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Original Paper

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 ([e50588](#))

Godfrey Katumba, Herman Mwanja, Jonathan Mayito, Betty Mbolanyi, Fred Isaasi, Daniel Kibombo, Judith Namumbya, David Musoke, Jonathan Kabazzi, Musa Sekamatte, Lillian Idrakua, Richard Walwema, Mohammed Lamorde, Francis Kakooza, Simon Etimu. 15

Peer Review Report

Peer Review 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”

Hojjat Borhany¹, MSc

Politecnico di Milano, Milan, Italy

Related Articles:

Companion article: <https://preprints.jmir.org/preprint/50588>

Companion article: <https://bio.jmirx.org/2024/1/e58949/>

Companion article: <https://bio.jmirx.org/2024/1/e50588/>

(*JMIRx Bio* 2024;2:e58901) doi:[10.2196/58901](https://doi.org/10.2196/58901)

KEYWORDS

antimicrobial resistance; surveillance system; water and environment sector

This is a peer-review report submitted for the paper “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

Specific Comments**Major Comments**

This paper [1] describes:

1. A stepwise and governmental approach for establishing antimicrobial resistance (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 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!

Minor Comments

1. The Objective section was missed in the structured abstract.
2. The abbreviations should be relocated before the reference section.
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!
4. No indicator was presented for the assessment of the limit of generated AMR data.
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.
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.
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.

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.

Conflicts of Interest

None declared.

Reference

1. Katumba G, Mwanja H, Mayito J, Mbolanyi B, Isaasi F, Kibombo D, et al. 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. JMIRx Bio 2024. [doi: [10.2196/50588](https://doi.org/10.2196/50588)]

Abbreviations

AMR: antimicrobial resistance

Edited by T Leung; submitted 27.03.24; this is a non-peer-reviewed article; accepted 27.03.24; published 07.05.24.

Please cite as:

Borhany H

Peer Review 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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Peer-Review Report

Peer Review 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”

Gerald Mboowa¹, PhD

Makerere University, Kampala, Uganda

Related Articles:

Companion article: <https://preprints.jmir.org/preprint/50588>

Companion article: <https://bio.jmirx.org/2024/1/e58949/>

Companion article: <https://bio.jmirx.org/2024/1/e50588/>

(*JMIRx Bio* 2024;2:e58903) doi:[10.2196/58903](https://doi.org/10.2196/58903)

KEYWORDS

antimicrobial resistance; surveillance system; water and environment sector

This is a peer-review report submitted for the paper “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

General Comments

This paper [1] is timely and presents data on antimicrobial resistance (AMR) surveillance in the water and environment sector in a resource-limited setting.

Specific Comments**Methodology**

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

“Conclusion” -> Check the spelling.

“CONFLICTS OF INTEREST” -> “CONFLICT OF INTEREST”

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.)

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 AMR since it reveals more about the complexity, evolution, and transmission of these pathogens as seen here.

Minor Comments**AMR Data Generation**

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

Discussion

Figure 1: It would be important to share this data via a public dashboard like here [2]. “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 [3].” And virulence factors [4].

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

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 here [5].

Conflicts of Interest

None declared.

Editorial notice: A peer reviewer conflict of interest was identified prior to publication: They work at the same institution or organization as an author. They have published with an author during the past 5 years.

References

1. Katumba G, Mwanja H, Mayito J, Mbolanyi B, Isaasi F, Kibombo D, et al. 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. *JMIRx Bio* 2024. [doi: [10.2196/50588](https://doi.org/10.2196/50588)]
2. MAAP country reports. African Society for Laboratory Medicine. URL: <https://aslm.org/what-we-do/maap/maap-country-reports> [accessed 2024-04-22]
3. Liguori K, Keenum I, Davis BC, Calarco J, Milligan E, Harwood VJ, et al. Antimicrobial resistance monitoring of water environments: a framework for standardized methods and quality control. *Environ Sci Technol* 2022 Jul 05;56(13):9149-9160. [doi: [10.1021/acs.est.1c08918](https://doi.org/10.1021/acs.est.1c08918)] [Medline: [35732277](https://pubmed.ncbi.nlm.nih.gov/35732277/)]
4. Kiyaga S, Kyany'a C, Muraya AW, Smith HJ, Mills EG, Kibet C, et al. Genetic diversity, distribution, and genomic characterization of antibiotic resistance and virulence of clinical strains in Kenya. *Front Microbiol* 2022;13:835403. [doi: [10.3389/fmicb.2022.835403](https://doi.org/10.3389/fmicb.2022.835403)] [Medline: [35369511](https://pubmed.ncbi.nlm.nih.gov/35369511/)]
5. National situation of antimicrobial resistance and consumption analysis from 2016-2018. African Society for Laboratory Medicine. URL: https://aslm.org/wp-content/uploads/2023/07/AMR_REPORT_UGANDA.pdf?x89467 [accessed 2024-04-22]

Abbreviations

AMR: antimicrobial resistance

TWG: technical working group

Edited by T Leung; submitted 27.03.24; this is a non-peer-reviewed article; accepted 27.03.24; published 07.05.24.

