Decision Letter (JCQ-2025-0031)

From: [redacted]
To:
CC:
BCC:

Subject: Journal of Clinical Question - Decision on Manuscript ID JCQ-2025-0031

Body: 11-Oct-2025

Dear Dr Sakata,

Manuscript ID JCQ-2025-0031 entitled "Recurrent Late-Onset Group B Streptococcal Invasive Infection: Prevention of Further Recurrence with Oral Ampicillin Prophylaxis in Family Members" which you submitted to the Journal of Clinical Question, has been reviewed. The comments of the reviewer(s) are included at the bottom of this letter.

The reviewer(s) have recommended publication, but also suggest some revisions to your manuscript. Therefore, I invite you to respond to the reviewer(s)' comments and revise your manuscript.

To submit your revised manuscript, follow the below steps.
1. Access to https://mc.manuscriptcentral.com/jcq and log into the site.
2. Click "Author" at the top left of the screen at "Home" page.
3. Click "Manuscripts with Decisions" on Author Dashboard page.
4. Click "create a revision" on the manuscript you are going to revise.
5. The system creates your revision manuscript form. Provide your comments about the revised points at the response field, fill in on each field step by step as same as you did for the original submission, and submit your revised manuscript.
IMPORTANT: Your original files are available to you when you upload your revised manuscript. Please delete any redundant files before completing the submission.
Your manuscript number has been appended to denote a revision.

You will be unable to make your revisions on the originally submitted version of the manuscript. Instead, revise your manuscript using a word processing program and save it on your computer. Please also highlight the changes to your manuscript within the document by using the track changes mode in MS Word or by using bold or colored text.

Once the revised manuscript is prepared, you can upload it and submit it through your Author Center.

When submitting your revised manuscript, you will be able to respond to the comments made by the reviewer(s) in the space provided. You can use this space to document any changes you make to the original manuscript. In order to expedite the processing of the revised manuscript, please be as specific as possible in your response to the reviewer(s).

IMPORTANT: Your original files are available to you when you upload your revised manuscript. Please delete any redundant files before completing the submission.

Because we are trying to facilitate timely publication of manuscripts submitted to the Journal of Clinical Question, your revised manuscript should be uploaded as soon as possible. If it is not possible for you to submit your revision in a reasonable amount of time, we may have to consider your paper as a new submission.

Once again, thank you for submitting your manuscript to the Journal of Clinical Question and I look forward to receiving your revision.

Sincerely,
Richard Isaacs
Journal of Clinical Question
jcqeic@gleampub.com

[Editor's Comments]
Associate Editor
Comments to the Author:
1. Check grammar and flow for minor errors.
2. Ensure all abbreviations are defined on first use in both abstract and main text.
3. Add ORCID IDs for authors if available

[Reviewer(s)' Comments]
Reviewer: 1

Comments to the Author
Major Comments
1. Introduction (line 51): Incidence statement
The frequency of recurrence is given as 1.4–3.7%, but the denominator is not specified (e.g., percentage of all GBS cases? neonates screened? hospital cohort?). Please clarify the population studied to allow readers to interpret this statistic correctly.
2. Maternal GBS screening (line 64)
The timing of the maternal GBS screening is critical (e.g., 35–37 weeks vs. at delivery). Please state explicitly when and how screening was performed.
3. Case description details (lines 68–69)
o Anterior fontanelle findings should be described more clearly. Was bulging present on the first admission, or only during the second?
o Please clarify whether cerebrospinal fluid FilmArray (or other multiplex PCR panels) was performed to rule out co-infections.
o It remains unclear if repeat CSF studies were performed during the first and/or second episodes, and whether clearance of GBS from CSF was confirmed. This information is important for treatment adequacy.
4. Microbiology
o Both episodes yielded GBS serotype III; however, please explicitly confirm whether the second isolate was indeed serotype III (line 80). If molecular typing (MLST or clonal complex determination) was performed, include results; if not, state this limitation.
o Please state whether antimicrobial susceptibility testing showed any unusual features.
5. Immunological evaluation (line 85)
Immunological screening is briefly reported, but important details are missing. Were lymphocyte transformation assays or lymphocyte blastogenesis tests performed? Please clarify.
Also, was an ENT evaluation or imaging (e.g., sinus CT) undertaken to exclude structural abnormalities as a predisposing factor?
6. Household screening and intervention (lines 88–89)
You mention that family members were given oral amoxicillin. Please clarify:
o Were throat, rectal, or skin cultures obtained from the parents and siblings before treatment?
o What were the results?
o Who bore the cost of prophylactic treatment (hospital vs. family)? This point may be relevant from an ethical and practical standpoint.
7. Follow-up and prognosis (line 90)
You describe the outcome as "normal development to date." Please specify the duration of follow-up (e.g., 6 months, 12 months). A clear timeframe is needed to judge the prognosis.
8. Immunization status
Since immunodeficiency was considered, it would be valuable to present the child's immunization schedule and whether any delays or abnormalities were noted.

