Authors' Response to Peer Reviews

Authors' Response to Peer Reviews of "Establishing Antimicrobial Resistance Surveillance in the Water and Environment Sector in a Resource-Limited Setting: Methodical Qualitative and Quantitative Description of Uganda's Experience From 2021 to 2023"

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KEYWORDS

antimicrobial resistance; surveillance system; water and environment sector

This is the authors' response to peer-review reports for "Establishing Antimicrobial Resistance Surveillance in the Water and Environment Sector in a Resource-Limited Setting: Methodical Qualitative and Quantitative Description of Uganda's Experience From 2021 to 2023".

Round 1 Review

Reviewer B [1]

General Comments

This paper [2] is timely and presents data on antimicrobial resistance surveillance in the water and environment sector in a resource-limited setting.

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Specific Comments

Methodology

"A stepwise approach was employed. Governance structures were streamlined and sector-specific AMR surveillance guiding documents developed" -> "were developed"

"Conslusion" -> Check the spelling.

Response: This section was revised and now reads "The Government of Uganda, through the MWE, with support from the Infectious Diseases Institute at Makerere University through the Fleming Fund Country Grant 2 project, instituted a step-wise approach with incremental targets and sequential phases from August 2021. This involved establishing a foundation; consolidating and refining gains; scaling up and further expansion of the surveillance system." Please see page 3 of the revised manuscript.

The spelling for "Conclusion" was also corrected. Please see page 9 of the revised manuscript.

"CONFLICTS OF INTEREST" -> "CONFLICT OF INTEREST"

Response: The suggested edit has been adopted. Please see page 10 of the revised manuscript.

Antimicrobial Resistance Governance Establishment and Enhancement

"To streamline the AMR governance in the water and environment sector, a sector-specific AMR technical working group (TWG) was instituted with identified a focal person to coordinate the surveillance activities in the sector." (Rewrite this.)

Response: This statement has been rewritten and now reads "A sector-specific AMR technical working group (TWG) and a focal person position were established to coordinate AMR containment efforts including surveillance activities in the sector."

Major Comments

Enhancement of the Microbiology Capacity of the National Water Quality Reference Laboratory

I would like to see a description of the testing platforms in this lab and plans for genomic surveillance of antimicrobial resistance (AMR) since it reveals more about the complexity, evolution, and transmission of these pathogens as seen here.

Response: The current testing platforms were described in the Methodology section under the "Pre-test and rollout of the AMR surveillance documents sub-section." Please see page 3 of the revised manuscript.

Minor Comments

AMR Data Generation

"The developed sector-specific AMR surveillance documents were pretested." (How was this done?)

Response: The steps followed during the pretest were included. This section now reads "The developed sector specific AMR surveillance documents were pre-tested through an active survey. This involved collection of samples from the Kampala-Wakiso region and analysing them at the NWQRL. Nine strategic surface water (non-point sources) and waste water (point sources) sampling sites were identified in Kampala and Wakiso and fifteen grab samples collected using the standard procedures as stipulated in the different surveillance documents. The samples were transported to the NWQRL under appropriate conditions and analysed using standard conventional culture-based procedures. The lessons learned during the pre-test were used to refine the surveillance documents." Please see page 3 of the revised manuscript.

Discussion

Figure 1: It would be important to share this data via a public dashboard like here [3]. "Liguori et al. have described the methods as fairly standardized, and an avenue for further analysis of the recovered isolates including sensitivity testing, sequence-based typing and whole genome sequencing, which aid in detecting and identifying antibiotic-resistant genes and genetic elements [4]." And virulence [5] factors.

Response: The section on data availability was added to the manuscript and reads "The data generated from the water and environment sector is a preserve of the Uganda MWE. It can be accessed by placing a request and concept on use to the Commissioner Water Quality Management Department in the Directorate of Water Resources Management, MWE." Please see page 9 of the revised manuscript.

Authors should also discuss making a sentence on the contribution of environmental wastewater sequencing.

Response: This has been included as advised and reads as "Thus, the AMR surveillance systems in the sector require appropriate expansion to include whole genome sequencing and environmental wastewater sequencing." Please see page 8 of the revised manuscript.

As a way forward, I wish to request the authors set up a public dashboard to share this important AMR surveillance data to stakeholders beyond the TWG as seen [6] here.

Response: The section on data availability was added to the manuscript and reads as "The data generated from the water and environment sector is a preserve of the Uganda MWE. It can be accessed by placing a request and concept on use to the Commissioner Water Quality Management Department in the Directorate of Water Resources Management, MWE." Please see page 9 of the revised manuscript.

