

EPIDEMIOLOGY OF ANTIMICROBIAL RESISTANCE AND THE WASH PROJECT: AVERTING A POTENTIAL PUBLIC HEALTH CRISIS IN NIGERIA USING THE UNITED KINGDOM AS A CASE STUDY

Abstract :

Aim: To assess the impact of WASH services in mitigating the proliferation of AMR in Nigeria, with the United Kingdom serving as a reference population.

Study Design: This is a review article.

Duration of study: An extensive review was conducted in relevant databases, specifically focusing on research studies published in peer-reviewed journals in English. These studies were conducted in both the United Kingdom and Nigeria, with the primary objective of investigating the relationship between Water, Sanitation, and Hygiene practices and Antimicrobial Resistance. The search spanned from May 2015, coinciding with the adoption of the global action on antimicrobial resistance by the World Health Assembly, to July 2023. The literature search was completed on August 10, 2023.

Methodology: The search involved electronic databases such as EBSCO, PubMed, Science Direct, and CINAHL Complete. Additionally, relevant literature was searched on the websites of organizations such as the World Health Organization, Nigeria Centre for Disease Control and Prevention, and the Centre for Disease Control and Prevention, Public Health England. The quality of the papers was evaluated using CASP tools to determine their reproducibility, credibility, dependability, and confirmability. Out of the initial 705 articles that were drawn from the different databases, 12 studies were included in the literature review.

Results: The review of the various literature showed that WASH interventions in Nigeria are geared toward disease transmission/infection prevention and control and not the combatting of AMR while studies in the UK have shown positive advances in tackling AMR utilizing WASH services.

Conclusion: Promoting the development and provision of WASH infrastructure in diverse Nigerian settings is crucial for addressing antimicrobial resistance (AMR). This literature review serves as a call to action for stakeholders at the national, regional, and local levels in Nigeria, emphasizing the necessity of nationwide investment in WASH infrastructure, the development of policies that support the implementation of WASH in all the communities and villages, extensive health promotion campaigns to raise awareness about AMR, and community-level interventions to contain the spread of AMR in Nigeria.

Key Words: AMR, antibiotic resistance, WASH, United Kingdom, Nigeria.

1.1 INTRODUCTION

Antimicrobial resistance (AMR) ensues when the efficacy of medications employed for treating infections or illnesses diminishes as a result of alterations in the structure of the microorganism which could be bacteria, fungi, viruses, or other microbes (Murray *et al.*, 2022). This phenomenon can transpire within the bodies of human or animal hosts, as well as in settings where the discharge of waste materials and the existence of antimicrobials and other contaminants erode or exhaust the predominant populations of the intended microorganisms. This depletion creates an opportunity for the surviving strains that possess resistance to flourish (Murray *et al.*, 2022). Consequently, this has led to the emergence of formidable pathogens such as Multi-drug-resistant *Mycobacterium tuberculosis* (MDR-TB), Methicillin resistant *Staphylococcus aureus* (MRSA) and Carbapenem-resistant Enterobacteriaceae (CRE).

WASH is an abbreviation that represents "water, sanitation, and hygiene." This acronym is extensively employed by non-profit organizations and humanitarian groups operating in less economically developed countries. The aims of delivering Water, Sanitation, and Hygiene (WASH) services include advancing public health, promoting individual dignity by addressing sanitation needs, ensuring access to water and sanitation as a basic human right, reducing the workload for women in terms of water collection, preventing gender-based violence, improving educational and health outcomes in schools and healthcare facilities, and reducing water contamination. A crucial water security component is access to WASH services (World Health Organization, 2015). Securing equitable, economically viable, and enduring access to Water, Sanitation, and Hygiene (WASH) services is a pivotal priority in global progress, and it forms the primary emphasis of the first two objectives outlined in Sustainable Development Goal 6 (SDG 6). Objectives 6.1 and 6.2 aspire to deliver fair and reachable water and sanitation provisions for all. By 2017, estimates revealed that 844 million people lacked access to safe and clean drinking water and that 2.3 billion people lacked basic sanitation facilities (World Health Organization and United Nations Children's Fund, 2017).

