Author’s response to reviews

Title: Laboratory Confirmed Puerperal Sepsis in a National Referral Hospital in Tanzania: Etiological Agents and Their Susceptibility to Commonly Prescribed Antibiotics

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Author’s response to reviews:

Editorial Office
BMC Infectious Diseases

RE: POINT BY POINT RESPONSE TO REVIEWERS’ COMMENTS

Reference is made to manuscript number INFD-S-18-02886 entitled “Laboratory confirmed Puerperal Sepsis in a National Referral Hospital in Tanzania: etiological agents and their susceptibility to commonly prescribed antibiotics”.

I hereby submit the revised manuscript and point by point responses to reviewers’ comments. In addition to these responses, the changes made to revised manuscript are highlighted in blue font colour.

Reviewer 1 - A Rottenstreich

Abstract

Comment: PS-avoid this abbreviation

tertiary Hospital-capital letter is not needed

Data was->Data were.

Notice that a space is required between numbers and following parenthesis, here and throughout the manuscript.
Was mostly caused E.coli-the word by should be between caused and E.coli

Response: Thank you for these observations, the abstract has been revised to accommodate all suggested changes

Introduction

Comment: PS-avoid this abbreviation

PS has declined-PS rate has declined

Bacterial pathogens causing.-this sentence suffers from poor English

Too many vaginal examinations->excessive number

CS is a single most->is the single most

Diverse of pathogens-> a variety of pathogens

Response: Thank you for these observations, the section has been revised to accommodate all suggested change

Methods

Comment: WHO criteria-please provide more information here and also in the results section which criteria was fulfilled and in what proportion of patients. If patients received antimicrobial prophylaxis during labor for any reason (GBS prophylaxis, fever during labor, suspected chorioamnionitis)-were they eligible?

Response: Information regarding WHO criteria has been expanded in methods and results sections. We excluded only patient who was on antibiotic for more than 6 days from time of screening for recruitment eligibility. The section has been revised accordingly

Comment: Please provide detailed information regarding the recruitment process. How many patients were screened for eligibility? During labor, before labor, after labor? More information regarding the delivery itself should be included-were they delivered at your center? Other hospitals? In home? How many deliveries do you in your center per year?

Response: We have provided more detail regarding recruitment process and delivery. However, this study dealt with patients admitted for postnatal care with clinical diagnosis of puerperal sepsis. As indicated in result section majority were seen between 8 and 14 days post-delivery
Comment: What was the institutional protocol regarding culture collection (blood and endocervical, what about urine, surgical site?), empiric treatment given (is there any difference at your center between CS vs. vaginal delivery, prolonged rupture of membranes?), GBS prophylaxis, antimicrobial prophylaxis prior to CS.

Response: The information regarding institutional protocol for management of puerperal sepsis has been included in methods section. Only cesarean sections are given prophylactic antibiotics before delivery. There is no GBS Prophylaxis

Results

Comment: 17 women were excluded-so how were they eligible in the first place?? -not clear

Response: We have revised the result section to clearly indicate that 214 women were admitted with diagnosis of puerperal sepsis in the study time frame while 197 were recruited in the study.

Comment: Half followed vaginal delivery and half CS-more information regarding the delivery itself should be included-duration of rupture of membranes, CS-before or during labor, indication for CS, fever during labor

Response: We have included in result section more information regarding the delivery. However Majority of participants were referred from other facilities for postnatal care and details during delivery were lacking

Comment: About 20% had unfavorable outcome-what is the general percentage of the outcomes mentioned at your area

The general unfavorable obstetrics outcome in the same hospital is 5.1%.

Response: This information has been added in discussion to related with our findings

Comment: Different regimens of ABX were given-according to which criteria? Was this based on physician's discretion?

Response: There is no specific criterion for antibiotic prescription; the protocol is to use broad spectrum antibiotic combination for aerobic and anaerobic pathogen. The different regimens given were based on physician’s opinion and availability

Comment: Please provide data regarding neonatal infection in these women?
Response: The current study focused on aetiology of puerperal sepsis and susceptibility pattern. We recorded only the early unfavorable neonatal outcome. We take this comment for consideration in future research.

Comment: More information regarding the clinical course of patients should be given-which type of infection? Response to antimicrobial treatment-duration of treatment? Length of stay? Need for interventional procedures-drainage of abscess, laparoscopy/laparotomy? Complications-ICU admission, septic shock etc.

Response: We have provided some information regarding the clinical course of patients in result section. However the focus of this study was on aetiology of puerperal sepsis and susceptibility pattern. We plan to perform detailed analysis on clinical course of patients diagnosed with puerperal sepsis, after collection of more data.