Reviewer BS [7]

Specific Comments

Major Comments

This paper describes:

1. A stepwise and governmental approach for establishing AMR surveillance in the environment and aquatic sector in a country with a resource-limited setting. This includes leveraging on previous experiments in the human and animal sector, and experimental methodology, namely, conventional culture-based

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bacteriology techniques, which is aligned with the current available equipment and infrastructure at the country scale.

2. The rationality of the passive and active monitoring was well presented and discussed. The quantification of antimicrobial susceptibility in priority microbial isolates were major findings in the study area, as they may cause a silent but life-threatening pandemic. However, no indicator was presented for the assessment of the limitation of the generated AMR data and the scale resolution associated the monitoring sites and sampling locations as well as experimental methodologies.

3. It also lacks a numerical comparison between the AMR values reported for the microbial isolates collected from point sources and nonpoint sources. The readability of the text is very satisfactory; however, there are still some parts that could be further improved!

Response: A comparison of the resistance observed among isolates collected from point and nonpoint sources was done. This section has been included and it reads as "Overall, there was no significant difference between the resistance observed in E. coli and Klebsiella spp isolates recovered from point and non-point sources. Among the Enterococcus spp isolates, a significant difference (OR 5.318182 (95% CI 1.793498-15.76977), p=0.003) was observed in the resistance to chloramphenicol between the isolates recovered from point and non-point sources. The Enterococcus isolates recovered from point sources were five times more likely to be resistant to chloramphenicol than those recovered from non-point sources." Please see page 6 of the revised manuscript.

Minor Comments

1. The Objective section was missed in the structured abstract.

Response: The Objective section has been included in the structured abstract, and it reads as "To describe Uganda's experience in establishing AMR surveillance in the Water and Environment sector." Please see page 1 of the revised manuscript.

2. The abbreviations should be relocated before the reference section.

Response: The list of abbreviations and acronyms used in the manuscript has been provided before the References section. Please see page 10 of the revised manuscript.

3. The map of the study area with the georeferenced location of the monitoring sites along with the compactness of the surveillance site per unit of area were not presented!

Response: A map of the study area has been developed and provided as a figure PNG file.

4. No indicator was presented for the assessment of the limit of generated AMR data.

Response: An explanation for this has been provided in the Discussion section. It reads "The representativeness of the AMR data generated is still limited as the active surveys are conducted in only the Kampala- Wakiso region. Therefore, the data may not be sufficient to generalize the prevalence of AMR in Uganda's water and environment sector. However, the data marks the first efforts to generate AMR data in the sector, but more efforts are required to increase the quantity of the sector AMR data." Please see page 9 of the revised manuscript.

5. Comparisons of many AMR values are reported to be similar to other studies, while a significant difference as high as two times was noticed during the peer review. It is recommended to include the values from other studies in the table to facilitate the comparison. Rewrite this section.

Response: The section has been rewritten as suggested. Please see page 7 of the revised manuscript.

6. Some points like "The program needs to be consolidated and expanded to include more sentinel sites, sample types, advanced AMR surveillance methodologies and techniques, and the surveillance of antimicrobial residues" presented in the conclusions are not supported in the main area of the paper.

Response: The Methodology and Results sections were revised to include the suggestions. Please see pages 3-7 of the revised manuscript.

7. Some information in the abstract, like 27% (n=160) of recovered isolates exhibited multidrug resistance and extensive drug resistance, was never presented in the main text.

Response: This text in the abstract was changed. The statement now reads "Up to 254 (64%) of the priority pathogens recovered exhibited multi and extensive resistance to the different antibiotics set." Please see pages 1 and 7 of the revised manuscript.

8. The Data Analysis section was totally unclear to me. Mainly, I cannot understand what steps were taken to analyze the data. It is recommended that the author adds some description with regard to that.

Response: The Data section was revised and more description was added. The section now reads "Microsoft Excel 2016 and Stata 16 were used for data entry, cleaning and analysis. Percentage resistance of the isolates to each antibiotic was generated and visuals (charts and graphs) developed. The Chi-square test and binary logistic regression were used to test whether resistance of the priority pathogens (E. coli, Klebsiella and Enterococcus spp) to the different antibiotics were significantly different across the point and non-point sources. A p-value of less than 0.05 indicated a significant statistical difference." Please see pages 4 of the revised manuscript.

Conflicts of Interest

None declared.

References

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Abbreviations

AMR: antimicrobial resistance
TWG: technical working group

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