Reviewer's report

Title: Characteristics of neonates with culture-proven bloodstream infection who have low levels of C-reactive protein (<10 mg/L)

Version: 2 Date: 20 April 2015

Reviewer: Roberto Santos

Reviewer's report:

I read with great interest the referenced manuscript. Kindly consider the following comments for corrections or rebuttal:

- Major Compulsory Revisions:
  1. Under CONCLUSION - can the conclusion simply answer the goal of the study i.e. to characterize neonates with culture proven BSI and CRP level ≤ 10 mg/L?

- Minor Essential Revisions:
  1. Under PATIENTS AND METHODS, 'Definitions' section - you may want to place spp (species) after Corynebacterium, Propionibacterium, Penicillium
  2. Under PATIENTS AND METHODS, 'Definitions' section - consider placing the microbiology assay system utilized in your hospital e.g. Vitek system, MALDI - TOF
  3. Under PATIENTS AND METHODS, 'Data on CRP' section - What's the limit of detection of CRP in your hospital? its coefficient of variation? if available
  4. Under PATIENTS AND METHODS, 'Data on CRP' section, last sentence of the last paragraph - There is a typographical error on 'intermediate (CRP 21 - 100 mg/L), this should be CRP 11 - 100 mg/L
  5. Under PATIENTS AND METHODS, 'Statistical analyses' section - I will leave it up to the journal's designated statistician the review of the appropriate statistical analyses utilized in this manuscript
  6. Under RESULTS section - Are there data available in your patients regarding the time CRP was obtained in reference to when clinical sepsis was recognized since the kinetics of CRP suggest it starts increasing by 6 hours and peaks at 48 hours (see INTRODUCTION section) suggesting that if CRP level was obtained too early it may be falsely low?
  7. Under RESULTS section - Are there data available in your patients regarding the liver synthetic function e.g. albumin since it may be possible that those premature infants with low CRP level do not have the substrate or with low hepatic reserve to produce CRP ab initio? Also, is it possible that these premature infants have no capacity to mount an immune response i.e. with low IL6 response affecting CRP level to be falsely low?
8. Under RESULTS section - if the levels of albumin are available in a subset of infants in your study, would it be possible to correlate it to CRP level?

9. Under RESULTS section, last paragraph before 'Microbiology' section - the episodes of BSI is significantly higher in the high CRP group versus low CRP group and not the intermediate CRP group?

10. Under RESULTS, 'Treatment and outcomes' section - instead of stating 'birth body weight' you may want to consider instead 'birthweight'

11. Under DISCUSSION, 3rd paragraph - can you provide the reference to the last statement

12. Under DISCUSSION, 3rd paragraph - the last statement provide some evidence why a subset of premature infants with culture proven BSI has falsely low CRP level

13. Under DISCUSSION, 4th paragraph - scientific name of organisms should be italicized e.g. Pseudomonas spp.

14. Under DISCUSSION, 4th paragraph - are there further identification of CoNS since some species e.g. S. lugdunensis behaves like S. aureus

15. Under DISCUSSION, 6th paragraph - can you provide reference for the 3rd statement

16. Under Table 1 - can you define NSD/CS under the table's legend?; in the legend section kindly check the spelling 'presences'

17. Under Table 2 - kindly correct 'Coagulase-negative Staphylococcus aureus', you may want to drop 'aureus'; under the legend, no need to capitalize the species name e.g. Neisseria meningitidis

- Discretionary Revisions: None

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

Site Principal Investigator, Duke Clinical Research Institute & Cempra Pharmaceuticals – Research Funding all paid to or will be paid to Albany Medical College, Albany, NY