1.2 THE DEVELOPMENT OF ANTIBIOTICS AND THE RISE OF ANTIMICROBIAL RESISTANCE

In the early 1900s, significant progress in the identification of antimicrobial drugs and the management of infections marked a turning point in human life expectancy. Particularly around bacterial infections, this progress was propelled by the discovery of penicillin in 1928 (Hu, *et al.*, 2020). The discovery of antibiotics ranks among the most pivotal revelations, significantly contributing to the reduction of illness and death. Across history, communicable diseases have afflicted humanity. For instance, during three years from 1347 to 1350, the bubonic plague resulted in the demise of roughly a third of Europe's population. The advent of antibiotics during the 1900s led to a drop in mortality rates, diminishing from 25% to 1% in England with the commencement of mass antibiotic production (Ribeiro da Cunha *et al.*, 2019). In the 20th century, the deployment of antibiotics in the United States wielded such a transformative effect on hygiene and public health that fatality rates from severe ailments, including endocarditis, plummeted by up to 75% (Gandra *et al.*, 2014). Consequently, considering the extensive research into the significance of the discovery of antibiotics, it can be agreed that the identification of antimicrobial agents stands as one of humanity's most crucial accomplishments in combating contagious diseases and curtailing illness and death (Aghamohammad and Rohani, 2023).

Undoubtedly, the revelation of antibiotics has substantially contributed to the alleviation of illness and mortality. However, the ascent of antibiotic resistance poses a formidable conundrum for medical practice. The chronicle of antibiotic resistance's emergence traces back to the early stages of antibiotic exploration. From the 1940s to the 1960s, a period marked as the golden era of antibiotic breakthroughs, the proliferation of resistant strains escalated swiftly, giving rise to prevalent occurrences of bacteria resistant to penicillin, tetracycline, macrolide, and even methicillin in clinical contexts (Friedman *et al.*, 2016).

1.3 ORIGINS OF ANTIMICROBIAL RESISTANCE

The emergence of AMR can be traced back to several factors, including the misuse and excessive use of antibiotics, their pervasive application in agriculture, and the pharmaceutical sector's limited focus on new antibiotic development (Ventola, 2015). Instances of inappropriate antibiotic utilization, the circulation of counterfeit antibiotics, inappropriate prescription practices, and patients' failure to adhere to prescribed antibiotic regimens all contribute to the proliferation of AMR. In approximately fifty percent of infection cases, errors in determining the need for treatment, the choice of appropriate antibiotics, and the duration of antibiotic therapy. Additionally, a significant sixty percent of antibiotics administered in intensive care units are either unnecessary, inappropriate or not the best choice (Ventola, 2015). Having inadequate antibiotic levels can create opportunities for the development of antimicrobial resistance by facilitating genetic changes, including alterations in gene expression, horizontal gene transfer, and mutagenesis. Antibiotic-induced changes in gene expression can enhance the virulence of pathogens, thereby increasing the occurrence of mutagenesis, which contributes to the spread of AMR (Ventola, 2015). Sometimes, protracted or inappropriate treatment regimens can unnecessarily cause bacteria to evolve and acquire resistance to drugs (Fair and Tor, 2014). The prevalence of incorrect antibiotic prescriptions is often associated with negligent regulations and ignorance regarding best practices. Furthermore, limited knowledge of the public about antibiotics can lead to their overuse, especially in regions like Nigeria where antibiotics can be obtained without prescriptions (Ndiokubwayo *et al.*, 2013).