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Peer Review of “Roles of Progranulin and FRamides in Neural Versus Nonneural Tissues on Dietary Restriction–Related Longevity and Proteostasis in *C. elegans* (Preprint)”

Anonymous

Related Article:Companion article: <https://www.biorxiv.org/content/10.1101/2024.02.06.579250v1>

(JMIRx Bio 2024;2:e60570) doi:10.2196/60570

KEYWORDS*C. elegans*; dietary restriction; lifespan; heat shock; proteostasis; neurodegeneration; motility

This is a peer-review report submitted for the preprint “Roles of Progranulin and FRamides in Neural Versus Nonneural Tissues on Dietary Restriction–Related Longevity and Proteostasis in *C. elegans*.”

Round 1 Review

General Comments

The manuscript titled “Roles of progranulin and FRamides in neural versus non-neural tissues on dietary restriction-related longevity and proteostasis in *C. elegans*” by Mir et al [1] examines the role of FMRamide-like neuropeptides in dietary restriction (DR)–mediated lifespan extension. To achieve this goal, the authors measured the survivability of animals under ad libitum (AL) and DR after knocking down these peptides specifically in the neuronal tissue or systemically (Figures 1 and 2). The authors did not obtain any significant results in these experiments and further performed other experiments to examine the impact of *pgrn-1* and *flp* knockdown in maintaining proteostasis in *eat-2* mutants (Figure 3) and influencing locomotion in the Alzheimer model of neurotoxicity (Figure 4). The data from all these experiments did not reveal any role for *pgrn-1* or *flp* genes in DR-dependent lifespan extension and proteostasis.

Specific Comments**Major Comments**

1. The premise of this study was that the authors found that *pgrn-1* and *flp* genes exhibited increased recruitment to polysomes upon DR. These data imply that these genes are translated to higher levels upon DR. Hence, increasing the levels of these under AL should recapitulate a DR-like state. However, the authors decided to examine the phenotypes associated with the knockdown of these genes. However, their data did not show any significant changes in DR-dependent lifespan enhancement. Hence, the logic of performing the experiments in Figures 3 and 4 is unclear.

2. There is no data to indicate the level (-fold decrease) of the FRamides or progranulin after RNA interference.

3. The lifespan experiments corresponding to Figure 2 have been performed two times, and the data are noted in Supplementary Table 3. However, the data from the two repeats (for *flp-5*, *flp-14*) are not reproducible, with one experiment showing a significant difference in lifespan under AL and DR and the second repeat showing no significant difference. These data indicate nonreproducibility, and ideally, no inference should be drawn from them without repeating them.

4. Supplementary Figure 2 data and conclusions are drawn from a single experiment only.

5. The title of the paper reflects that progranulin and FRamides play a role in DR-mediated extension of lifespan; however, all the results noted indicate the opposite (lines 205 and 206, 213-217, 336-339, and 345-348). Hence, the rationale for continuing to assess the role of these genes in the DR pathway by performing experiments in Figures 3 and 4 is unclear. Moreover, the authors also concluded that knocking down the expression of *pgrn-1* or *flp* does not have any role in proteostasis, and their role in neural proteotoxicity is complex (lines 369-372). Based on the data from Figure 4, the authors conclude that downregulation of *pgrn-1* or *flp* has minimal or no effect on motility during adulthood under DR conditions. Overall, the findings indicate that though there is increased translation of *pgrn-1* or *flp* genes upon DR, these genes do not function as DR effectors.

Hence, a more appropriate title would be “Progranulin and FRamides do not play a role in DR-related longevity and proteostasis.” Moreover, a more detailed explanation of the results in Figures 3 and 4 might be helpful for the readers to understand the role of these genes in motility and why there are differences in young and late ages. Unfortunately, I cannot recommend this manuscript for publication in its current state.

Conflicts of Interest

None declared.

Editorial Notice

The authors of the preprint under review declined the opportunity to revise the preprint in response to the feedback in the peer reviews and publish it in the journal JMIRx Bio. The editors thank the peer reviewers for providing their feedback on this preprint.

Reference

1. Mir DA, Cox M, Horrocks J, Ma Z, Rogers A. Roles of progranulin and FRamides in neural versus non-neural tissues on dietary restriction-related longevity and proteostasis in *C. elegans*. bioRxiv. Preprint posted online on February 8, 2024 2024 [[FREE Full text](#)]
-

Abbreviations

AL: ad libitum

DR: dietary restriction

Edited by G Eysenbach; submitted 15.05.24; this is a non-peer-reviewed article; accepted 15.05.24; published 17.06.24.

Please cite as:

Anonymous

*Peer Review of "Roles of Progranulin and FRamides in Neural Versus Nonneural Tissues on Dietary Restriction-Related Longevity and Proteostasis in *C. elegans* (Preprint)"*

JMIRx Bio 2024;2:e60570

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Peer Review of “Roles of Progranulin and FRamides in Neural Versus Nonneural Tissues on Dietary Restriction–Related Longevity and Proteostasis in *C. elegans* (Preprint)”

Anonymous

Related Article:

Companion article: <https://www.biorxiv.org/content/10.1101/2024.02.06.579250v1>

(*JMIRx Bio* 2024;2:e60571) doi:[10.2196/60571](https://doi.org/10.2196/60571)

KEYWORDS

C. elegans; dietary restriction; lifespan; heat shock; proteostasis; neurodegeneration; motility

This is a peer-review report submitted for the preprint “Roles of Progranulin and FRamides in Neural Versus Nonneural Tissues on Dietary Restriction–Related Longevity and Proteostasis in C. elegans.”

Round 1 Review

General Comments

Mir et al [1] is a study designed to understand the role of progranulin and FRamides in neural and nonneural tissues through a dietary restriction approach.

