The African Wastewater Resistome

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In Africa, the prevalence of Antimicrobial Resistance (AMR) in wastewater is of particular concern due to the inadequate sanitation and wastewater treatment facilities, coupled with the overuse and misuse of antibiotics in healthcare and agriculture.

low- and middle-income countries environmental health public health

1. Introduction

Antimicrobial resistance (AMR) has been recognised by countries and organisations worldwide as one of the biggest threats to public health in recent times [1][2][3]. It is estimated that without appropriate preventive or remedial measures, the world may experience approximately 10 million losses of lives and over USD 100 trillion annually in the global economy by 2050 [4].

Although microorganisms possess intrinsic resistance to naturally occurring stressors, the indiscriminate use of pharmaceuticals has been recognised as the most significant contributor to acquired resistance in these organisms, thus escalating the threat to human health [5][6]. For example, the massive and increasing demand for animal protein has engendered an unparalleled use of antibiotics in food animal production, which in 2017 was estimated at 93,309 tons per year globally, with an expected 11.5% increase by 2030 [7]. Furthermore, in humans, misdiagnosis of infections results in the inappropriate prescription of many antibiotics [8]. Therefore, to curb this ill, the World Health Organization (WHO) has identified critical factors driving AMR, including the abusive use of these pharmaceuticals, nonavailability of clean water, sanitation and hygiene (WASH) for human and animal use, inadequate measures to control and prevent infections and diseases in health and animal production settings, inaccessibility to good, and cost-effective medications, vaccines and test procedures, unawareness and lack of knowledge regarding the problem, and nonenforcement of legislation [9].

However, a considerable proportion of the antibiotics consumed by humans and animals are mostly excreted in partially or completely unmetabolised forms, usually containing active ingredients [10][11]. This results in the inevitable discharge of these pharmaceutically active compounds into the environment, especially water bodies, with the major consequence being the potential selection for the survival of resistant microorganisms. With this, wastewater treatment plants (WWTPs) have been recognised as being among the hotspots for the discharge of antibiotics, their residues and antibiotic-resistant bacteria into the environment [12][13][14][15][16][17].

Despite the perceived role of these WWTPs on the spread of AMR, studies evaluating their impact are limited, especially in low- and middle-income countries (LMICs) such as South Africa, where such facilities are usually nonfunctional or function sub-optimally. Furthermore, where such studies are available, the link between environmental and clinical isolates is not apparent, probably because of the basic analyses performed that usually have low discriminating powers to establish such associations. Moreover, the lack of proper reporting of findings influences the acquisition of such data in the public domain. Thus, the present research evaluated the existing literature on AMR in Africa between 2012 and 2022, emphasising South Africa as a case study, to identify gaps that need to be filled to inform future preventive and mitigation measures towards AMR.

2. Overview of African Studies between 2012 and 2022

In Africa, the prevalence of AMR in wastewater is of particular concern due to the inadequate sanitation and wastewater treatment facilities, coupled with the overuse and misuse of antibiotics in healthcare and agriculture. African countries, especially in the sub-Saharan region, have the highest disease burdens in the world, with infectious diseases accounting for over 227 million healthy life years and over USD 800 billion yearly productivity loss globally [18]. The ripple effect of this health situation has been identified as the primary factor driving the excessive rate of antimicrobial prescriptions within the continent [19]. For example, consumption of antibiotics in the WHO Watch list increased by 165% in LMIC (including African countries) compared to approximately 28% in their high-income counterparts between 2000 and 2015 [19].

This high antibiotic use implies that wastewater in these countries would be rich in antibiotic residues, antibiotic-resistant bacteria (ARB) and their associated antibiotic resistance genes (ARGs). For example, a study in Ghana investigated resistance genes, and mobile genetic elements (MGEs), from drainage and canalizations before and after three hospitals and an urban waste treatment plant [20]. The main idea was to establish the relationship between the hospital and the wastewater resistome. The authors used a combination of culture-dependent and independent methods, including high-throughput whole-genome sequencing on two sequencing platforms, Nanopore (long reads) and Illumina (short reads). The authors recorded higher resistance rates to carbapenems in the canalization after the hospitals, indicating that the hospital wastewater contributed significantly to the dissemination of resistant bacteria in the environment. Furthermore, the study identified several carbapenemase/β-lactamase genes, including novel variants, such as $bla_{\text{DIM-1}}$, $bla_{\text{VIM-71}}$, $bla_{\text{CARB-53}}$, and $bla_{\text{CMY-172}}$, with some of these genes associated with MGEs, meaning that these could easily be transferred within and between bacterial communities.

In Nigeria, Akpan et al. [21] isolated Gram-negative bacteria from an abattoir’s wastewater and tested them for antibiotic resistance against five antibiotics to determine the impact of the abattoir on the environmental resistome. The organisms isolated included *Salmonella* spp., *E. coli*, *Klebsiella* spp., *Shigella* spp., *Pseudomonas* spp. and *Enterobacter* spp. The authors observed that a significant proportion of the isolates (~67%) were resistant to all antibiotics tested, with a 77% multidrug resistance recorded across the samples. However, no extended-spectrum β-lactamase (ESBL)-producing traits were observed in any of the isolates. This study demonstrated that abattoirs contributed considerably to AMR in the aquatic environment.

Tesfaye et al. [22] investigated antimicrobial resistance in *Enterobacteriaceae* in wastewater collected from health settings, an abattoir, and a WWTP, including downstream of a river in Addis Ababa, Ethiopia. The authors obtained 54 isolates, including *E. coli*, *Salmonella* spp., *Klebsiella pneumoniae*, *Enterobacter aerogenes*, *Citrobacter* spp., *Klebsiella oxytoca* and *Enterobacter cloacae*. Antibiotic susceptibility testing revealed that all the isolates were multidrug resistant, while two isolates were resistant to all the 12 antibiotics tested. ESBL production was also recorded in 27.3% of the resistant isolates. Furthermore, the hospital wastewater had a higher percentage of resistance than all the other sites, again identifying hospital wastewater as a hotspot for AMR dissemination.

A major shortcoming in all the studies reviewed is that most focused on a one-off sampling, usually resulting in a very limited number of isolates or samples. Such small sample sizes would make it challenging to draw strong conclusions and would require further investigations. Furthermore, many studies used culture or sequencing and only a few used both. Using only the culture methods could underestimate the microbial load due to viable but non-culturable isolates, reducing the reported resistome. On the other hand, using only genomic approaches could overestimate the risk associated with AMR in wastewater. Nevertheless, the presence of any resistance genes and MGEs would signify the possible transmission to other related or even unrelated species. A summary of some studies on wastewater resistome in Africa is provided in **Table 1**.

Table 1. Summary of some studies on AMR in wastewater in Africa between 2012 and 2022.

Country	& Wastewater Type/Source	Duration of Study	Sample Size	Targeted Resistance	Phenotypic (P)/Genotypic (G) Resistance	Method	Reference
* South Africa	WWTP	Two campaigns—actual duration not mentioned	# Not indicated	Cefotaxime-resistance	P	Culture	[23]
Algeria	WWTP	3 days in 2 months	Not indicated	ESBLs and associated quinolone resistance	P, G	Culture; PCR	[24]
Botswana	WWTP	$ One-off sampling	one	Overall resistome	G	Shotgun metagenomics	[25]
Botswana	WWTP	Monthly for 1 year	72	General resistance—9 antibiotics tested	P	Culture	[26]
Burkina Faso	Urban channel	6 months	101	ESBLs	P	Culture	[27]

Country	& Wastewater Type/Source	Duration of Study	Sample Size	Targeted Resistance	Phenotypic (P)/Genotypic (G) Resistance	Method	Reference
Burkina Faso	WWTP	Monthly for 5 months	15	General resistance—19 antibiotics	P	Culture	[28]
Cameroon	Open-air canals	One-off	6 (composite) samples	Overall resistome	G	Shotgun metagenomics	[29]
Ethiopia	Hospital wastewater	3 months	27	General resistance—13 antibiotics	P	Culture	[30]
Ethiopia	Hospital wastewater	4 months	40 (composite samples)	General resistance—13 antibiotics	P	Culture	[31]
Ghana	WWTP	Monthly—6 months	30	General resistance	P	Culture	[32]
Kenya	University WWTP	4 months	Not mentioned	Overall resistome	P, G	Culture; whole-genome sequencing	[33]
Kenya	Septic tank	2 months	Not mentioned	General resistance	P	Culture	[34]
Kenya	WWTP	6 months (covering the dry and rainy seasons)	24	General resistance	P	Culture	[35]
Nigeria	Hospital WWTP	Weekly for 4 months	Not mentioned	ESBLs	P, G	Culture; PCR	Adekanmbi
Senegal	Slaughterhouse wastewater and WWTP	Not mentioned	Not mentioned	General resistance—16 antibiotics	P	Culture	[36]
South Africa	WWTP	7 months (Every two weeks)	81	Overall resistome	P, G	Culture; whole-	[37]

Country	[&] Wastewater Type/Source	Duration of Study	Sample Size	Targeted Resistance	Phenotypic (P)/Genotypic (G) Resistance	Method	Reference
						genome sequencing	
Tanzania	WWTP	2013/2014 (Not specific)	52	General resistance—14 antibiotics	P	Microdilution	[38]
Tunisia	WWTP	Not mentioned	Not mentioned	*intI1*, ARGs *bla*$_{CTX-M}$, *bla*$_{TEM}$, *qnr*A, *qnr*S, *sul* I, *erm*B	G	PCR	[39]
Uganda	Multiple sources	Not mentioned	Not mentioned	General resistance—15 antibiotics	P	Culture	[40]
Zambia	Wastewater ponds	Not mentioned	5 samples	General resistance—8 antibiotics	P	Culture	[41]
Zimbabwe	Abattoir wastewater	3 months	600 samples	General resistance—16 antibiotics	P	Culture	[42]

[*] Part of a multinational (22 countries) study in Europe, Asia, Africa, Australia, and North America. [#] A total of 472 samples were collected from all the countries. [$] Analysed once and used to irrigate soil. Focus was not on the monitoring of the wastewater resistome but on the impact of the wastewater on the soil resistome. [&] Includes influent or effluent or both.

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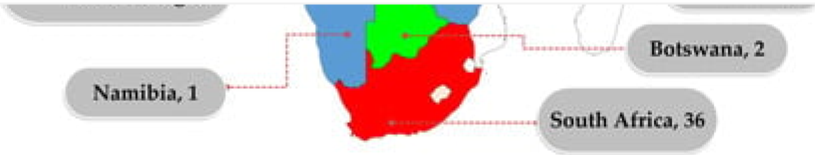

Figure 1. Distribution of African studies on AMR in wastewater between 2012 and 2022. Numbers represent the number of studies identified within the reviewed period. Only counties that reported at least one study in the review period are labelled.

However, it is evident that wastewater as a reservoir and source of AMR is gaining attention in Africa, as seen by the increasing trend of studies focusing on wastewater (**Figure 2**).

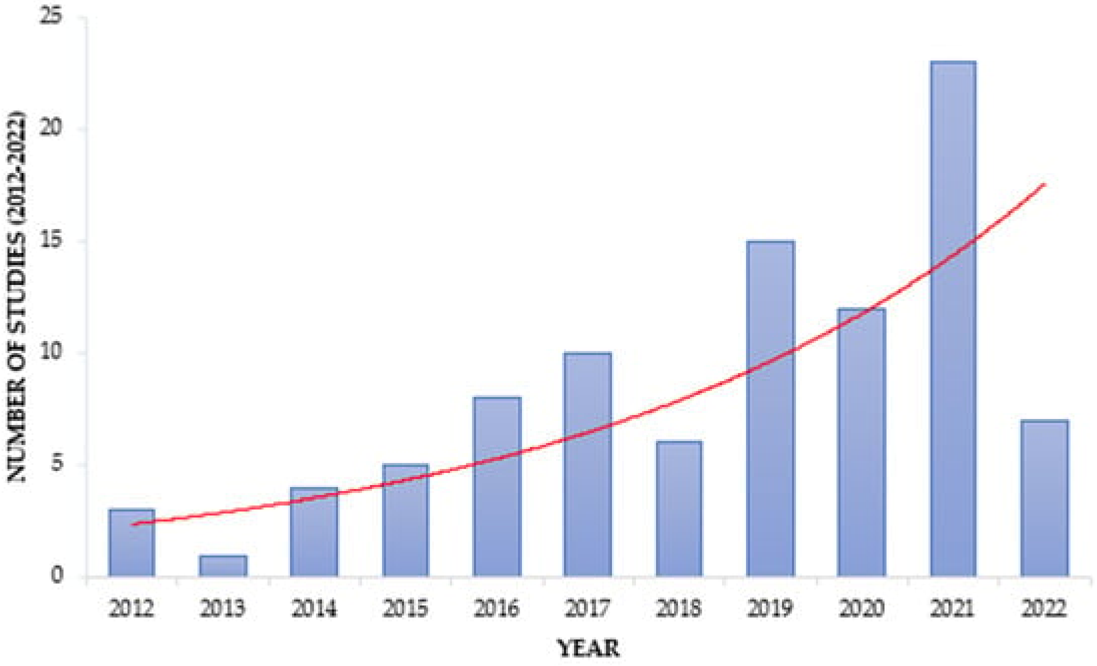

Figure 2. Trend in ARM studies focusing on wastewater. The red line shows the increasing trend within the reviewed period.

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