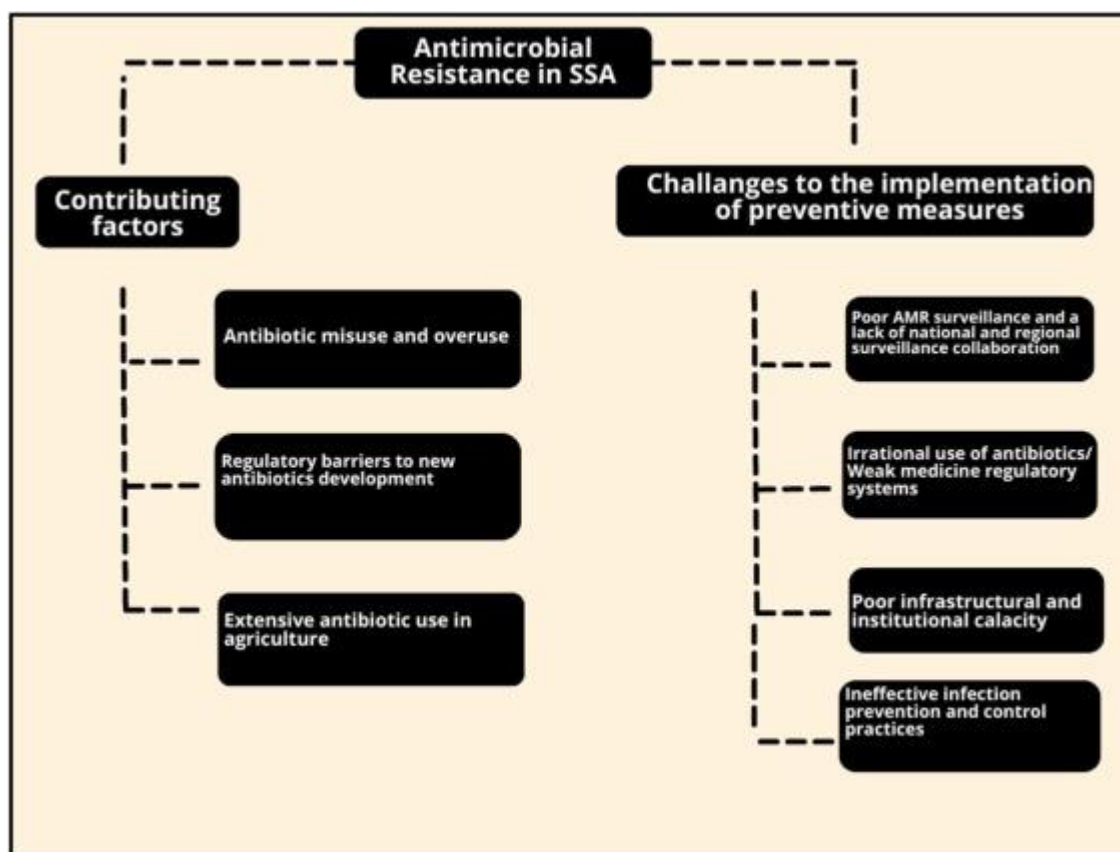


Figure 1.: Factors that contribute to antimicrobial resistance (AMR) and the obstacles encountered in executing preventive measures (Moyo *et al.*, in 2023).

1.4 DISSEMINATION OF ANTIMICROBIAL RESISTANCE ACROSS VARIOUS REGIONS OF THE WORLD

The propagation of AMR arises from a confluence of antimicrobial misuse, extending beyond just humans to encompass animals, agricultural methodologies, and the environment. This encompasses aspects like regulating post-antibiotic utilization in soils and water bodies (O'Neill, 2015). Globally, resistance to carbapenem antibiotics, the last-line treatment for *Klebsiella pneumoniae* infections, has spread across all regions of the world (WHO, 2018). In specific nations, due to resistance, carbapenem antibiotics no longer elicit desired effects in over fifty percent of individuals undergoing treatment for *K. pneumoniae* infections (Peleg and Hooper, 2010). Resistance in *E. coli* is pervasive. Fluoroquinolone antibiotics, commonly used for treating urinary tract infections, have now become ineffectual in over fifty percent of patients in numerous regions (Shaikh *et al.*, 2015). The inability to effectively treat gonorrhea using third generation cephalosporins such as cefixime, cefdinir, and cefpodoxime (often considered the last option in medical treatment) has been confirmed in at least ten different nations including Australia, Austria, France, Canada, Japan, Norway, South Africa, Sweden, Slovenia, and the United Kingdom of Great Britain and Northern Ireland (WHO, 2018). The occurrence of resistance in

Staphylococcus aureus is widespread. People suffering from methicillin-resistant *Staphylococcus aureus* (MRSA) infections are at a significantly increased risk of mortality, estimated at 64%, compared to those with non-resistant infections. For Enterobacteriaceae-induced life-threatening infections resistant to carbapenems, colistin stands as the ultimate treatment. However, colistin resistance has recently surfaced across multiple nations and territories, as these bacteria are essentially impossible to treat (Ventola, 2016).