The idea of using multiple mutants to understand the effect of *flp-5*, *flp-14*, *flp-15*, and *pgrn-1* is interesting. While I like the overall idea and the experimental setup, I have a few questions regarding the study.

Specific Comments

1. I would have liked to see another control where wild-type worms were taken and heat treated at 35 °C alongside an

unheated control group. This way I could have seen a more direct and indirect comparison between the groups.

2. I would have liked to understand the reason behind carrying out motility assays at 25 °C when the worms were maintained at 20 °C. Is it because it is ideal?

3. It could be that I might have read it wrong, but to me, the labels in [Figures 1, 2, and S2](#) seem to be off. They don't match the alphabetical order, or I might be missing something here.

4. For the motility assay, where they compared the GRU102 strain against GRU102 crossed with TU3335, I see that all the results were compared to one universal control. I would have liked to see mutant controls alongside the GRU102 and GRU102 crossed with TU3335. Again, by doing this, I would have had a direct comparison of the control, mutant controls, and mutants under conditions. Here, I cannot see how the mutants were performing on day 1 as the authors show the mutant data started from day 4.

Conflicts of Interest

None declared.

Editorial Notice

The authors of the preprint under review declined the opportunity to revise the preprint in response to the feedback in the peer reviews and publish it in the journal JMIRx Bio. The editors thank the peer reviewers for providing their feedback on this preprint.

Reference

1. Mir DA, Cox M, Horrocks J, Ma Z, Rogers A. Roles of progranulin and FRamides in neural versus non-neural tissues on dietary restriction-related longevity and proteostasis in *C. elegans*. bioRxiv. Preprint posted online on February 8, 2024 2024 [[FREE Full text](#)]
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Peer Review of “Roles of Progranulin and FRamides in Neural Versus Nonneural Tissues on Dietary Restriction-Related Longevity and Proteostasis in C. elegans (Preprint)”

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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"

Godfrey Katumba^{1*}, MSc; Herman Mwanja^{2*}, BEHS; Jonathan Mayito^{2*}, MBChB, MMed; Betty Mbolanyi¹, MSc; Fred Isaasi², MPH; Daniel Kibombo², MPH; Judith Namumbya¹, MSc; David Musoke³, PhD; Jonathan Kabazzi^{2,4}, BMLS; Musa Sekamate⁵, MPH; Lillian Idrakua¹, MSci; Richard Walwema², MBA; Mohammed Lamorde², PhD; Francis Kakooza², PhD; Simon Etimu¹, MSci

¹Ministry of Water and Environment, Government of Uganda, Kampala, Uganda

²Infectious Diseases Institute, Makerere University, Kampala, Uganda

³School of Public Health, Makerere University, Kampala, Uganda

⁴National Health Laboratory and Diagnostics Services, Ministry of Health, Kampala, Uganda

⁵One Health Coordination Office, Ministry of Health, Kampala, Uganda

*these authors contributed equally

Corresponding Author:

Herman Mwanja, BEHS

Infectious Diseases Institute

Makerere University

Makerere University Main-Campus

Kampala

Uganda

Phone: 256 0770781589

Email: hmwanja@idi.co.ug

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Companion article: <https://bio.jmirx.org/2024/1/e50588/>

(*JMIRx Bio* 2024;2:e58949) doi:[10.2196/58949](https://doi.org/10.2196/58949)

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.

Specific Comments

Methodology

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

“Conclusion” -> 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

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.

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Abbreviations

AMR: antimicrobial resistance
TWG: technical working group

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Original Paper

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

Godfrey Katumba^{1*}, MSc; Herman Mwanja^{2*}, BEHS; Jonathan Mayito^{2*}, MBChB, MMed, PhD; Betty Mbolanyi¹, MSc; Fred Isaasi², MPH; Daniel Kibombo², MPH; Judith Namumbya¹, MSc; David Musoke³, PhD; Jonathan Kabazzi^{2,4}, BMLS; Musa Sekamatte⁵, MPH; Lillian Idrakua¹, MSci; Richard Walwema², MBA; Mohammed Lamorde², PhD; Francis Kakooza², PhD; Simon Etimu¹, MSci

¹Ministry of Water and Environment, Government of Uganda, Kampala, Uganda

²Infectious Diseases Institute, Makerere University, Kampala, Uganda

³School of Public Health, Makerere University, Kampala, Uganda

⁴National Health Laboratory and Diagnostics Services, Ministry of Health, Kampala, Uganda

⁵One Health Coordination Office, Ministry of Health, Uganda, Kampala, Uganda

*these authors contributed equally

Corresponding Author:

Herman Mwanja, BEHS

Infectious Diseases Institute

Makerere University

Makerere University Main Campus

Kampala, P.O. Box 22418

Uganda

Phone: 256 0770781589

Email: hmwanja@idi.co.ug

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Abstract

Background: Antimicrobial irrational use and poor disposal in the human and animal sectors promote antimicrobial resistance (AMR) in the environment as these antimicrobials and their active ingredients, coupled with resistant microbes, are released into the environment. While AMR containment programs in the human and animal sectors are well established in Uganda, those in the water and environment sector still need to be established and strengthened. Therefore, the Ministry of Water and Environment set out to establish an AMR surveillance program to bolster the One Health efforts for the containment of AMR under the National Action Plan 2018-2023.

Objective: This study aims to describe Uganda's experience in establishing AMR surveillance in the water and environment sector.

