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OPEN PEER REVIEW

Primary Carrier Status and Alteration in the Colonization of the Extended-Spectrum β-Lactamase Producing *Enterobacteriaceae* Among Children in Pediatric Intensive Care Unit During the Hospital Stay

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About this report

This open peer review (OPR) report shows the public comments made on this article during peer review, by the reviewers, the associate editor and the editor-in-chief, for every revision round, together with the authors' replies. Comments appear only with the consent of the people who wrote them. Reviewers who chose to sign their report are named; the others are shown as "Referee". Comments are edited for language only, and confidential remarks to the editors are not included.

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1 Original submission

2 comments · 16 Jun 2023 – 18 Jun 2023

Referee 1 Reviewer

MINOR REVISION 16 Jun 2023

Manuscript ID: 138044
Manuscript Title: Primary carrier status and alteration in the colonization of the extended2 spectrum β-lactamase producing Enterobacteriaceae among children in 3 Pediatric Intensive Care Unit during hospital stay
1- Please ensure that your manuscript's style correctly matches that of Archives of Pediatric Infectious Disease Journal.
2- The manuscript needs to be edited; some sentences are unclear and must be rewritten.
3-Keywords must be chosen based on their role in the manuscript, so words like children and carrier state must be deleted.
4- In the methods section, there is no information about the total number of samples.
5- The authors do not use demographic information.
5- Were only Escherichia, Klebsiella, and Enterobacter identified in the stool examination?
Or did the authors choose them?
6- In line 124, the reference to CLSI must be edited.
7- The PCR conditions are not mentioned.
8- The dose of each antibiotic disk must be written.
9- Parts: 3.4 & 3.5 must be rewritten.

Referee 2 Reviewer

MINOR REVISION 18 Jun 2023

Dear author, please pay attention to the comments below:
Comment 1: In table 2, you reported some p-values equal to 1. A p-value is generally not found to be 1. It becomes 1 when the values of both groups are the same (identical), so it's better to report the p-value as 0.999 instead of 1.
Comment 2: In table 3, what do you mean by the AB usage column? Please explain it further.

Comment 3: In table 3, which variable does the p-value in the final column relate to?

Comment 4: Did you interpret the significant p-value in table 3 in the results section?

Comment 5: In line 198, you stated, "resistance in children received special antibiotic compared with those patients with no history of the prescription"; didn't you report the results in a table?
Comment 6: Did you use sampling or a census in your study? Please explain this in the methods section.
Comment 7: Please explain the sample size in your study. Did you consider all PICU patients from July 2021 to June 2022 at Mofid 97 Children's Hospital in Tehran?

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Revision 1

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Dear Editor-in-Chief of APID,

Thanks for considering our manuscript for review in your valuable journal. The reviewers' comments were responded and related changes were done in the revised file. A point-by-point response to each comment is shown below. All the changes are highlighted in yellow color in the revised file.

Regards,

M. A., on behalf of the authors

19 July 2023

Reviewer 1:
Comments
1: *The English of the manuscripts needs improvement*
Response: The manuscript was revised thoroughly.

2. Abstract Line 10: Enterobacteriacea (ESBL-E). ESBL-E is not an abbreviation of the Enterobacteriaceae. Please correct it.

Response: Thank you for your remark. The phrase was corrected.

3. Methods
Line 109: Escherichia, Klebsiella, and Enterobacter are not correct. After the genus of bacteria, the species of that or the spp. Should be written. (Please correct the whole of the text)

Response: Thank you for the remark. Names of the bacteria were corrected throughout the manuscript body.

4. Lines 121 and 122: the charge of the antibiotic disc should be written

Response: Thank you. The antibiotics charge for discs were included according to the comment.

5. Line 124: the M100 of CLSI includes the reference table for antibiotic susceptibility testing.

Response: Thank you. The writing mistake was corrected. The full name of the standard protocol was added to the references.

6. Line 124: CLSI should be written like; " Clinical and Laboratory Standards Institute" for the first time.

Response: Thank you. The full name of the standard protocol was added to the references.

7. *Line 125: ESBL detection should be done by "cefotaxime and cefotaxime-clavulanic acid" and " ceftazidime and ceftazidime-clavulanic acid" according to the CLSI guideline. Please explain your method.*

Response: Thanks for your remark. Due to the limitation for screening of the ESBL-*E* isolates using ceftazidime and ceftazidime-clavulanic acid discs, which were not available at the time of the current study, further confirmation was done by polymerase chain reaction (PCR) using specific primers, as described below. This limitation was described in the revised section.