In the year 2019, Sub-Saharan Africa (SSA) experienced the highest number of deaths attributed to antimicrobial resistance. Within that timeframe, around 1.1 million fatalities in SSA were linked to AMR, while approximately two hundred and fifty thousand deaths within the region were attributed to AMR (Murray *et al.*, 2022). The predominant microbes driving these fatalities related to AMR in SSA encompassed *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aureus*, *Staphylococcus aureus*, *Streptococcus pneumoniae*, and *Acinetobacter baumannii* (Murray *et al.*, 2022). In Mali and the Central African Republic, roughly 60–80% of *Staphylococcus aureus* strains exhibited methicillin resistance. In Zambia and Zimbabwe, fifty to seventy percent of *Escherichia coli* strains displayed resistance to third generation cephalosporins. South Africa observed 50–60% resistance in *Acinetobacter baumannii* isolates against carbapenem. Moreover, over eighty percent of *Klebsiella pneumoniae* isolates in Ethiopia, Mozambique, and Zambia were resistant to third generation cephalosporins in 2019 (Murray *et al.*, 2022). While *Streptococcus pneumoniae* was the primary contributor to AMR-related fatalities in SSA in 2019 when compared to other bacterial strains, the situation varied in different parts of the world. In central Asia, central and eastern Europe, Latin America, and the Caribbean, as well as South Asia, *Escherichia coli* emerged as the primary cause of AMR-linked fatalities. In the Middle East, Southeast Asia, East Asia, Oceania, and North Africa, *Staphylococcus aureus* took precedence as the main contributor to AMR-induced deaths (Murray *et al.*, 2022). AMR's impact has reverberated across the global battle against various infectious diseases such as COVID-19, tuberculosis, Hepatitis B, HIV, and malaria. In the absence of effective AMR prevention measures, projections suggest that the global toll could escalate to around ten million deaths by 2050, with Africa alone accounting for approximately four million of these deaths due to AMR (Dadgostar, 2019).

1.5 THE GLOBAL MENACE OF ANTIMICROBIAL RESISTANCE

Antimicrobial resistance (AMR) stands as a pressing worldwide concern that demands immediate attention. The assessment of antimicrobial resistance, initiated by the UK government, argued that in less than thirty years, AMR could result in the death of ten million individuals annually (O'Neill, 2016). The O'Neill report, conducted on behalf of the UK government, projected that AMR would claim 10 million lives each year by 2050, surpassing the number of deaths caused by cancer (which accounts for 8.2 million yearly). Between 2000 and 2010, the rapidly growing economies of BRICS nations (Brazil, Russia, India, China, and South Africa) accounted for approximately eighty percent of the increase in antibiotic usage. Statistics show that the leading consumers during that period were India, with over twelve billion units, China, with ten billion units, and the USA, with almost seven billion units in 2010 (O'Neill, 2016). Within BRICS nations, the surge in antibiotic misuse stemmed in part from population growth, along with enhanced drug accessibility and improved standard of living. Another important factor was the lack

of well-defined antibiotic regulations. Notably, the United States of America exhibited the highest prevalence of antibiotic abuse across both human and livestock domains and additionally, there is a dearth of comprehensive antimicrobial stewardship programme implementation (Ghafur, 2015). This situation is further compounded by the scarcity of new antimicrobial medicines entering the market. The AMR report from 2015 also highlighted that a wide range of common medical conditions, such as tuberculosis, methicillin-resistant *Staphylococcus aureus* infections, vancomycin-resistant *Enterococci* infections, HIV/AIDS, malaria, urinary tract infections, bloodstream infections, and food poisoning, had acquired resistance to many antimicrobial drugs. This situation necessitates the use of costly, high-risk last-line antimicrobials, which are frequently inaccessible or unaffordable in lower and middle-income countries (Hu *et al.*, 2020).

The Sustainable Development Goals (SDGs) regard antimicrobial resistance (AMR) as a matter of urgent public health attention both in society and globally, and the success of the SDGs might be impeded by the presence of AMR (Gajdács *et al.*, 2021). An international plan for addressing global antimicrobial resistance was approved by the World Health Assembly in May 2015, consisting of five objectives, with the third objective focusing on strategies for preventing infections. On a global scale, up to May 6, 2023, the number of fatalities attributed to COVID-19 has exceeded 6.9 million (WHO, 2023). By comparison, the annual impact of AMR is twice as high, yet the responses to COVID-19 and AMR have been notably dissimilar.