Methods: A methodical qualitative and quantitative description of the steps undertaken between August 2021 and March 2023 to establish an AMR surveillance system in the water and environment sector is provided. The Uganda Ministry of Water and

Environment used a stepwise approach. Governance structures were streamlined, and sector-specific AMR surveillance guiding documents were developed, pretested, and rolled out. The National Water Quality Reference Laboratory infrastructure and microbiology capacity were enhanced to aid AMR detection and surveillance using conventional culture-based methods. A passive and targeted active surveillance hybrid was used to generate AMR data. Passive surveillance used remnants of water samples collected routinely for water quality monitoring while targeted active surveys were done at selected sites around the Kampala and Wakiso districts. Excel and Stata 15 statistical software were used for data analysis.

Results: A sector-specific technical working group of 10 members and focal persons is in place, providing strategic direction and linkage to the national AMR surveillance program. The National Water Quality Reference Laboratory is now at biosafety level 2 and conducting microbiology testing using conventional culture-based techniques. Up to 460 water samples were processed and 602 bacterial isolates were recovered, of which 399 (66.3%) and 203 (33.7%) were priority pathogens and nonpriority pathogens, respectively. Of the 399 priority pathogens, 156 (39.1%), 140 (35.1%), 96 (24.1%), and 7 (1.8%) were *Escherichia coli*, *Klebsiella* species, *Enterococcus* species, and *Salmonella* species, respectively. *E. coli* showed resistance to ampicillin (79%), ciprofloxacin (29%), and ceftriaxone (29%). Similarly, *Klebsiella* species showed resistance to ampicillin (100%), ciprofloxacin (17%), and ceftriaxone (18%). *Enterococcus* species showed resistance to ciprofloxacin (52%), vancomycin (45%), and erythromycin (56%). Up to 254 (63.7%) of the priority pathogens recovered exhibited multiple and extensive resistance to the different antibiotics set.

Conclusions: Initial efforts to establish and implement AMR surveillance in the water and environment sector have succeeded in streamlining governance and laboratory systems to generate AMR data using conventional culture-based methods.

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KEYWORDS

antimicrobial resistance; surveillance system; water and environment sector

Introduction

Antimicrobial resistance (AMR) occurs when microorganisms survive after exposure to antimicrobials that would normally kill them, inhibit their metabolism, or stop their growth [1]. This also includes antibiotic resistance in bacteria [2]. As a result, antibiotics become ineffective against disease-causing bacteria, leading to AMR evolving into a silent pandemic [2,3], which is projected to account for over 10 million human deaths by 2050 [3]. This imparts a substantial financial burden on the health care system [4]. AMR is a “One Health” issue, highlighting the complex interconnectedness between the health and well-being of animals, people, plants, and their shared environment [5]. This results from the transmission of resistant microorganisms, their genes, or mobile genetic elements between these compartments [6]. Thus, making AMR one of the top threats to global health, with increasing trends in resistant infections in humans and animals, tending toward a postantibiotic era [7].

Globally, AMR in the environment has been a neglected issue whose public health importance, burden, and implication are yet to be explored comprehensively [8], especially in resource-limited settings [9]. Over the past decades, global health research has increasingly shown that the environment plays a key role in the proliferation and exacerbation of AMR and its effects [9-12]. Most antimicrobials used in humans and animals are excreted or indiscriminately disposed of into the environment in their raw or active forms [13]. Sublethal levels of antimicrobials, contaminants, and resistant bacteria in effluents from pharmaceutical industries, households, agricultural runoffs, and health care settings are released into the environment [3,14]. This creates an unnatural selective pressure in the environment [3,15] that, coupled with direct contact between natural bacterial communities and the

discharged resistant bacteria, drives the evolution, selection, and emergence of resistant strains within the environment [3,13,16].

In Uganda, AMR surveillance and containment efforts have mainly focused on the human and animal sectors [17], partly due to the lack of a structured surveillance program with consensus on standard methodologies and targets in the water and environment sector on both the national and global scale [7]. Currently, there is no benchmarking or threshold data in the sector to inform epidemiological, evolutionary, and risk modeling efforts [7,12]. The Uganda Ministry of Water and Environment (MWE) and its partners, therefore, undertook efforts to establish an AMR surveillance program in the water and environment sector to bolster a One Health approach in curbing AMR, guided by the AMR National Action Plan 2018-2023. Instituting AMR surveillance in the sector was done in cognizance of the country’s environmental concerns, local contexts, and a structured framework [13,18-20]. We, therefore, present Uganda’s experience in establishing an AMR surveillance program and the emerging data on the status of AMR in the environment sector between August 2021 and March 2023.

Methods

Overview

A methodical qualitative and quantitative description of the steps undertaken between August 2021 and March 2023 to establish an AMR surveillance system in the water and environment sector is provided. Several surveillance documents, guidelines, and reports were reviewed to collect data appropriately aligned to AMR surveillance in a low-resource setting [21]. The description below provides the steps (processes and methods) undertaken to set up the program.

AMR Governance Establishment and Enhancement

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 stepwise approach with incremental targets and sequential phases from August 2021. This involved establishing a foundation, consolidating and refining gains, scaling up, and further expanding the surveillance system.

