Challenges in Tackling Antimicrobial Resistance in Resource-limited settings: A Cameroonian Case study

Patrice Landry Koudoum[1,2*], Angyiba Serge Andigema[1,2#], Abena Jerry[1,2#], Moise Matakone[1]

[1] Department of Microbiology, Hematology and Immunology, University of Dschang, Cameroon;

[2]Oli Health Magazine Organization, Research, and Education, Yaoundé, Cameroon.

#These authors contributed equally

*Corresponding author

Department of Microbiology, Hematology, and Immunology

University of Dschang, Dschang, Cameroon

Email: patricekoudoum@gmail.com

ABSTRACT

Antimicrobial resistance (AMR) remains a global public health threat, especially in resource-limited countries. AMR contributors and exacerbators vary greatly depending on the country's resources, development, and containment strategies. To properly address the AMR menace, it is important to understand the current local drivers and provide country-tailored solutions. The main drivers of AMR such as inadequate water sanitation and hygiene, antimicrobial misuse, and overuse in both humans and animals in resource-limited countries are not adequately managed to reduce the emergence and spread of AMR in community and hospital settings. Tackling AMR will require a multisectoral One Health approach with the contribution of stakeholders, policymakers, health professionals, and the community. If AMR is not adequately handled in resource-limited countries, it will always find its way to spread globally as it has no respect for local, regional, and intercontinental boundaries. The objective of this review is set to highlight the major challenges faced in tackling AMR in resource-limited settings with Cameroon as a case study and proposed possible control measures.

KeyWords: Antimicrobial resistance, Cameroon, resource-limited countries.

Introduction

Antimicrobial resistance (AMR) has grown to be a worldwide threat with tremendous health and socioeconomic implications (R. C. Founou, Founou, & Essack, 2017). According to a recent systematic review, in 2019, antibiotic-resistant infections claimed close to 5 million lives and 1.27 million deaths were directly attributable to bacterial AMR (Murray et al., 2022). It has been predicted that if no prompt actions are taken, AMR will emerge as the leading cause of mortality by 2050, claiming 10 million lives yearly and costing $US100 trillion to the global economy (O'Neill, 2016).

AMR is present across the globe, but its burden is disproportionately higher in developing countries (R. C. Founou et al., 2017). The highest mortality rates caused by bacterial AMR in 2019 were recorded in South Asia and sub-Saharan Africa (SSA) which are two sub-regions comprised mainly of developing countries (Murray et al., 2022). AMR is evolving at a fast pace, with the most communicated accelerators being the overuse and misuse of antimicrobials in both animals and humans and a dry antimicrobial development pipeline (O'Neill, 2016). Cameroon is not escaping this upward trend in AMR. A study conducted at a national reference laboratory

analysing over 10000 bacteria isolates collected in 2010 and 2017 found that almost all bacteria groups acquired resistance. Alarmingly, significant increases in acquired resistance were found in critical bacteria listed by the WHO for the development of new antibiotics (WHO, 2017b) including but not limited to carbapenem-resistant *Acinetobacter* (+248%), carbapenem-resistant *Pseudomonas* (+74%), 3rd generation-resistant *Enterobacterales* (+66%) and methicillin-resistant *Staphylococcus aureus* (+69%) (Massongo et al., 2021). To properly address the AMR menace, it is important to understand local drivers and provide country-tailored solutions. Curbing the growing threat caused by AMR, requires a holistic and multi-sectorial approach with the implication of health professionals, stakeholders, and the community (Pokharel, Raut, & Adhikari, 2019). Below are presented major challenges faced in containing AMR in resource-limited countries with Cameroon as a case study and proposed possible way-out solutions.

Study context

Cameroon is one of the low- and middle-income countries with a population of over 27,2 million and situated in the Central African region where it is limited by the Central African Republic, Chad, Equatorial Guinea, Gabon, and Nigeria (World Bank 2023). Cameroon has a pyramidal health system organised into three levels with each level characterised by administrative and health-care structures (World Health Organization 2017). Only 3.6% of the national GDP is dedicated to the health sector in 2023 (MINFI, 2023). Most of the peripheral health facilities don't have enough operational laboratories, which leads to frequent stock-out reagents and the unavailability of competent laboratory technicians (World Bank 2019).