1.6 RATIONALE OF STUDY/ANTIMICROBIAL RESISTANCE AND ITS IMPACT IN NIGERIA

The Nigeria Centre for Disease Control and Prevention (NCDC) has characterized antimicrobial resistance as a subtle, gradual epidemic, distinct from the pronounced waves and peaks observed during the COVID-19 pandemic. The NCDC has identified several obstacles that need to be overcome for Nigeria's response to antimicrobial resistance. These challenges include insufficient coordination among relevant sectors, limited diagnostic services leading to inadequate surveillance and response mechanisms, insufficient funding, subpar adoption and implementation of standardized infection prevention and control measures in both communities and healthcare facilities, and various other difficulties. An investigation into the awareness of AMR within Nigeria, conducted by Chukwu *et al.*, 2020, provided insights into the extent of AMR awareness and antibiotic usage among the wider Nigerian populace. The research findings indicated that approximately 30% of the Nigerian population uses antimicrobial drugs without obtaining a prescription. Moreover, the general comprehension of antimicrobial resistance and proper antimicrobial use among respondents was notably inadequate. Nigeria's existing surveillance framework primarily targets the detection and management of epidemics, but lacks a dedicated AMR policy, despite having other policies that address the drivers of AMR within the healthcare system (Adeniji, 2018).

Numerous studies conducted across Nigeria have well-documented the improper utilization of antimicrobials (Fadareet *et al.*, 2019, Fadareet *et al.*, 2015a, Ekwochiet *et al.*, 2014). However, there remains a scarcity of information regarding the specific impact of AMR within Nigeria. This is concerning not only due to the potential for adverse effects and drug interactions, but also due to the economic ramifications, particularly since only a limited portion of Nigeria's population currently benefits from health

insurance coverage (Fadareet *al.*, 2015b). Information regarding the availability and effectiveness of Antimicrobial Stewardship Programs within Nigerian hospitals is currently lacking. This information gap requires immediate attention, particularly considering Nigeria's large population compared to other African countries, coupled with the escalating rates of AMR within Nigeria (Olufunmisoet *al.*, 2017, Bernabe *et al.*, 2017, Adenipekunet *al.*, 2016).

Consequently, the necessity for this literature review becomes evident. Notably, the significance of WASH measures in curbing the spread of AMR in Nigeria has yet to be documented, however, analyzing data from countries that have achieved success in implementing WASH strategies like the United Kingdom would be crucial in mitigating AMR transmission within Nigeria.

METHODOLOGY

2.1 LITERATURE SEARCH

An extensive literature review was conducted in relevant databases, specifically focusing on research studies published in peer-reviewed journals in English. These studies were conducted in both the United Kingdom and Nigeria, with the primary objective of investigating the relationship between Water, Sanitation, and Hygiene practices and Antimicrobial Resistance. The search spanned from May 2015, coinciding with the adoption of the global action on antimicrobial resistance by the World Health Assembly, to July 2023. The literature search was completed on August 10, 2023, and it encompassed multiple internationally recognized databases to gather pertinent information from publications. The electronic databases utilized for this purpose included CINAHL Complete, EBSCO, PubMed, and Science Direct. Furthermore, data was explored from authoritative sources such as The World Health Organization, the Nigeria Centre for Disease Control and Prevention, the Nigerian Ministry of Health, and the Centers for Disease Control and Prevention, as well as the Public Health England websites, in the quest for relevant literature. The databases were searched for MeSH terms that included antimicrobial, resistance, antibiotic, disease burden, morbidity, mortality, water, sanitation, hygiene, wastewater, United Kingdom, Nigeria, and antibiotics (see Appendix 1). Also, Boolean words AND, and OR were employed during database search to exclude unrelated studies (see Appendix 2). The exact search words were “Antimicrobial Resistance and WASH and Nigeria”, “Antimicrobial Resistance and WASH and United Kingdom”, “Antibiotic Resistance and WASH and Nigeria”, “Antibiotic Resistance and WASH and United Kingdom”, AMR OR Antimicrobial, AMR OR Antimicrobial (see Appendix 2). A Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram was utilized to record inclusion and exclusion criteria.