A 10-member sector-specific AMR technical working group (TWG) with focal persons was established to coordinate the AMR containment efforts, including surveillance activities in the sector. The TWG developed AMR surveillance documents (plan, protocol, and standard operating procedures) focused on the monitoring of priority environmental bacteria (*Escherichiacoli*, *Klebsiella* species, *Enterococcus* species, and *Salmonella* species) in water samples. These documents were aligned to the different international and national guidelines [22-25]. The National Water Quality Reference Laboratory (NWQRL) was identified as the sentinel site for AMR surveillance in the sector using conventional culture-based techniques. One sample type (water samples) was also designated for the initial AMR surveillance efforts. The TWG also reviewed the generated AMR data to inform AMR programming and policy formulation in the sector.

Enhancement of the Microbiology Capacity of the NWQRL

The NWQRL microbiology section was equipped and its infrastructure was enhanced. The human resource capacity was enhanced through in-service microbiology, biosecurity and biosafety, and laboratory quality management system trainings and mentorships. This capacity enhancement was done through a One Health approach, leveraging the established AMR surveillance capacity in the human and animal sectors. The NWQRL was also enrolled in the national laboratory external quality assessment and proficiency testing scheme of the Uganda National Health Laboratory and Diagnostic Services to enhance the microbiology testing quality.

Pretest and Rollout of the AMR Surveillance Documents

The developed sector-specific AMR surveillance documents were pretested through an active survey. This involved the collection of samples from the Kampala-Wakiso region and analyzing them at the NWQRL. A total of 9 strategic surface water (nonpoint sources) and wastewater (point sources) sampling sites were identified in Kampala and Wakiso, and 15 grab samples were collected using the standard procedures as stipulated in the different surveillance documents. The samples were transported to the NWQRL under appropriate conditions and analyzed using standard, conventional, culture-based procedures. The lessons learned during the pretest were used to refine the surveillance documents.

The documents were then rolled out to generate AMR surveillance data through a hybrid of passive and active surveillance. The initial efforts focused on nonpoint sources or surface water sources (rivers, streams, and other open channels), drinking water (national water grid and other potable water),

and point sources or wastewater (sewer, wastewater treatment plants and ponds, and septic tanks) samples. Passive surveillance used remnants of samples routinely referred from across the country to the NWQRL for water quality monitoring. Active surveillance used samples collected through quarterly targeted surveys from strategic sites (shown in the map provided in [Multimedia Appendix 1](#)) in the Kampala-Wakiso region as stipulated in the surveillance protocol. This region was chosen because it has vast human economic activities that involve the intense use of antibiotics and thus provided an ideal setting for integrated AMR surveillance in the sector.

Conventional culture-based bacteriology techniques were used for the enumeration, isolation, and identification of priority bacteria. Water sample enrichment was done by inoculating 2-5 ml of the sample into 10 ml of brain heart infusion and incubating for 16-18 hours at 37 °C. Following the enrichment, culture media and biochemical tests were used to isolate and identify the bacteria.

For *E coli* and *Klebsiella* species, MacConkey agar with crystal violet was used for the primary culture and purity plating. The distinct colonies (*E coli*: pink/red lactose-fermenting colonies; *Klebsiella* species: pink-yellow mucoid lactose-fermenting colonies) that grew after 18-24 hours of incubation at 37 °C were subjected to Gram stain (microscopy) and biochemical tests including oxidase, urea, citrate, triple sugar iron, and sulfide indole motility tests using standard procedures.

For *Salmonella* species, MacConkey agar with crystal violet was used for the primary culture. The distinct colonies (colorless colonies) that grew after 18-24 hours of incubation at 37 °C were purity plated on xylose lysine deoxycholate media. The distinct colonies (red colonies with black centers) that grew after 18-24 hours of incubation at 37 °C were subjected to Gram stain and biochemical tests including oxidase, urea, citrate, triple sugar iron, and sulfide indole motility tests using standard procedures. For *Enterococcus* species, Slanetz and Bartley agar was used for the primary culture. The distinct colonies (red or purple colonies) that grew after 18-24 hours of incubation at 37 °C were purity plated on 5% sheep blood agar media. The distinct colonies (white or gray colonies) that grew after incubation were subjected to Gram stain (microscopy) and biochemical tests including catalase and bile esculin tests.

Other than the priority bacterial isolates, we also recovered other bacteria species including *Citrobacter freundii*, *Enterobacter*, *Pseudomonas*, *Proteus*, *Providencia*, and *Raoultella* species.

AMR Data Generation

Antimicrobial susceptibility testing was done using the Kirby-Bauer disc diffusion method with the appropriate isolate-antibiotic combinations and techniques as stipulated in the 31st edition of the Clinical and Laboratory Standards Institute guidelines [26]. Penicillins, fluoroquinolones, cephalosporins, aminoglycosides, carbapenems, glycopeptides, macrolides, oxazolidinones, folates (sulphonamide-trimethoprim), tetracycline, and phenicol were the antibiotic classes considered. Isolates were cryopreserved in a 20% glycerol and brain heart infusion and archived at the Uganda National Biorepository at the Central Public Health

Laboratories and National Animal Diseases Diagnostics and Epidemiology Center laboratory at -80°C .

Data Analysis

Excel 2016 (Microsoft Corporation) and Stata 16 (StataCorp) were used for data entry, cleaning, and analysis. The percentage resistance of the isolates to each antibiotic was generated and visuals (charts and graphs) were developed. The chi-square test and binary logistic regression were used to test whether the resistance of the priority pathogens (*E. coli*, *Klebsiella*, and *Enterococcus* species) to the different antibiotics was significantly different across the point and nonpoint sources. A P value $<.05$ indicated a significant statistical difference.

Ethical Statement

The work reported here is part of the Uganda National AMR surveillance program that was approved by the National AMR Sub-Committee of the National One Health Platform.

Results

Streamlining of AMR Governance in the Water and Environment Sector

The sector-specific TWG was constituted and comprised of 10 members from the three directorates of the MWE, including the directorates of water resources management, water development, and environmental affairs. Focal persons for AMR surveillance in the sector were identified. The TWG finalized the sector surveillance documents that stipulate the target priority pathogens and sample type, designated the NWQRL as the sentinel site, designed the routine and targeted surveys, and reviewed and reported the AMR data generated to the MWE. The TWG also published a report on the AMR burden in the sector in the annual Natural Resources, Environment, Climate Change, Land and Water Management Program Performance Report 2022 [27]. Further, the TWG functioned as a linkage for the sector surveillance program to the national AMR surveillance program under the National AMR Sub-Committee of the National One Health Platform, the human and animal sector-specific AMR surveillance programs, the academia, and implementing partners.

Microbiology Laboratory Capacity Enhancement in the Sector

Following the infrastructural and equipment enhancement, the NWQRL now houses a fully-fledged biosafety level 2 microbiology laboratory, the minimum level required for AMR surveillance. The laboratory has staff trained in microbiology, including antimicrobial susceptibility testing, biosafety biosecurity, AMR data management, and laboratory quality management systems. These staff have supported the laboratory analysis of environmental samples to generate AMR data.

Bacterial Isolates Recovered

Up to 460 samples were collected and processed at the NWQRL between August 2021 and March 2023, of which 363 (78.9%) were from passive surveillance while 97 (21.1%) were from active surveillance. Of the 460 samples, 158 (34.3%) were from point sources (wastewater samples), while 284 (61.7%) were

from nonpoint sources: 108 (23.5%) ground, 95 (20.7%) surface, and 81 (17.6%) drinking water samples. Up to 328 (71.3%) samples had significant growth and yielded 602 bacterial isolates, of which, 399 (66.3%) and 203 (33.7%) were priority and nonpriority pathogens, respectively. Of the 602 isolates, 223 (37%), 166 (27.6%), 132 (21.9%), and 67 (11.1%) were from waste, surface, ground, and drinking water sources, respectively. Of the 602 isolates, 399 (66.3%) were priority pathogens: 156 (39.1%) *E. coli*, 140 (35.1%) *Klebsiella* species, 96 (24.1%) *Enterococcus* species, and 7 (1.8%) *Salmonella* species. The 203 nonpriority isolates were *Citrobacter* species ($n=57$, 28.1%), *Enterobacter* species ($n=52$, 25.6%), *Proteus* species ($n=23$, 11.3%), *Pseudomonas* species ($n=19$, 9.4%), *Acinetobacter* species ($n=8$, 3.9%), and other bacterial species ($n=44$, 21.7%).

The Burden of AMR in the Water and Environment Sector

E. coli ($n=156$) had a resistance of 79% to ampicillin, 55% to trimethoprim/sulfamethoxazole, 29% to ceftriaxone and ciprofloxacin, 18% to cefepime and chloramphenicol, 11% to imipenem, and 0% to amikacin and meropenem. Other antibiotic resistance is shown in Table 1.

Klebsiella species isolates ($n=140$) had a resistance of 100% to ampicillin, 33% to trimethoprim/sulfamethoxazole, 28% to amoxicillin-clavulanate, 27% to cefuroxime, 17% to ciprofloxacin, 2% to imipenem, and 0% to amikacin. *Salmonella* species isolates ($n=7$) had a resistance of over 50% to ampicillin, ciprofloxacin, ceftriaxone, trimethoprim/sulfamethoxazole, and tetracycline. *Enterococcus* species ($n=96$) had a resistance of 45% to vancomycin, 56% to erythromycin, 54% to tetracycline, and 52% to ciprofloxacin (Table 1).

Overall, there was no significant difference between the resistance observed in *E. coli* and *Klebsiella* species isolates recovered from point and nonpoint sources. Among the *Enterococcus* species isolates, a significant difference (odds ratio 5.318182, 95% CI 1.793498-15.76977; $P=.003$) was observed in the resistance to chloramphenicol between the isolates recovered from point and nonpoint sources. The *Enterococcus* isolates recovered from point sources were 5 times more likely to be resistant to chloramphenicol than those recovered from nonpoint sources.

Several isolates recovered exhibited nonsusceptibility to more than one antibiotic and to two or more antibiotic classes, a phenomenon referred to as multidrug resistance (MDR) and extensive drug resistance, respectively. Up to 254 (63.7%) of the 399 priority pathogens recovered exhibited MDR or extensive drug resistance, of which 99 (39%), 85 (33.5%), 65 (25.6%), and 5 (2%) were *E. coli*, *Enterococcus* species, *Klebsiella* species, and *Salmonella* species, respectively. Of the MDR *E. coli* isolates ($n=99$), 40 (40%), 25 (25%), 18 (18%), 12 (12%), 1 (1%), and 3 (3%) showed resistance to 2, 3, 4, 5, 6, and 7 antibiotics from different classes, respectively. Of the MDR *Enterococcus* species isolates ($n=85$), 27 (32%), 34 (40%), 16 (19%), and 8 (9%) showed resistance to 2, 3, 4, and 5 antibiotics from different classes, respectively. Of the MDR *Klebsiella* species isolates ($n=65$), 36 (55%), 20 (32%), 2 (3%),

6 (9%), and 1 (2%) showed resistance to 2, 3, 4, 5, and 7 antibiotics from different classes, respectively ([Table 2](#)).

