Reviewer’s report

Title: Effect of metallo-beta-lactamase production and multidrug-resistance on clinical outcomes in patients with Pseudomonas aeruginosa bloodstream infection: a retrospective cohort study

Version: 2 Date: 16 September 2013

Reviewer: Barry Neish

Reviewer’s report:

This could be a very interesting piece of work. Unfortunately there are a number of major points outlined below that make interpretation of the data presented here difficult.

Major Compulsory Revisions

Study design and definitions paragraph 2-
The definition of multi-drug resistant Pseudomonas lacks an aminoglycoside. In the literature the most common definition consists of at least two beta lactams (usually a ureido-penicillin plus a cephalosporin and/or a carbapenem), a fluoroquinolone and an aminoglycoside. This definition is unusual because it lacks the aminoglycoside. Reference 18 used to define multi-drug resistance is in German, I am unable to comment on its appropriateness for this paper. See Falagas et al 2006, J.Med.Micro, 55(12):1619-1629 for a good review where the majority of definitions of multi-resistance includes an aminoglycoside.

MBL detection and susceptibility profiles paragraph 2-
34 isolates were tested for MBL production, no statement is made regarding the reasoning for this number.

Table 1-
Providing the zone sizes does not add anything to the interpretation, as a result this table is very confusing. Just providing number of antimicrobial resistant isolates with percentage in brackets would be enough.

According to EUCAST all Pseudomonas should at least intermediate to aztreonam, therefore using the authors definitions all Pseudomonas would automatically be reported as resistant to aztreonam prior to testing (intermediate reported as resistant).

Table 2-
Please show number of patients with each parameter and the percentage (to 1 decimal place) in brackets, please be consistent with the presentation of data.

The number of meropenem resistant isolates (28.32% =32 patients) does not match with the number of isolates tested for MBL=34 as stated in MBL detection and susceptibility profiles paragraph 2.
Study population characteristics paragraph 2 and Table 3-
Is the 4MRGN-PA group necessary? It is a sub-group of 34MRGN-PA and does not show any extra significance or add additional discussion points. I recommend removal of this group and only present MBL-PA and 34MRGN-PA.

Table 4-
This is an overly large and confusing table. It would help immensely to have the HR consistently presented to 2 decimal places only.
I don’t think the HR for discharge including the deceased patients is necessary. The same impact would be generated using only the HR for deaths and the discharge time of survivors.
The laboratory parameters are not discussed at all in the text therefore they should be removed.
Very few of the comorbid conditions show any significance, therefore they can be removed from the table and a line inserted in the results text saying that not significance observed with these conditions.
Together this reduces the size and complexity of the table.

Table 5-
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Discussion paragraph 1-
The authors state that MBL-PA BSI results in higher mortality, while this is true, no mention is made that there is also higher mortality with 34MRGN-PA, therefore this seems to bias the interpretation of the data towards increased significance of MBL and away from appropriate antimicrobial prescribing which should be the more central theme.

Minor Essential Revisions

Table 1-
Add e to the end of ceftazidim

Table 4and 5 titles-
It should read "Hazard ratios", not "rations".

Clinical outcomes paragraph 2-
No P-values mentioned for HR in multivariate models

Discretionary Revisions
Could discuss the standard empiric therapy for treatment of Pseudomonas infections and how that would be affected by an increase in MBL.

Impact of other resistance mechanisms, e.g. porin loss and active transport/export

**Level of interest:** An article of limited interest

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests