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OPEN PEER REVIEW

Determination of *MCR-1* Gene and Antibiotic-Resistant *Escherichia coli* Isolates from Clinical and Non-clinical Samples

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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

1 comment · 23 Oct 2024

Referee 1 Reviewer

REJECT 23 Oct 2024

Dear Authors,

I would like to express my appreciation for the effort you've put into your manuscript on the Determination of the MCR-1 Gene and Antibiotic-Resistant Escherichia coli Isolates from Clinical and Non-Clinical Samples. While the topic is not novel, I believe it aligns well with the journal's scope. However, after careful consideration, I regret to inform you that your manuscript is not suitable for publication for the following reasons:

1. The rationale behind comparing the antibiotic resistance of E. coli in clinical and non-clinical isolates is unclear. Additionally, I am puzzled as to why human samples included urine cultures while animal samples were sourced from feces. These two sources may yield results that are not directly comparable, suggesting that the study design did not adequately meet its objective.

2. The data were collected over five years ago, leading me to view the findings as outdated. Given the passage of time, it is likely that the antibiotic resistance patterns in isolated samples have evolved.

3. The discussion section needs to be developed further. Currently, it reads as a literature review. I expect comparative analysis between your findings and those of previous studies, along with an explanation of the etiology behind any differences or similarities.

4. There are many grammatical errors throughout your manuscript.

Best regards,

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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

Thanks to the reviews and valuable comments of the respected reviewers, the answers of the reviewers are attached.

Reviewer 1:

1-It is recommended provide more context about the global impact of antibiotic resistance, particularly focusing on the significance of the MCR-1 gene in enhancing resistance to colistin, an antibiotic of last resort.

Antibiotic-resistant infections have increased globally. For instance, the WHO reported that around 700,000 deaths occur annually due to drug-resistant infections. This number is projected to rise, potentially reaching 10 million deaths per year by 2050 if current trends continue. Multi-drug resistant organisms, particularly Gram-negative bacteria such as Escherichia coli and Klebsiella pneumoniae, are major contributors to this crisis. Colistin, a polypeptide antibiotic, is often viewed as a last-resort option for treating infections caused by multidrug-resistant Gram-negative bacteria. Its use has surged due to ineffective alternatives, especially in critical care settings. The MCR-1 gene encodes an enzyme that modifies the bacterial cell membrane, reducing colistin's efficacy. This gene can confer resistance not only to colistin but also to other antibiotics, complicating treatment protocols. The significance of the MCR-1 gene highlights a critical aspect of the antibiotic resistance crisis, particularly in the context of colistin as a last-resort antibiotic. The global spread of this gene and the associated resistance it confers underline the urgent need for coordinated action to combat antibiotic-resistant infections.

2- Provide more information on the statistical methods used to analyze the data. Clearly describe how significance was determined and any specific tests apart from descriptive statistics used for comparisons.

To analyze the antibiotic resistance model of Escherichia coli isolates, clinical and animal samples were used, and the number and percentage of resistant and sensitive isolates were presented for each antibiotic.To evaluate the significance, the p value can be calculated from the Chi-square test. A p-value <0.05 usually indicates a statistically significant difference between groups.

3- Expand the discussion to better compare this study’s findings with previous research on MCR-1 prevalence. Explore possible reasons for any differences observed and address the implications for public health in more depth.

Previous studies have reported varying prevalence rates of the MCR-1 gene in E. coli isolates from clinical and agricultural settings. For instance, European research may show lower

prevalence rates (often below 5%), while studies in Asia, particularly China, could report significantly higher rates (over 20%). Comparing these rates with the findings presented in this study can illuminate patterns related to local agricultural practices, antibiotic use, and public health interventions. The variation in prevalence might also arise from differences in sample sources. Studies focused on human clinical isolates may yield different resistance patterns compared to those from livestock or environmental sources. The geographical context and temporal aspects play significant roles in resistance profiles. Regions with intensive agriculture and high antibiotic usage in livestock are more likely to report elevated MCR-1 prevalence. Similarly, recent studies reflecting the impact of stricter antibiotic regulations might show declining prevalence over time, contrasting with older reports where less stringent controls were in place. The usage of colistin as an antibiotic in agricultural settings has been a point of concern. In regions where colistin is frequently used for growth promotion or disease prevention in livestock, higher prevalence rates of MCR-1 are often observed. If the current study reveals high resistance in livestock, this may correlate with historical or current agricultural practices. Variations in infection control practices between hospitals and farms can influence the spread of resistant strains. Increased biosecurity measures in one region might lead to lower transmission, whereas lax practices in another may facilitate the spread of resistant bacteria.

4- Clearly outline the study's limitations, such as sample size or potential biases in sample collection, and suggest directions for future research to build upon these findings

This study is considered with limitations such as small sample size, financial limitations, examination of other antibiotics, etc., and it is also possible to suggest suitable solutions by examining other genes in antibiotic resistance.

5- Conduct a detailed proofreading session to address any spelling, grammar, or typographical errors. This will enhance the readability and professionalism of the manuscript.

Ok,Done

Reviewer 2:

1-The rationale behind comparing the antibiotic resistance of E. coli in clinical and non-clinical isolates is unclear. Additionally, I am puzzled as to why human samples included urine cultures while animal samples were sourced from feces. These two sources may yield results that are not directly comparable, suggesting that the study design did not adequately meet its objective.

The key rationale behind comparing antibiotic resistance in E. coli isolates from clinical (human) and non-clinical (animal) settings is to assess the potential transmission pathways of resistant strains. Given that E. coli is a commensal organism in the gut of humans and animals, analyzing both sources can shed light on how resistance genes, such as MCR-1, may circulate between them. This has substantial implications for public health. Identifying and comparing resistance in both settings can help elucidate the sources of resistance emergence and spread. If significant differences in resistance rates are observed, this may indicate that certain antibiotics used in livestock are contributing to resistance seen in human infections.

2- The data were collected over five years ago, leading me to view the findings as outdated. Given the passage of time, it is likely that the antibiotic resistance patterns in isolated samples have evolved.

It is completely true, but due to the financial limitations and the difficult process of conducting the tests, this process has been prolonged, but the article has tried to point out and compare the new findings.

3- The discussion section needs to be developed further. Currently, it reads as a literature review. I expect comparative analysis between your findings and those of previous studies, along with an explanation of the etiology behind any differences or similarities.

Ok,Done

4- There are many grammatical errors throughout your manuscript.

Ok,Done

2 Revision 1

0 comments

No public comments in this round.