Table 1. Antimicrobial resistance profiles for the different isolates recovered between August 2021 and March 2023

Isolate name, antibiotic class, and antibiotic name	Isolates tested for AST ^a , n	Resistance (%)
<i>Escherichia coli</i> (n=156)		
Penicillins		
Ampicillin	151	79
Fluoroquinolones		
Ciprofloxacin	141	29
Levofloxacin	38	21
Cephalosporins		
Cefuroxime	38	39
Ceftriaxone	115	29
Ceftazidime	38	26
Cefepime	66	18
Aminoglycosides		
Gentamicin	150	9
Amikacin	38	0
Carbapenems		
Meropenem	38	0
Imipenem	148	11
Beta-lactamase		
Piperacillin-tazobactam	53	4
Amoxicillin-clavulanate	38	13
Sulfonamide-trimethoprim		
Trimethoprim/sulfamethoxazole	146	55
Tetracyclines		
Tetracycline	50	30
Amphenicols		
Chloramphenicol	94	18
Glycyclines		
Tigecycline	50	30
<i>Klebsiella</i> species (n=140)		
Penicillins		
Ampicillin	137	100
Fluoroquinolones		
Ciprofloxacin	89	17
Levofloxacin	71	7
Cephalosporins		
Ceftriaxone	92	18
Ceftazidime	71	15
Cefepime	80	11
Aminoglycosides		
Gentamicin	134	4
Amikacin	71	0

Isolate name, antibiotic class, and antibiotic name	Isolates tested for AST ^a , n	Resistance (%)
Carbapenems		
Meropenem	71	1
Imipenem	134	2
Beta-lactamase		
Piperacillin-tazobactam	75	3
Amoxicillin-clavulanate	71	28
Sulfonamide-trimethoprim		
Trimethoprim/sulfamethoxazole	135	33
Tetracyclines		
Tetracycline	10	30
Amphenicols		
Chloramphenicol	56	4
Glycyclines		
Tigecycline	71	4
<i>Salmonella</i> species (n=7)		
Penicillins		
Ampicillin	7	86
Fluoroquinolones		
Ciprofloxacin	7	71
Cephalosporins		
Ceftriaxone	5	60
Carbapenems		
Imipenem	7	29
Sulfonamide-trimethoprim		
Trimethoprim/sulfamethoxazole	7	57
Tetracyclines		
Tetracycline	4	75
Amphenicols		
Chloramphenicol	7	43
<i>Enterococcus</i> species (n=96)		
Penicillins		
Ampicillin	74	30
Fluoroquinolones		
Ciprofloxacin	60	52
Gentamicin-Syn	51	0
Glycopeptides		
Vancomycin	88	45
Macrolides		
Erythromycin	88	56
Oxazolidinones		
Linezolid	51	2
Sulfonamide-trimethoprim		

Isolate name, antibiotic class, and antibiotic name	Isolates tested for AST ^a , n	Resistance (%)
Trimethoprim/sulfamethoxazole	66	89
Tetracyclines		
Tetracyclines	80	54
Amphenicols		
Chloramphenicol	40	50
Glycyclines		
Tigecycline	71	0

^aAST: antimicrobial susceptibility testing.

Table 2. Isolates that exhibited multidrug resistance and extensive drug resistance tendencies among the priority isolates recovered.

Number of antibiotics for which resistance is shown	Frequency of resistant isolates
Two antibiotics	
<i>Enterococcus</i> species	27
<i>Klebsiella</i> species	36
<i>Escherichia coli</i>	40
Three antibiotics	
<i>Enterococcus</i> species	34
<i>Klebsiella</i> species	20
<i>Escherichia coli</i>	25
Four antibiotics	
<i>Enterococcus</i> species	16
<i>Klebsiella</i> species	02
<i>Escherichia coli</i>	18
Five antibiotics	
<i>Enterococcus</i> species	8
<i>Klebsiella</i> species	6
<i>Escherichia coli</i>	12
Six antibiotics	
<i>Enterococcus</i> species	0
<i>Klebsiella</i> species	0
<i>Escherichia coli</i>	1
Seven antibiotics	
<i>Enterococcus</i> species	0
<i>Klebsiella</i> species	1
<i>Escherichia coli</i>	3

Discussion

AMR surveillance in the Uganda water and environment sector is taking shape, including the streamlining of the sector AMR governance structures. This has expanded the One Health approach to AMR surveillance in the country. A TWG, a national AMR reference laboratory, and an AMR focal person were constituted and provided with terms of reference. This is in alignment with the road map for the participation of low- and

middle-income countries in the Global Antimicrobial Surveillance System [21]. This program has been established using a phased/stepwise approach where one sentinel site, the NWQRL, was identified and its capacity enhanced and is now used for AMR surveillance. This is a prerequisite for establishing targeted and well-monitored public health surveillance of AMR in low-income settings [21,28]. The alignment of the efforts in the sector with national and international guidelines allows national and international

comparisons of established surveillance systems to identify areas of improvement [29].

The program has succeeded in profiling the resistance patterns of the bacterial pathogens recovered from different water types from both point and nonpoint sources of AMR determinants in the environment as categorized by Khurana and Sinha [30]. Wastewater samples represent the point sources as the resistant microorganisms in these samples either emerge directly or after antimicrobials reach and contaminate the different environment compartments. The ground, drinking, and surface water samples constitute the nonpoint sources of resistant organisms since these indicate the interface and spillage of resistant microorganisms from the environment to the human and animal populations [30].