Challenges faced in tackling AMR and what can be done

   1. **Inadequate access to water sanitation and hygiene (WASH)**

Inappropriate WASH is known to be a significant risk factor for infections especially diarrheal diseases worldwide. This concerns particularly resource-limited settings where there is a higher burden of infectious diseases, resulting in higher use of antimicrobials for treatment and thus the rapid emergence and spread of AMR (Pokharel et al., 2019). In Cameroon, the rate of access to drinking water is 66% and sanitation 45% and it is currently argued that it is unlikely for Cameroon to reach universal access to WASH in rural settings by 2030 (Victor Dang et al., 2022). It is currently estimated that, 60% of all diarrheal diseases treated using antimicrobials can be prevented by providing universal access to water and sanitation (Pokharel et al., 2019).

Because prevention is better than cure, it is judicious that the Cameroon government invests more to provide adequate WASH and community-based programmes to the population thereby reducing the occurrence of infectious diseases and the eventual use of antimicrobials which triggers the emergence and spread of AMR.

   2. **Sub-optimal infection prevention and control strategies**

Infection prevention and control (IPC) in hospital settings is a cornerstone in combatting AMR as it prevents the acquisition and spread of hospital-acquired resistant infections (HAIs). Sub-optimal hospital hygiene is more evident in resource-limited settings resulting in a higher burden of HAIs (Ayobami, Brinkwirth, Eckmanns, & Markwart, 2022). In Cameroon, a study conducted in two referral hospitals of Yaoundé in 2015 found that 99% (141/143) of hospital surface samples, 92% (33/36) of air samples from operation rooms, and 75% (12/16) of water samples were positive for bacteria (Gonsu et al., 2015). These results strongly underscore the role of the hospital environment as an important reservoir and source of bacteria (whether resistant or not) causing HAIs.

These results serve as a clarion call for Cameroon policymakers to develop and implement national guidelines for the microbiological monitoring of hospital environment surfaces to prevent the spread of antimicrobial-resistant microorganisms in the hospital milieu. Also, it will be a life-saving action to observe IPC measures as it has been estimated that, the washing of hands alone by healthcare workers in hospital settings could reduce antimicrobial use and infectious diseases by 40% (Erasmus et al., 2010).

3. Misuse and overuse of antimicrobials by humans

Antimicrobial misuse and overuse by humans are significant exacerbators of AMR as it triggers a selective pressure on microbes (Denyer Willis & Chandler, 2019). Antimicrobial misuse is often driven by inadequate knowledge of antimicrobial use, poverty, and availability of these drugs over-the-counter (OTC) among others (Pokharel et al., 2019). For instance, a recent study on 402 Cameroonians purchasing antibiotics at private pharmacies found that nearly half (47%) bought these antibiotics without a medical prescription and 90% reported that antibiotics can kill all microbes (Elong Ekambi et al., 2019). More worrisome is that, unregulated drug dispensaries are rampant in Cameroon and they are often a source for OTC purchase of antimicrobials by community members, yet their contribution to AMR remains unassessed.

It is more than urgent to develop and implement appropriate guidelines for the use of antimicrobials in Cameroon and also provide high-quality training to healthcare professionals and raise community members on AMR and the appropriate use of antimicrobials.

4. Increasing antimicrobial use in animals

Antimicrobial use in food animals for growth promotion, therapeutic, prophylactic, and metaphylactic purposes is on the rise globally. It has been forecasted that there will be a 67% rise in antimicrobial consumption in livestock between 2010 and 2030 (Van Boeckel et al., 2015). More worrisome is that 73% of the sales of all medically important antimicrobials are for use in food animal production (Van Boeckel et al., 2019). Cameroon is not escaping this global trend as a study reported that between 2014 and 2019, 217.67 tons of antimicrobials were imported for veterinary use in Cameroon and there has been a 104% increase in the importation between 2014 and 2019 with 34% of these antimicrobials being of critical importance to human medicine according to the WHO AwaRe categorization (Mouiche et al., 2020).

The use of antibiotics in food animals is known to trigger a selective pressure on the bacteria colonizing or infecting the animal and thus promote the selection of resistant bacteria which can then be spread to humans either through direct contact with the animal or animal secretions or indirectly via shared environmental surfaces (L. L. Founou, Founou, & Essack, 2021).

AMR has been termed a quintessential One Health issue (Robinson et al., 2016) as it cannot be addressed properly if the components (human, animal, and the environment) of the one health triad are not taken into account as antimicrobial-resistant microorganisms and genes can always emerge from one of the interfaces and spread to the others (L. L. Founou et al., 2021). It is therefore capital to observe antimicrobial stewardship in the three sectors to curb the growing threat of AMR.

5. Lack of political will

Weak governance is a commonplace in resource-limited settings and this often leads to weakened healthcare policies, lack of infrastructures, inadequate IPC and WASH, corruption, socio-economic instability, poverty, and non-optimal investment in the healthcare sector (Pokharel et al., 2019). In such settings, high rates of infectious diseases prevail, leading to a refuge towards antimicrobials which serves as a "quick-fix", resulting in high antimicrobial use and eventually the escalation of AMR (Denyer Willis & Chandler, 2019). Cameroon for example is undermined by political instability in its North West and South West regions (so called Anglophone crisis) since 2016, terrorist attacks in the Far North region, poverty (with over 40% of the population living under the poverty limit), corruption and slow economic growth (Worldbank, 2023). In Cameroon, only 3.6% of the country's gross domestic product has been allocated for public health according to the law of finance of 2023 (MINFI, 2023).

There is allegedly weak commitment with regard to AMR in Cameroon. Since the adoption of the National Action Plan in May 2018 for implementation by 2020, almost no effort and progress has been made and since 2018, no budget has been allocated for that (Amin et al., 2021). Omitting strong political commitment, the implementation of the Cameroon NAP and the de-escalation of AMR

will remain unrealistic.

6. Inadequate diagnostic and empirical regimens

While antimicrobials remain readily accessible OTC in resource-limited settings, peripheral hospital laboratories lack appropriate facilities and skilled personnel to rapidly detect infections and perform antimicrobial susceptibility testing (AST) (Pokharel et al., 2019). An external evaluation in September 2017 by the World Health Organisation (WHO) in Cameroon revealed for instance that, only four research laboratories, one animal health laboratory, and 13 public health laboratories were adequately equipped to detect and report cases of antimicrobial resistance (WHO, 2017a). In the absence of adequate diagnostic and AST results, healthcare professionals rely on empirical antimicrobial regimens which are not often adapted to the local AMR epidemiology as they are often burrowed from the Western world (Okeke et al., 2005).

It is now more than a necessity for developing countries to leverage their diagnostic capacity with regards to AMR and to fill data gaps regarding AMR epidemiology in their local population in order to set up country-tailored treatment guidelines. Also, computerized nationwide real-time monitoring platforms for infectious diseases and AMR is needed for robust AMR surveillance and to inform on long-term trends in resistance.

7. Inadequate wastewater treatment and disposal

The environment seems to be the neglected component of the one health triad whereas its contribution to the emergence and spread of AMR is enormous but yet insufficiently assessed (Essack, 2018). Both municipal and hospital wastewater are known to be important reservoirs of antibiotic-resistant bacteria and genes (Tiwari et al., 2022). In developing countries, there is a lack of stringent policies regulating the pre-treatment of hospital wastewater before disposal, as such, wastewater is often eliminated without prior treatment resulting in the elimination of resistant bacteria and genes in the community. In community settings, municipal wastewater treatment plants (where they exist) often function at sub-optimal capacities, resulting in ARB and ARGs from influent passing to effluent water and subsequently disposed to adjacent water bodies (Abia, Baloyi, Traore, & Potgieter, 2023). In Cameroon, the recent analysis of raw sewage used for urban agriculture using state-of-the-art metagenomics has recently revealed that the environmental resistome is highly diverse and dense (Bougnom, McNally, Etoa, & Piddock, 2019). The wastewater resistome is a significant contributor to AMR emergence and dissemination and as such, adequate treatment and disposal coupled with wastewater AMR surveillance are a requisite for the containment of AMR.

Conclusion

In the next foreseeable future, AMR will remain a global public health concern, especially in resource-limited settings if no urgent actions are taken. As related in this review, basic necessities such as adequate WASH and IPCs are overlooked contributors to AMR in Cameroon, just as in other resource-limited countries. Tackling AMR will require a multisectoral One Health approach with the contribution of stakeholders, policymakers, health professionals, and the community. If AMR is not adequately handled in resource-limited countries, it will always find its way to spread globally following, humans, animals, food, and water movement as AMR has no respect for local, regional, and intercontinental boundaries.

References

Abia, A. L. K., Baloyi, T., Traore, A. N., & Potgieter, N. (2023). The African Wastewater Resistome: Identifying Knowledge Gaps to Inform Future Research Directions. *Antibiotics (Basel), 12*(5). doi:10.3390/antibiotics12050805

Amin, E. T., Omeichu, A. A., Shu, D. M., Ekome, S. R. E., Njumkeng, C., & van der Sande, M. A. B. (2021). Control of antimicrobial resistance in Cameroon: Feasibility of implementing the National Action Plan. *Trop Med Int Health, 26*(10), 1231-1239. doi:10.1111/tmi.13649

Ayobami, O., Brinkwirth, S., Eckmanns, T., & Markwart, R. (2022). Antibiotic resistance in hospital-acquired ESKAPE-E infections in low- and lower-middle-income countries: a systematic review and meta-analysis. *11*(1), 443-451. doi:10.1080/22221751.2022.2030196

Bougnom, B. P., McNally, A., Etoa, F. X., & Piddock, L. J. (2019). Antibiotic resistance genes are abundant and diverse in raw sewage used for urban agriculture in Africa and associated with urban population density. *Environ Pollut, 251*, 146-154. doi:10.1016/j.envpol.2019.04.056

Denyer Willis, L., & Chandler, C. (2019). Quick fix for care, productivity, hygiene and inequality: reframing the entrenched problem of antibiotic overuse. *BMJ Glob Health, 4*(4), e001590. doi:10.1136/bmjgh-2019-001590

Elong Ekambi, G. A., Okalla Ebongue, C., Penda, I. C., Nnanga Nga, E., Mpondo Mpondo, E., & Eboumbou Moukoko, C. E. (2019). Knowledge, practices and attitudes on antibiotics use in Cameroon: Self-medication and prescription survey among children, adolescents and adults in private pharmacies. *PLoS One, 14*(2), e0212875. doi:10.1371/journal.pone.0212875

Erasmus, V., Daha, T. J., Brug, H., Richardus, J. H., Behrendt, M. D., Vos, M. C., & van Beeck, E. F. (2010). Systematic review of studies on compliance with hand hygiene guidelines in hospital care. *Infect Control Hosp Epidemiol, 31*(3), 283-294. doi:10.1086/650451

Essack, S. Y. (2018). Environment: the neglected component of the One Health triad. *Lancet Planet Health, 2*(6), e238-e239. doi:10.1016/s2542-5196(18)30124-4

Founou, L. L., Founou, R. C., & Essack, S. Y. (2021). Antimicrobial resistance in the farm-to-plate continuum: more than a food safety issue. *Future Sci OA, 7*(5), Fso692. doi:10.2144/fsoa-2020-0189

Founou, R. C., Founou, L. L., & Essack, S. Y. (2017). Clinical and economic impact of antibiotic resistance in developing countries: A systematic review and meta-analysis. *PLoS One, 12*(12), e0189621. doi:10.1371/journal.pone.0189621

Gonsu, K. H., Guenou, E., Toukam, M., Ndze, V. N., Mbakop, C. D., Tankeu, D. N., . . . Takongmo, S. (2015). Bacteriological assessment of the hospital environment in two referral hospitals in Yaoundé-Cameroon. *Pan Afr Med J, 20*, 224. doi:10.11604/pamj.2015.20.224.4433

Massongo, M., Ngando, L., Pefura Yone, E. W., A, N. Z., Mbanzouen, W., Fonkoua, M. C., . . . Tejiokem, M. C. (2021). Trends of Antibacterial Resistance at the National Reference Laboratory in Cameroon: Comparison of the Situation between 2010 and 2017. *Biomed Res Int, 2021*, 9957112. doi:10.1155/2021/9957112

MINFI. (2023). Cameroon Ministry of Finance. The Law of finance 2023. Retrieved from https://www.dgb.cm/wpfd_file/projet-de-loi-de-finance-2023/ [Accessed 1Jul 2023].

Mouiche, M. M. M., Moffo, F., Betsama, J. D. B., Mapiefou, N. P., Mbah, C. K., Mpouam, S. E., . . . Awah-Ndukum, J. (2020). Challenges of antimicrobial consumption surveillance in food-producing animals in sub-Saharan African countries: Patterns of antimicrobials imported in Cameroon from 2014 to 2019. *J Glob Antimicrob Resist, 22*, 771-778. doi:10.1016/j.jgar.2020.06.021

Murray, C. J. L., Ikuta, K. S., Sharara, F., Swetschinski, L., Robles Aguilar, G., Gray, A., . . . Naghavi, M. (2022). Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. *The Lancet, 399*(10325), 629-655. doi:10.1016/S0140-6736(21)02724-0

O'Neill, J. (2016). Tackling drug-resistance infections globally: final report and recommendations, 2016.Available:https://amrreview.org/sites/default/files/160518_Final%20paper_with%20cover.pdf [Accessed 1Jul 2023].

Okeke, I. N., Klugman, K. P., Bhutta, Z. A., Duse, A. G., Jenkins, P., O'Brien, T. F., . . . Laxminarayan, R. (2005). Antimicrobial resistance in developing countries. Part II: strategies for containment. *Lancet Infect Dis, 5*(9), 568-580. doi:10.1016/s1473-3099(05)70217-6

Pokharel, S., Raut, S., & Adhikari, B. (2019). Tackling antimicrobial resistance in low-income and middle-income countries. *BMJ Glob Health, 4*(6), e002104. doi:10.1136/bmjgh-2019-002104

Robinson, T. P., Bu, D. P., Carrique-Mas, J., Fèvre, E. M., Gilbert, M., Grace, D., . . . Woolhouse, M. E. (2016). Antibiotic resistance is the quintessential One Health issue. *Trans R Soc Trop Med Hyg, 110*(7), 377-380. doi:10.1093/trstmh/trw048

Tiwari, A., Kurittu, P., Al-Mustapha, A. I., Heljanko, V., Johansson, V., Thakali, O., . . . Heikinheimo, A. (2022). Wastewater surveillance of antibiotic-resistant bacterial pathogens: A systematic review. *Front Microbiol, 13*, 977106. doi:10.3389/fmicb.2022.977106

Van Boeckel, T. P., Brower, C., Gilbert, M., Grenfell, B. T., Levin, S. A., Robinson, T. P., . . . Laxminarayan, R. (2015). Global trends in antimicrobial use in food animals. *Proc Natl Acad Sci U S A, 112*(18), 5649-5654. doi:10.1073/pnas.1503141112

Van Boeckel, T. P., Pires, J., Silvester, R., Zhao, C., Song, J., Criscuolo, N. G., . . . Laxminarayan, R. (2019). Global trends in antimicrobial resistance in animals in low- and middle-income countries. *Science, 365*(6459). doi:10.1126/science.aaw1944

Victor Dang, M., Paul Blaise, M., Célestin, D., Paul Fabrice, N., Anil Kumar, M., & Auguste, O. (2022). Perspective Chapter: Access to Rural Water and Sanitation Services in Cameroon within the Context of Sustainable Development Goals (SDGs). In T. Sonja Šostar & R. Urška (Eds.), *Hygiene and Health in Developing Countries* (pp. Ch. 2). Rijeka: IntechOpen.

WHO. (2017a). Evaluation externe conjointe des principales capacités RSI de la République du Cameroun. . Retrieved from https://www.minsante.cm/site/?q=en/content/evaluation-externe [Accessed on June 12 2023]

WHO. (2017b). *Prioritization of Pathogens to Guide Discovery, Research and Development of New Antibiotics for Drug-Resistant Bacterial Infections, Including Tuberculosis;* World Health Organization: Geneva, Switzerland, 2017; pp. 1–88.

Worldbank. (2023). Cameroon Data. Retrieved from https://data.worldbank.org/country/cameroon [Accessed on June 12 2023]