Author’s response to reviews

Title: Burden and Risk Factors of Invasive Group B Streptococcus Disease among Neonates in a Chinese Maternity Hospital

Authors:

Qunhua Ying (ssbx1972@163.com)
Shutan Wang (526141016@qq.com)
Xiuming Lou (290465240@qq.com)
Jinlong Ding (41041924@qq.com)
Jiefeng Ding (djfyd@163.com)

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Author’s response to reviews:

Dear Dr. Nath:

On behalf of my co-authors, we thank you very much for giving us an opportunity to revise our manuscript, we appreciate editor and reviewers very much for your positive and constructive comments and suggestions on our manuscript entitled "Burden and Risk Factors of Invasive Group B Streptococcus Disease Among Neonates in a Chinese Maternity Hospital" (INFD-D-17-01173R1). We have studied reviewer’s comments carefully and have made revision which marked in red in the paper. We have tried our best to revise our manuscript according to the comments. Attached please find the revised version, which we would like to submit for your kind consideration.

We would like to express our great appreciation to you and reviewers for comments on our paper. Looking forward to hearing from you.

Thank you and best regards,

Yours sincerely

Qunhua Ying

E-mail: ssbx1972@163.com
Dear Editors and Reviewers:

Thank you for your letter and for the reviewers’ comments concerning our manuscript entitled "Burden and Risk Factors of Invasive Group B Streptococcus Disease Among Neonates in a Chinese Maternity Hospital" (INFD-D-17-01173R1). Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our researches. We have studied comments carefully and have made some changes which we hope meet with approval. These changes will not influence the content and framework of the paper. Revised portion are marked in red in the paper. The main corrections in the paper and the response to the reviewer’s comments are as flowing:

Reviewer #1:

Special thanks to Dear Dr. Gassiep for your good comments and suggestion.

General:

There are many grammatical and punctuation errors throughout the manuscript.

Response: We deeply appreciate your consideration of our manuscript. We have tried our best to correct grammatical and punctuation errors throughout the manuscript and have had the manuscript reviewed by AJE.

There are many inconsistencies with reporting of data in numbers and or words, as well as including and excluding total numbers and percentages.

Response: It is really true as you suggested that we have made correction according to the Reviewer’s comments.

The results section was cumbersome and difficult to read.

Response: Considering the Reviewer’s suggestion, we have deleted some part and re-worded.

I agree with the authors comments that they methods of GBS detection at their facility are not sensitive given the samples taken and lack of enrichment. This may have led to a significant false-negative rate, and thus true incidence and outcome data may be skewed currently.
Response: It is really true as Reviewer suggested. We have made progress in sample taken since 2018. This may led to more screening positive and more prevention procedure. Data have not been collected.

Timing of antibiotics is pertinent and not included.
Response: We have re-written this part according to the Reviewer’s suggestion.

Susceptibility data was collected but not reported.
Response: We didn’t report because antibiotic resistance of GBS is similar to common reports. All the strains are sensitive to Penicillin G and ampicillin.

There are a number of statements that require clarification and or rewording as detailed below.
Response: We have re-written this part according to the Reviewer’s suggestion.

Changes:

Abstract
Line 32, the statements of “child” were corrected as “paediatric”.
Line 33, the statements of “death” were corrected as “mortality”.
Line 37, the statements of “incidences” were corrected as “incidence”.
Line 37, “The total writing of EOD & LOD” were added.
Line 39, We have re-written this sentence as “pneumonia accounted 63.1% (41/65) of EOD, and sepsis accounted 88.9% (8/9) cases of LOD”.
Line 41/41: "Predictors of mortality were sepsis and false negative screening." We are very sorry for our negligence of relevant statistics and have corrected it.

Keywords:
7. Line 50: I am uncertain that "burden" is a sufficiently targeted keyword. Could also consider "neonatal sepsis" as opposed to "neonates", and "GBS risk factors".
Response: We have made correction according to the Reviewer’s comments.
Methods:

Line 67: "Gynaecology and Obstetrics and Paediatrics." were corrected as “Gynaecology, Obstetrics and Paediatrics.”

Line 69: First use of abbreviation IAP, the total writing was added.

Line 69-74: We have added a reference according to the Reviewer’s comments.

Line 75: GBS disease incidence is higher in non-resident and membrane stripped mother. It was found in this study. We have added in the results section according to the Reviewer’s comments.

Study design:

Line 84: Reference about definitions of EOD & LOD were added.

Line 88: "and the two groups were matched on birth date." was deleted.

Microbiological identification and susceptibility testing:

Line 91: The statements of "NICU (neonatal intensive care unit)", were corrected as “neonatal intensive care unit (NICU)”. The same for CSF.

Line 94: "3D microbial system", were corrected as "BacT/ALERT 3D Microbial Identification System."

Line 95: "Positive blood culture bottles were subsequently plated onto Columbia blood agar…” were rephrased. And the company which agar sourced was added.
Line 96: "35 degrees" were corrected as “35°C”.

Line 97: "which were also plated onto Columbia blood culture bottles." were corrected as “CSF samples were inoculated into 3D blood culture bottles.”

Line 100: "GBS-like colony morphologies." was corrected as "morphology".

Line 100 - 102: "GBS was identified by positive Gram staining and presumptive identification by the CAMP test." Gram stain results & CAMP test results were clarified.

Data collection:
Line 106 - 122: All this information were deleted.

Line 112 - 114: This was deleted.

Line 115: "Maternal urinary tract culture was seldom performed." were removed to result point.

Statistical analysis:
Line 122: "are presented as the mean ± standard deviation (SD) or median." were corrected as “median (range)”.

Line 122 - 126: It is really true as Reviewer suggested that we had deleted the redundant description.