Discussion

Comment: Should discuss recent important articles-Wilkie et al. Obstetrics & Gynecology 2019-Microbiology and antibiotic resistance in peripartum bacteremia-

Rottenstreich et al. CMI 2018-Risk factors clinical course and outcomes of pregnancy-related GAS infections

Response: The suggested references has been added and discussed as suggested

Comment: The limitation of lack of ability to detect anaerobic pathogens is discussed. A similar discussion should be mentioned regarding GAS-see above reference, and its important implications.

Response: We have revised the limitation to include discussion as suggested.

Comment: The phrase "we note" is used excessively.

Response: The phrase “we note” has been reduced by rephrasing the sentences.

Comment: Conclusions should appear after Limitations.

Response: We have rearranged, now conclusion appear after limitation.

Comment: Overall, I think the article provide some important findings. However, the aforementioned changes should be made in order to make it eligible for publications.
Response: Thanks for compliments and constructive comments provided. We have addressed all suggested changes.

Reviewer 2: Jennifer E Kaiser, MD, MA

1. It is not clearly stated until the limitations section that this study only investigated aerobic causes of puerperal sepsis. Adding this to the title, abstract, and concluding statements would provide clarity

Response: We have now stated in the abstract, and methods to indicate that the study only investigated aerobic cause of puerperal sepsis

Comment: Is it known what proportion of puerperal sepsis cases are due to aerobic vs anaerobic bacteria in similar populations?

Response: The proportion of puerperal sepsis cases due to aerobic vs anaerobic bacteria in similar populations is not known. This is due to limited facilities for anaerobic culture

2. Consider adding the larger aim of this study to the introduction (i.e. improve empiric treatment).

Response: The background section has been revised to add a statement of the large aim of the study

3. Did an IRB or equivalent approve the study?

Response: As indicated in the declaration section, the ethical approval for the study was obtained from the IRB (Senate Research and Publication Committee) of the Muhimbili University of Health and Allied Sciences

4. How was convenience sampling done - only women on certain wards or at certain times of day were approached for participation? Convenience sampling should also be a consideration in the limitations in terms of possible bias introduced using this sampling method

Response: Sampling of women for recruitment was done at Maternity wards only for those suspected having puerperal sepsis. The limitation has been revised to include a statement on convenient sampling

5. How many women in the study time frame were admitted with PS versus how many recruited?
Response: We have rephrased the result section to clearly indicate that 214 women were admitted with diagnosis of puerperal sepsis in the study time frame while 197 were recruited in the study.

6. How was the "required sample size" determined?

Response: Sample size was calculated using Kish Lisle formula; we have revised the methods section to add a statement on how the sample size was estimated.

7. Consider a participant flow chart. Were any women excluded for having received prophylactic antibiotics for cesarean section due to the exclusion criteria of antibiotic use within the past week?

Response: The participant flow chart provide summary of flow of participants through each stage of the study. We think our study has only two stages of which information is well presented in the result section. We excluded only patient who was on antibiotic for more than 6 days from time of screening for recruitment eligibility. The section has been revised accordingly.

8. Please clarify if blood and cervical cultures were collected prior to antibiotic initiation. The blood and endocervical samples for culture were taken prior antibiotics initiation.

Response: This information has been added to the methods section.

9. I am not familiar with what an "endocervix gator," but it is unclear whether endocervical cultures were obtained during a speculum exam with attention to avoiding vaginal contamination.

Response: gator-means anatomical area of endo-cervix. We have revised specimen collection subsection to indicate that endocervical cultures were obtained during a speculum exam.

10. Please define acronyms used (MRSA, ESBL)

Response: Definition of acronyms is available under List of abbreviations.

11. Consider expanding on generalizability in the discussion.

Response: Thanks for this comments, we have revised the discussion and conclusion to expand on generalizability.
12. Other limitations that need further consideration in the limits section: convenience sampling, overall sample size, small numbers of isolated bacterial species, and extrapolating treatment recommendations from these small numbers (i.e. Pseudomonas, Enterococci, etc).

Response: The limitation section has been revised to include these suggestions.

Comments from Editor

1. STROBE guidelines

Response: The STROBE guidelines has been followed.

2. Add consent to participate statement under the "Ethics approval and consent to participate" section

Response: The statement on consent to participate has been added in the Ethics approval and consent to participate section.

3. Rename the heading Ethics approval to "Ethics approval and consent to participate"

Response: The heading has been rephrased.

4. Role of funder

Response: It has been clearly indicated that the funder had no role in design, data collection, analysis and manuscript writing.