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: 1 May 2015

Reviewer: Evelien Verstraete

Reviewer's report:

General comment: interesting topic; since CRP has low sensitivity it might be more interesting to look in all blood culture samples and compare CRP in blood culture proven with non-blood culture proven sepsis

Major compulsory revisions: difficult to read; not well structured; not always concise; need for more explanatory analyses (post hoc)

TITLE: The research is not solely conducted on neonates with low CRP levels, it is a comparison of groups

ABSTRACT
1. Results: ....tended to have; low CRP group; .....relatively more common: please give numbers
2. Results: In the methods, distinction is made for three groups, the results only reported on two of them, who are the high CRP group (is not defined in the abstract; abstract needs to be completely self-explanatory)
3. Conclusion: more caution in interpretation of the results; ..... to rule out sever sepsis....: add culture-proven sepsis, because this was your study population

METHODS
1. I miss a definition of clinical sepsis
2. I miss data on how many blood cultures are taken per year (any difference in indication practice during the study period?)
3. Any specialist service(s) of this university hospital? (important to know the study population)
4. Time interval of CRP measurement: I think you need to reduce the maximum time interval between measurement and blood culture sampling or better include only CRP measurements preceding sampling; now, if I interpret well, CRP measurements are included closest to blood culture sampling on the same day of sampling, so could be 23h after sampling; CRP rises steadily or quickly already after 6h so including a time interval of 23h might introduce bias.

RESULTS
1. Highlight the most important results (the ones you discuss) because you have too much overlap with Table 1 and Table 2.
2. Table 2: other subcategories of Gram-positive pathogens: CoNS; S. Aureus; Group-D Strep; Group-B Strep; other Strep

3. I am interested in the group of neonates (n=82) with an increased CRP response after antibiotic treatment: inappropriate treatment? Changes in clinical presentation? Specify median CRP and ‘a few days after’

4. Last sentence subtopic microbiology: Among 96 episode of CoNS HABSI… had CoNS in their blood cultures: CHECK!!! Also same sentence: …. without a CRP response….: CHECK!!!, I think you mean with a CRP response….

5. I would like to see the data on regression analysis plus Kaplan-Meier curves and I think it is better to do a post hoc analysis with birth-weight subgroups

DISCUSSION
Reorganize: start with mentioning your principal results; compare pathogen distribution with others; paragraph 2 is for introduction; flow needs to be improved; include discussion on post hoc analyses for better understanding of the results

Discretionary Revisions

INTRODUCTION
1. Add more and the major publication on incidence of late-onset BSI: Verstraete et al. (2014); Stoll et al. (2002)

2. Difficult to read: e.g. Although some studies have demonstrated…..

3. Add appropriate references on predictors for late-onset BSI; recently, a meta-analysis on predictive signs for healthcare-associated sepsis is published in Pediatrics: Verstraete E, et al. (2015)

METHODS
1. Episode of BSI was defined according to clinical criteria: which clinical criteria? Rephrase first sentence

RESULTS
1. Table 1: add median (Q1-Q3) where appropriate

DISCUSSION
1. p13 A high CRP level is predictably associated: what do you mean by predictably associated?

2. More appropriate comparison with late-onset sepsis studies: search for Modi et al. (2009); Mahieu et al. (2000)

Minor Essential Revisions

METHODS
1. For CoNS BSI….. blood culture positive for CoNS…: double info

2. Last sentence: intermediate group CRP 11 instead of 21

RESULTS
Table 1: insert n (%) in the table for every characteristic group (e.g. perinatal history, n (%); Clinical septic symptoms, n (%)

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

**Quality of written English:** Needs some language corrections before being published

**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