Line 127: All the “univariate” and “multivariate” were changed to “univariable” and “multivariable” respectively according to the Reviewer’s comments.
Results:

Line 143 - 147: We think the numbers of cases and delivery women annually are needed apart from the incidence presented in Figure 1. We are very sorry to better describe about them.

Line 150: We have clarified as “pneumonia accounted 63.1% (41/65) of EOD, and sepsis accounted 88.9% (8/9) cases of LOD, respectively.”

Line 151: "Nineteen (25.7%) cases occurred…” was deleted. We have checked consistent use of words and numbers.

Line 153 - 155: suggest writing as two sentences not one. Second sentence "39/74(52.7%) women who received IAP." No need to list all antibiotics listed in table.

Response: It is really true as Reviewer suggested and we have deleted it.

Line 156: "Antibiotic dose and exposure duration before delivery differed." were added.

Line 157: "26 women who underwent caesarean delivery and whose infant developed EOD,25…”

Response: Percentages were added with raw numbers.

Line 162: "though the results were poor", has been reworded.

Line 168: "LOD was 23 minutes (5minutes-6days) and 17days (7-51days), respectively." Statistical analysis data were added.

Line 157 - 183: could be streamlined, as it is currently difficult to read.

Response: We are very sorry for our poor English and have clarified again.
Line 189: "hospitalization among fatal cases was 4.83 days, which was less than the average…"
Response: This is from date of admitted into NICU, and difference between EOD & LOD were added.

Line 208: "and mothers' status as a native or migrant worker…" was reworded as “non-resident mother”.

Discussion:
Line 221: "Over the past decades, GBS has been recognized 221 as a main cause of neonatal…"
Response: A second reference more recent than 1973 to better clarify this statement was added.

Line 233: "Our study confirms that GBS is an important pathogen in fatal neonatal pneumonia…"
Response: Non-fatal neonatal pneumonia and sepsis without pneumonia were added.

Line 242: "because infants aged >1 month go to other general hospitals." Is the author's center specifically for neonatal care or also general pediatrics? If general, then it may not be due to the reason given in the text.
Response: We have corrected as our NICU is only for neonates aged < 1 month. Infants > 1 month maybe go to another local hospital too.

Line 243: "antibiotics at home may lead to negative culture results", there is no mention of antibiotic receipt pre-admission, and was this data collected?
Response: This data was not collected but taking antibiotics at home is common.
Line 245: "The higher incidence of EOD may result from our neonatal doctors thinking highly of diagnostic evaluations." This sentence is unclear. Also, it may not stand to reason, as it would appear that patients with suspected infection were investigated the similarly.

Response: We have made correction according to the Reviewer’s comments.

Line 246 - 247: "Wortham reported that 13% of early onset infections had no documented symptoms, including 9% who remained asymptomatic at 72 hours." What are the numbers for LOD and did the authors find a difference in their data?

Response: Wortham’s report was not refer to LOD.

Line 249 - 251: "they received a limited diagnostic evaluation (blood cell count and blood/throat swab culture). This resulted in early detection, early diagnosis and early treatment." These statements seem contradictory; as the authors mention "limited" evaluation, but then mention that this resulted in "early detection".

Response: “Limited ” was deleted.

Line 253 - 254: "and thus the prevalence of low pathogenic bacteria might be another factor", difficult to infer low pathogenic strains. Would suggest considering the combination of host-pathogen interaction. Also no strain data provided.

Response: It is really true as Reviewer suggested that we have re-written this part according to the Reviewer’s suggestion.

Line 254 - 256: "Clinically diagnosed meningitis accounted for 3/65 EOD and 2/9 LOD cases, respectively; this lower morbidity may be caused by a strain with low virulence." Firstly, the numbers are low in the LOD cohort. Secondly, was there a clinical outcome difference to suggest a difference in virulence?

Response: It is really true as Reviewer suggested that the reason is not clear.

Line 256: "CPS type III", first use of abbreviation, please expand.

Response: The complete spelling was added.
We appreciate for your warm work earnestly, and hope that the correction will meet with approval.

Reviewer #2:

Special thanks to Dear Dr for your good comments and suggestion.

REQUESTED REVISIONS:

1. Consider retrospective power calculation to check whether the study had enough significant power to detect the important difference

Response: It is really true the numbers are low in the LOD cohort. We understand that in the unconditional logistic regression model, the number of cases and controls should be at least 30-50 cases. When we calculate Risk factors for GBS- EOD the cases and controls should be enough. LOD cases and matched controls were not enough to conduct multivariable analysis. At the same time the P value was greater than 0.05 in the univariable analysis for GBS-LOD cases. Thus we can not find the risk factors for LOD.

2. Reporting of odds ration - consider reducing to two decimal places

Response: As Reviewer suggested, we have reduced to two decimal places.

3. For all results, it is usually preferable to refer to the Table first, before describing the results and not usually at the end.

Response: We have made correction according to the Reviewer’s comments.

4. 'Risk factors for early onset invasive GBS' lines 206 to 216. It is not clear whether odds ratios were coming from? The reported odds ratios are completely different from the ones reported in Table 4?

Response: We are very sorry for our negligence of this and have corrected them.
5. For the risk factors, it will be nice if the authors can also include the direction and magnitude of associations for all the odds ratios reported.

Response: We added an explanation of the direction and magnitude of OR in the "statistical analysis" section. The risk factors were ranked in OR order too.


Response: We have changed “univariate” and “multivariate” to “univariable” and “multivariable” respectively.

7. Study strengths and limitations not discussed.

Response: Because study strengths have been identified, we added limitations in the conclusion according to the Reviewer’s suggestion

Once again, thank you very much for your comments and suggestions.

Thank you and best regards,

Yours sincerely

Qunhua Ying

E-mail: ssbx1972@163.com