The program used culture-based methods as these were better aligned with the current laboratory infrastructure in the Uganda water and environment sector and the country at large. Liguori et al [7] 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. However, these culture-based methods recover fewer microorganisms as the majority of the environmental microbes are not readily cultured, yet they may pose public health challenges [31]. Thus, the AMR surveillance systems in the sector require appropriate expansion to include whole genome sequencing and environmental wastewater sequencing.

E coli, *Klebsiella* species, *Enterococcus* species, and *Salmonella* species used for surveillance in the Ugandan sector are globally recommended for the environment sector [32,33]. An expert survey conducted among 105 experts from different fields and parts of the world found that Enterobacterales (mainly *E coli* and *Salmonella* species) and *Enterococcus* species were the most selected culture target microorganisms for AMR surveillance in the environment [7]. These microorganisms are similar to those recommended for AMR surveillance in the human [34,35] and animal health [36] sectors. This makes the comparison, quantification, and evaluation of the occurrence of these organisms across the different sectors in low-resource settings feasible [3,37]. They are classified as the major clinically relevant multidrug-resistant pathogens prevalent in the different environmental compartments [3,32,33,38] that can cause life-threatening illnesses in humans and animals [24].

The high *E coli* resistance to ampicillin and trimethoprim/sulfamethoxazole observed in our evaluation is similar to that observed in South Africa, where *E coli* had high resistance to sulfamethoxazole (100%) and ampicillin (90%) [39]. Moges et al [40] in Ethiopia observed that the recovered *E coli* had 100% resistance to ampicillin and 38% resistance to trimethoprim/sulfamethoxazole. This ampicillin resistance is similar to that found by Nabadda et al [41] among recovered *E coli* isolates from human samples in Uganda, which had more than 90% resistance to ampicillin. Amaya et al [42] also found that some *E coli* recovered from groundwater from wells in León, Nicaragua showed very high resistance of 100% to ampicillin, ciprofloxacin, and trimethoprim/sulfamethoxazole.

This indicates a similarity in the resistance of *E coli* recovered from humans and the environment, which requires further assessment using whole genome sequencing techniques to elucidate the interrelatedness.

The high resistance of *Klebsiella* species against ampicillin observed in the Uganda program correlates to the high ampicillin intrinsic resistance (100%) observed in the *Klebsiella* species isolates from environmental samples in a study in Pakistan from 2017 to 2019 [43]. Holt et al [44] similarly found 100% resistance to ampicillin among the different *Klebsiella* species recovered [45]. This phenomenon of *Klebsiella* species' intrinsic resistance to ampicillin is demonstrated in the Clinical and Laboratory Standards Institute guidelines [26] and the European Committee on Antimicrobial Susceptibility Testing guidelines [46,47]. The moderate *Klebsiella* species resistance (below 50%) to gentamicin, imipenem, and trimethoprim/sulfamethoxazole observed in the program is consistent with that observed in an Iraqi study on the resistance patterns of *Klebsiella* species isolates from clinical and environmental samples [48].

Resistant *Salmonella* species isolated from some of the samples indicate contamination of these sources by human and animal waste [49,50]. This points to a potential risk for an outbreak of salmonellosis within the animal or human populations residing in the surroundings of the sample source [51,52]. Such an observation can be used to predict the health profile of the human and animal populations in a given catchment area using environmental samples [20].

Enterococcus species resistance to tetracycline (54%), vancomycin (45%), erythromycin (56%), and ciprofloxacin (52%) in this program were all higher (in some instances double) than the resistance of the *Enterococcus* species from environmental samples in an area of intensive poultry production in Canada [53]. Another study in France also showed high resistance of *Enterococcus* species isolates to erythromycin (100%), vancomycin (85.7%), and tetracycline (57.1%) [54].

The MDR exhibited by the isolates recovered in the program is consistent with the findings of studies conducted in several parts of the world. For example, a 96.4% MDR occurrence was observed in the bacterial strains recovered from samples collected from different aquatic environments in a study in France [54]. Another study in Ghana by Odonkor and Addo [55] found that 63% of the *E coli* strains recovered were resistant to at least 3 antibiotics from different classes. Further, a study conducted in the United States also found that 65% of the isolates recovered from combined sewage overflows (wastewater) were resistant to 6 or more antibiotics from different classes [56]. Human and animal exposure to and infection with such highly resistant bacteria in the environment through complex interactions impacts the economy of countries as such infections are harder to treat. This increases medical costs, hospital stays, the risk of infection spread, severity, and mortality rates [57].

Our evaluation had one major limitation. 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.

Efforts to implement AMR surveillance in the water and the environment sector succeeded in streamlining AMR surveillance governance and isolating resistant pathogens from different

water types (waste, drinking, surface, and groundwater). 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. Sustained surveillance in the sector and interlinkages with the human and animal sectors' surveillance systems are also required to inform concerted strategies to control AMR in the country.

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Data Availability

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.

Conflicts of Interest

None declared.

Multimedia Appendix 1

Map showing the environment sector antimicrobial resistance surveillance sampling points in Kampala and Wakiso.

[\[PNG File , 656 KB - xbio_v2i1e50588_app1.png\]](#)

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Abbreviations

AMR: antimicrobial resistance

MDR: multidrug resistance

MWE: Ministry of Water and Environment

NWQRL: National Water Quality Reference Laboratory

TWG: technical working group

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