Reviewer's report

Title: Quantifying the clinical virulence of Klebsiella pneumoniae producing carbapenemase Klebsiella pneumoniae simultaneously though an in-vivo insect model and translated patient outcomes

Version: 1 Date: 17 September 2013

Reviewer: Jason J Pogue

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McLaughlin and colleagues present a very interesting analysis in an attempt to truly identify the attributable mortality with KPC bloodstream infections. While, I commend them for their translational approach, and do not necessarily disagree with their premise that it is the patient population that acquire KPC that are associated with mortality rather than the virulence of the organism, I think several limitations of these data limit the ability of the authors to make the conclusions that they do. The major issues are discussed below

1) Probably the most important issue with these data are that there are only 15 KPC BSI cases, and for the primary outcome of mortality there are only 12 events. This makes multivariate modeling with three variables nearly impossible. While it appears in table 4 it appears that the virulence score attenuated the independent risk of mortality with KPC, I do not think this is an appropriate interpretation of these data. By forcing three variables into the model the authors have made the model unstable. KPC falling out as a risk factor is more an artifact of too many variables (as seen by the extremely large confidence interval that on its upper end surpasses a 30-fold risk), rather than an effect of the virulence score. In fact, the virulence score has an OR of 1.01, suggesting that it had zero impact on mortality.

2) I would strongly consider using patients with ESBL infections as the source population for the controls. These patients are likely more similar to KPC patients and would serve as a better reference than pan-susceptible isolates. While a case-case control study is ideal for risk factor studies, it would not be appropriate as uninfected controls could not make it into the animal model.

3) What was the source of bacteremia in patients, and was it the same between the groups?

4) I would consider refocusing this study on the animal model. I find those data to be very intriguing and of interest. If the authors disagree with this then they will need to collect a larger sample of KPC patients to validate their model

Level of interest: An article whose findings are important to those with closely related research interests
Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

'I declare that I have no competing interests'