Minor Comments
1. Language and style
o Some grammatical errors (e.g., "stratagies" in the abstract, line 29) should be corrected.
o Consider shortening long sentences in the case presentation for clarity.
2. Figures and timeline
Figure 1 is informative, but it would benefit from clearer labeling of the two admission periods and treatments. Including CSF results on the timeline would enhance comprehensibility.
3. Discussion
The discussion appropriately references prior reports, but the limitations of this case (e.g., lack of comprehensive family culture data, absence of genotyping of isolates) should be emphasized more explicitly.

Reviewer: 2

Comments to the Author
The author presents research on Group B Streptococcus, which could be a major cause of invasive neonatal infection. Recurrent late-onset invasive GBS infection can be life-threatening. Therefore, preventive measures need to be improved.
Major comments:
1. We also need to pay more attention to the limitations of these methods. This is particularly important for newborns.
2. The author needs to provide their own suggestions in this manuscript.

Date Sent: 11-Oct-2025

Author's Response to Decision Letter for (JCQ-2025-0031)

Recurrent Late-Onset Group B Streptococcal Invasive Infection: Prevention of Further Recurrence with Oral Ampicillin Prophylaxis in Family Members

Dear Reviewers,
We sincerely thank you for your thorough and constructive comments on our manuscript. Your insights have been invaluable in enhancing the clarity and robustness of our study. Our point-by-point responses to your comments are provided below, along with the corresponding revisions made to the manuscript, in which the revised parts are shown in red.

Reviewer: 1
Major comments
1. Introduction (line 51): Incidence statement. The frequency of recurrence is given as 1.4–3.7%, but the denominator is not specified (e.g., percentage of all GBS cases? neonates screened? hospital cohort?). Please clarify the population studied to allow readers to interpret this statistic correctly.
Response: Thank you for your valuable comment. We have confirmed that the denominator represents the percentage of all infant invasive GBS cases. We have clarified this point in the revised manuscript (lines 54–55).

2. Maternal GBS screening (line 64). The timing of the maternal GBS screening is critical (e.g., 35–37 weeks vs. at delivery). Please state explicitly when and how screening was performed.
Response: We appreciate the review's thoughtful feedback. We have confirmed that maternal GBS screening was performed at 35 weeks of gestation by veginal and rectal swab culture, and the result was positive. We have revised the manuscript accordingly (line 67).

3. Case description details (lines 68–69). o Anterior fontanelle findings should be described more clearly. Was bulging present on the first admission, or only during the second?
Response: Thank you for your valuable comment. On the first admission, the anterior fontanelle was normal. We have added this information to the case description (line 70-71).
o Please clarify whether cerebrospinal fluid FilmArray (or other multiplex PCR panels) was performed to rule out co-infections.
Response: Thank you for your comment. We did not perform cerebrospinal fluid FilmArray or other multiplex PCR tests to rule out co-infections, because bacteremia was detected shortly after admission.
o It remains unclear if repeat CSF studies were performed during the first and/or second episodes, and whether clearance of GBS from CSF was confirmed. This information is important for treatment adequacy.
Response: Thank you for your valuable comment. During the second episode, repeat cerebrospinal fluid (CSF) studies were conducted. The first follow-up CSF study, performed one week after treatment initiation, showed a negative culture but persistently elevated cell count and low glucose levels. CSF examinations were subsequently performed at regular intervals, especially after the completion of antibacterial therapy. Until discharge, CSF cultures remained negative. We have added this information to the revised manuscript (lines 97-98, 99-100).

