Reviewer's report

**Title:** Reappraisal of the outcome of healthcare-associated and community-acquired bacteremia: a prospective cohort study.

**Version:** 1  **Date:** 6 March 2013

**Reviewer:** Majdi Al-Hasan

**Reviewer's report:**

The manuscript examines the effect of healthcare-associated (HCA) acquisition of bloodstream infections (BSI) on mortality over a brief period of time in multiple hospitals in Spain. I have several comments about this manuscript.

**Major comments:**

1- The biggest issue here is that the mortality results were, in part, previously published (reference #10). In fact, the entire Table 1 is copied from the same reference, which the authors acknowledge. Is it really worth running a multivariable model to analyze mortality if there was no difference in the univariate model between HCA and community-acquired (CA) BSI as already shown in reference #10, Table 1 and mentioned in the Introduction section of the manuscript? The only interesting finding in the mortality analysis is that inappropriate therapy was associated with mortality, but this is not news.

2- It is obvious why there was no mortality difference between CA and HCA BSI in this report. First, more patients with HAC BSI had coagulase-negative Staph than CA BSI (10% vs. 5%). BSI due to coagulase-negative Staph is known to have very low mortality, if any. Second, it is almost certain that patients with HCA BSI received broader spectrum antibiotics than those with CA BSI. It would be interesting to show that difference in the manuscript.

3- It would be interesting to examine mortality for Gram-positive and Gram-negative BSI separately. I assume mortality is higher for HCA BSI due to Gram-negative bacilli than CA BSI due to Gram-negative bacilli, given higher proportions of BSI due to P. aeruginosa and Enterobacter spp in the HCA group. The limitation of this analysis is that the study may not have adequate power to detect the difference in mortality if stratified by Gram-positives and Gram-negatives.

4- My suggestion is to focus on the risk factors for inappropriate antimicrobial therapy in community-acquired (not community-onset) and HCA BSI in 2 separate models. This will help identify the group of patients with community-acquired BSI who should receive broader spectrum antimicrobial coverage. I agree with the authors that the time has come to expand the definition of HCA BSI to include patients with outpatient invasive (urinary) procedures, etc., to capture more cases of BSI due to resistant organisms that usually end up receiving inappropriate therapy (which is associated with mortality as in the current and past literature).
5- On the same note. It would be very interesting to explore the 23 patients with CA BSI who received inappropriate therapy in more detail. Did they receive a third-generation cephalosporin for P. aeruginosa or ESBL producing (or cefotaxime-R) E. coli or Klebsiella spp? Did they receive a fluoroquinolone for a FQ-R Gram-negative bacillus? Or did the majority of them receive no antimicrobial agents in the first 24h. It would be as interesting also to discuss antimicrobial therapy in detail for the 34 patients with HCA BSI who received inadequate therapy (how many did not receive antipseudomonal agents? How many did not receive vancomycin for empiric therapy of Gram-positive BSI? How many received FQ for FQ-R Gram-negative bacillus? etc.) This will generate very interesting data on why did some patients receive inappropriate therapy and provide opportunities for improvement. Summarizing this data in a table would be very useful.

6- Resistance: The study is not powered to examine antimicrobial resistance for any individual organism. For example, there were only 57 and 71 HCA and CA E. coli BSI (the most common organism) in the study, respectively. Fluoroquinolone resistance was clearly more common in HCA than in CA E. coli BSI (37% vs 25%) and methicillin resistance was more common in HCA than CA S. aureus BSI (27% vs 0%). Both were not statistically significant due to under power. That needs to be clearly stated in the Discussion section.

Minor comments:
1- Please use the term BSI throughout the title and text for consistency. You may use “bacteremia” as a key word.
2- I would use the term HCA, not HCA-CO, throughout the text to make things less confusing for readers.
3- Please define STROBE, SAEI and SAMPAC prior to first use.
4- The word “Enterobacteriaceae” is misspelled in Page 4, line 71.
5- Did the study run from October 1 to December 31? Please specify.
6- Please use “0” in Table 1 instead of “-“.
7- The authors cite the wrong reference for the Pitt bacteremia score (reference #19). They should cite one of the original papers that described or updated the score such as the one by Paterson DL, et al in Annuals of Internal Medicine in 2004.
8- Table 3: Regarding the odds ratio for Pitt score, is this per point or per the entire range?
9- Was BSI due to Candida spp included in the study. If not, then please mention this in the Methods section.

Level of interest: An article of importance in its field

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