12 penicillin-resistant strains in contemporary isolates (9 strains with intermediate resistance instead of 11 strains and three strains with high resistance)). In the present revised manuscript we corrected this data in the results section and penicillin resistance in contemporary isolates remained 18.2% (12/66).

2. Page 7, paragraph 2. I disagree with the authors, there was not a higher percentage of penicillin-resistant pneumococcal pneumonia among patient with PSI classes IV-V than among classes I-III (see table 1: PSI classes IV-V was 74.1% in penicillin-resistant strains vs 76.6% in penicillin-susceptible strains).
   Authors’ response: Effectively, when we analysed penicillin-resistance pneumococcal pneumonia among patient with PSI classes IV-V versus among classes I-III there was not difference (28% vs 25%). As the reviewer suggest, in the present revised manuscript we have rewritten this paragraph in the discussion section.

3. Page 7, paragraph 5: Mortality rate associated to initial inappropriate treatment was 12.5% (1/8).
   *Authors’ response: Effectively, mortality rate associated to initial inappropriate treatment was 12.5% (1/8). This error has been corrected in the present revised manuscript.

   *Author's response: We are sorry. This mistake has been corrected in the present revised manuscript and now “Mufson et al manuscript” corresponds to reference 23.

5. Table 1. Third column. Chronic renal disease 7 (25.9%)
   Table 1. Fifth column. Chronic liver disease 9 (8.7%)
   *Author's response: We are sorry. This mistake has been corrected in the present revised manuscript.

6. Table 3. Fifth column. There is two missing penicillin-resistant strains in the
contemporary isolates. As described in results section, it should be 14 penicillin-resistant strains.

*Authors’ response: As we commented above, we made a mistake in the results section and there were 12 penicillin-resistant strains in contemporary isolates (9 strains with intermediate resistance instead of 11 strains and 3 strains with high resistance). We have corrected this data in the present revised manuscript.