4. Microbiology. Both episodes yielded GBS serotype III; however, please explicitly confirm whether the second isolate was indeed serotype III (line 80). If molecular typing (MLST or clonal complex determination) was performed, include results; if not, state this limitation. Please state whether antimicrobial susceptibility testing showed any unusual features.
Response: We appreciate the reviewer's thoughtful feedback. The GBS isolates obtained from blood culture in both episodes, as well as the isolate from the cerebrospinal fluid culture of the second episode, were analyzed for serotype and sequence type. All three isolates were identified as serotype III. Multilocus sequence typing revealed sequence type 17. Antimicrobial susceptibility testing demonstrated susceptibility to PCG, ABPC, CTX, MEPM, CPFX, and VCM, but resistance to EM and CLDM. We have added this information to the revised manuscript (line 93-98).

5. Immunological evaluation (line 85) Immunological screening is briefly reported, but important details are missing. Were lymphocyte transformation assays or lymphocyte blastogenesis tests performed? Please clarify. Also, was an ENT evaluation or imaging (e.g., sinus CT) undertaken to exclude structural abnormalities as a predisposing factor?
Response: We appreciate the reviewer's helpful comment. Lymphocyte transformation tests showed normal proliferative responses to PHA (SI = 28.6) and ConA (SI = 44.7). We have added these data to the Case Presentation (line 87-89). Cerebrospinal fluid and blood tests were performed at discharge (mentioned at line 99-100), but no additional imaging studies were conducted before discharge.

6. Household screening and intervention (lines 88–89) You mention that family members were given oral amoxicillin. Please clarify: Were throat, rectal, or skin cultures obtained from the parents and siblings before treatment? What were the results? Who bore the cost of prophylactic treatment (hospital vs.

family)? This point may be relevant from an ethical and practical standpoint.
Response: We appreciate the reviewer's thoughtful feedback. Cultures were obtained only from the mother, and the results are described in lines 101–102. Due to institutional regulations, cultures could not be performed for the father and siblings. And we mentioned it in limitations (lines 156-158). The cost of prophylactic treatment was borne by the hospital.

7. Follow-up and prognosis (line 90) You describe the outcome as "normal development to date." Please specify the duration of follow-up (e.g., 6 months, 12 months). A clear timeframe is needed to judge the prognosis.
Response: Thank you for your valuable comment. We have added the follow-up information to clarify the developmental progress and duration. The patient showed normal developmental milestones: rolling over at 5 months, sitting without support at 8 months, walking independently at 11 months, and speaking words at 15 months of age. She continues to demonstrate normal development at 15 months of follow-up (line 106-109).

8. Immunization status. Since immunodeficiency was considered, it would be valuable to present the child's immunization schedule and whether any delays or abnormalities were noted.
Response: We appreciate the reviewer's helpful comment. The patient received all immunizations according to the national schedule without any adverse reactions. We have added this information to the Case Presentation (lines 104–106).

Minor comments
1. Language and style. o Some grammatical errors (e.g., "stratagies" in the abstract, line 29) should be corrected. o Consider shortening long sentences in the case presentation for clarity.
Response: We appreciate the reviewer's helpful comment. We have carefully revised the manuscript for grammatical accuracy and improved readability. The typographical error "stratagies" has been corrected to "strategies." In addition, several long sentences in the Case Presentation have been shortened to enhance clarity.

2. Figures and timeline. Figure 1 is informative, but it would benefit from clearer labeling of the two admission periods and treatments. Including CSF results on the timeline would enhance comprehensibility.
Response: We appreciate the reviewer's helpful suggestion. Figure 1 has been revised to clearly indicate the two admission periods and the corresponding treatments. In addition, CSF results have been incorporated into the timeline.

3. Discussion. The discussion appropriately references prior reports, but the limitations of this case (e.g., lack of comprehensive family culture data, absence of genotyping of isolates) should be emphasized more explicitly.
Response: We appreciate the reviewer's insightful comment. We have added a statement in the Discussion to more clearly emphasize the limitations of this case, including the lack of comprehensive family culture data (lines 156–160).

Reviewer: 2
Major comments
1. We also need to pay more attention to the limitations of these methods. This is particularly important for newborns.
Response: We appreciate the reviewer's helpful comment. We have added a statement in the Discussion to emphasize the limitations of current preventive methods (lines 156–160).
2. The author needs to provide their own suggestions in this manuscript.
Response: Thank you for your valuable comment. We have revised the Clinical question box and conclusion to include our own suggestions for the prevention of recurrent invasive GBS infection, particularly in cases without immunological abnormalities and with negative maternal GBS screening results (lines 22–26, 168–169).

Best Regards

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