8. The definition of the MDR, XDR, and PDR should be written in the method part with references.

Response: Thanks for your remark. The related reference was added and a description of these resistance phenotypes in the methods section was referred to the study of Magiorakos AP et al.

9. Results
In the result, the part author should be explained the other isolated rectal swab.

Response: This study was aimed to investigate the frequency of ESBL-phenotype among isolates of *Escherichia*, *Klebsiella*, and *Enterobacter* spp. Members of *Enterobacteriaceae* that differ from the noted genera and non-Enterobacteriaceae isolates were excluded from the study. A description line was added to the methods section according to the reviewer's comment.

10. ESBL in Table 3: Please specify whether the enzyme has been confirmed using a phenotypic or molecular method.

Response: Thank you. This table is related to phenotypic results. The heading of Table 3 was revised.

11. References
- The author should use up-date references.

Response: Thanks for your comment. More related references were used in the current manuscript as high as possible. There are limited studies on the fecal carriage of ESBL-*E* in PICU-admitted pediatrics, and a few older references, due to this limitation, were used in the discussion section for discussing some of the findings.

Reviewer 2:

1. Please ensure that your manuscript's style matches with Archives of Pediatric Infectious Disease Journal correctly.

Response: Thank you. The standard style of the journal was considered.

2. Manuscript needs to be edited, some sentences don't have a good meaning and must be rewrite.

Response: Thank you. The manuscript was revised thoroughly and sentences were rewritten.

3.Key words must be chosen on their role in manuscript, so words like: children and carrier

Response: Thank you for your remark. The keywords were corrected.

4. in part methods, there is not any information about total number of samples.

Response: Thank you for your remark. More details were included in the text.

5.Authors don't use of Demographic information.

Response: Thanks for your remark. Demographic data were included in the first paragraph of the results section.

6. Only Escherichia, Klebsiella , and Enterobacter were identified in stool exam?
Or authors chose them?

Response: Yes, the study aimed to detect ESBL phenotype in these three genera. To describe the method of selection for these three genera, a new sentence was added to section 3.2 of the methods.

7. In line 124, referring to CLSI, must be edited.

Response: Thank you. The full name of the standard protocol was added to the references

8. PCR condition is not mentioned.

Response: Thank you. In Table 1, the reference primers used are mentioned and for more details, they are included in the sources.

9. Dose of each antibiotic disks, must be written.

Response: Thank you. The antibiotics charge for discs were included according to the comment.

10. Part: 3.4 & 3.5 must be rewrite.

Response: Thank you. Rewritten.

Reviewer 3:

1. In table 2, you reported some of p-values equal to 1, p value generally not found to be 1. It becomes 1 when values of both groups are same(identical), so it's better you report the p-value equal to 0.999 instead of 1.

Response: Thank you for your remark. It was corrected.

2.In table 3, what do you mean by AB usage column? please more explain about it.

Response: Thank you for your remark. A description was added to the table legend.

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3. In table 3, is p-value in the final column, related to what variable?

Response: Thank you for your remark. A description was added to the legend.

4. did you interpret the significant p-value in table 3, in results section?

Response: Thank you for your remark. . A description was added to the legend.

5. in line 198, you stated about resistance in children received special antibiotic compared with those patients with no history of the prescription", didn't you report the results in a table?

Response: Thank you for your remark. The correlation between antibiotic usage and antibiotic resistance is described in Table 3 and the paragraph below this table. This paragraph was revised.

6.did you do sampling or census in your study, please explain about it in methods section.

Response: Thank you. Rectal swab samples were obtained from the admitted patients. The sampling method is described in section 3.2.

7. please explain about the sample size in your study? Did you consider all of PICU patients from July2021 to June2022 in Mofid 97 Children's Hospital in Tehran.

Response: Thank you for your remark. Details about the sampling method were added to section 3.1 to describe the selection and sampling better. *Enterobacteriaceae* is a member of the normal flora of the gastrointestinal tract in all children and adults. All the 80 patients who were included to this study on admission carried at least one of the target bacteria, including *Escherichia*,

Enterobacter, or *Klebsiella*. Accordingly, all the patients who were randomly included at admission time were resampled at discharge time.

2 Revision 1

0 comments

No public comments in this round.