The quality of the papers was evaluated to ensure their reliability, credibility, trustworthiness, and confirmability using the CASP tools as outlined in Appendix 3. The data obtained from the literature search was synthesized by combining information from the different papers and creating a narrative that outlined the impact of the WASH project on the management and control of Antimicrobial Resistance.

2.2 DATA MANAGEMENT/ANALYSIS

Data management and analysis involved the process of choosing studies based on the specified inclusion criteria and quality assessment. The relevant studies for the

literature review were assessed and papers that met the stipulated inclusion criteria were retained for further review.

2.3 SELECTION OF RELATED STUDIES

To identify relevant studies, the inclusion and exclusion criteria were applied. Papers that met the inclusion criteria were chosen for further examination and content assessment. Notably, certain types of papers were excluded, including grey literature, extended abstracts, presentations, keynotes, review articles, and papers not written in English. Additionally, publications that addressed Antimicrobial Resistance without explicitly mentioning "Antimicrobial resistance" and "WASH" in their titles, keywords, or abstracts were included especially for the studies carried out in Nigeria due to the lack of published research linking the two terms. Studies carried out in the United Kingdom without both "WASH" and "AMR" were excluded because these publications did not align with the scope of this literature review, which focused on evaluating the impact of WASH in reducing AMR in the United Kingdom as a case study.

The modified PICO criteria were employed, as detailed in Table 1 (Naylor *et al.*, 2018), to screen abstracts, titles, and full texts during the selection process.

Table .1: Inclusion/Exclusion Criteria

Criteria (PICO)	Inclusion criteria	Exclusion criteria
Population	Research involving individuals of diverse age and gender groups Sewage and various aquatic environments	Research involving animals Studies focusing on plants
Study methodology	Cross-sectional Studies Case-Control studies Cohort Studies Quasi-experimental studies Randomized Control Trials	Blog analyses Case series Case studies Reports from conferences Assessment of interventions Individual correspondence Editorial pieces

Outcome	Studies with findings on patterns of antimicrobial resistance in water sources. Studies presenting results on the impact of WASH on antimicrobial resistance.	Results that are limited to molecular biology findings exclusively. Results that are limited to epidemiological data Results containing antimicrobial resistance patterns only
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2.4 ASSESSMENT OF RESEARCH QUALITY

Each piece of literature was assessed using a set of criteria derived from four quality assessment questions:

QA1: Were the inclusion and exclusion criteria of the review clearly defined and suitable for the study?

QA2: Is it probable that the literature search encompassed all pertinent studies related to the subject?

QA3: Did the chosen publication involve blinded reviewers who evaluated the study's quality and validity?

QA4: Was the mention and description of Antimicrobial Resistance and Water, Sanitation, and Hygiene in the publication adequate and comprehensive?

2.5 DATA SYNTHESIS

The phase of data synthesis involved both extracting and organizing important information from the chosen papers to gain insights and reach conclusions. Data extraction consisted of identifying and retrieving relevant data from the selected papers. To fulfil the objectives of the literature review, the variables of interest were categorized into two groups: general attributes of the articles and particular parameters used to evaluate, quantify, or depict AMR and WASH. General article details encompassed publication years, types of analyses (quantitative, qualitative, or mixed methods), study characteristics and scope, as well as the geographical locations of the studies.

RESULT

3.1 SEARCH RESULTS

The overall screening procedures and the sequence for identifying relevant literature are presented in Figure 1. Initially, 584 articles were collected from ScienceDirect, 90 from PubMed, 26 from EBSCO, 4 from CINAHL, and 5 from various other sources. Following the exclusion of certain types of literature such as grey literature, blog reports, extended abstracts, editorial pieces, presentations, conference reports, book chapters, and non-English language papers, the final number of retained articles was reduced to 432, which were then subjected to a detailed review of their titles. Subsequently, only 126 articles met the eligibility criteria and proceeded to the abstract review stage.

Following the review of article abstracts, a total of 96 articles remained for comprehensive analysis of their main content. During this comprehensive review, duplicate papers and articles lacking clear information on AMR and WASH were removed. Ultimately, 12 publications were identified that fully satisfied all the inclusion criteria applied in this literature review (Figure2). After reading the article abstract, only 96 articles remained for the main body reading. During the main body reading, duplicated papers and articles that lacked clear AMR and WASH information were manually removed. In the end, 12 publications have remained that fulfilled all the inclusion criteria used in this literature review

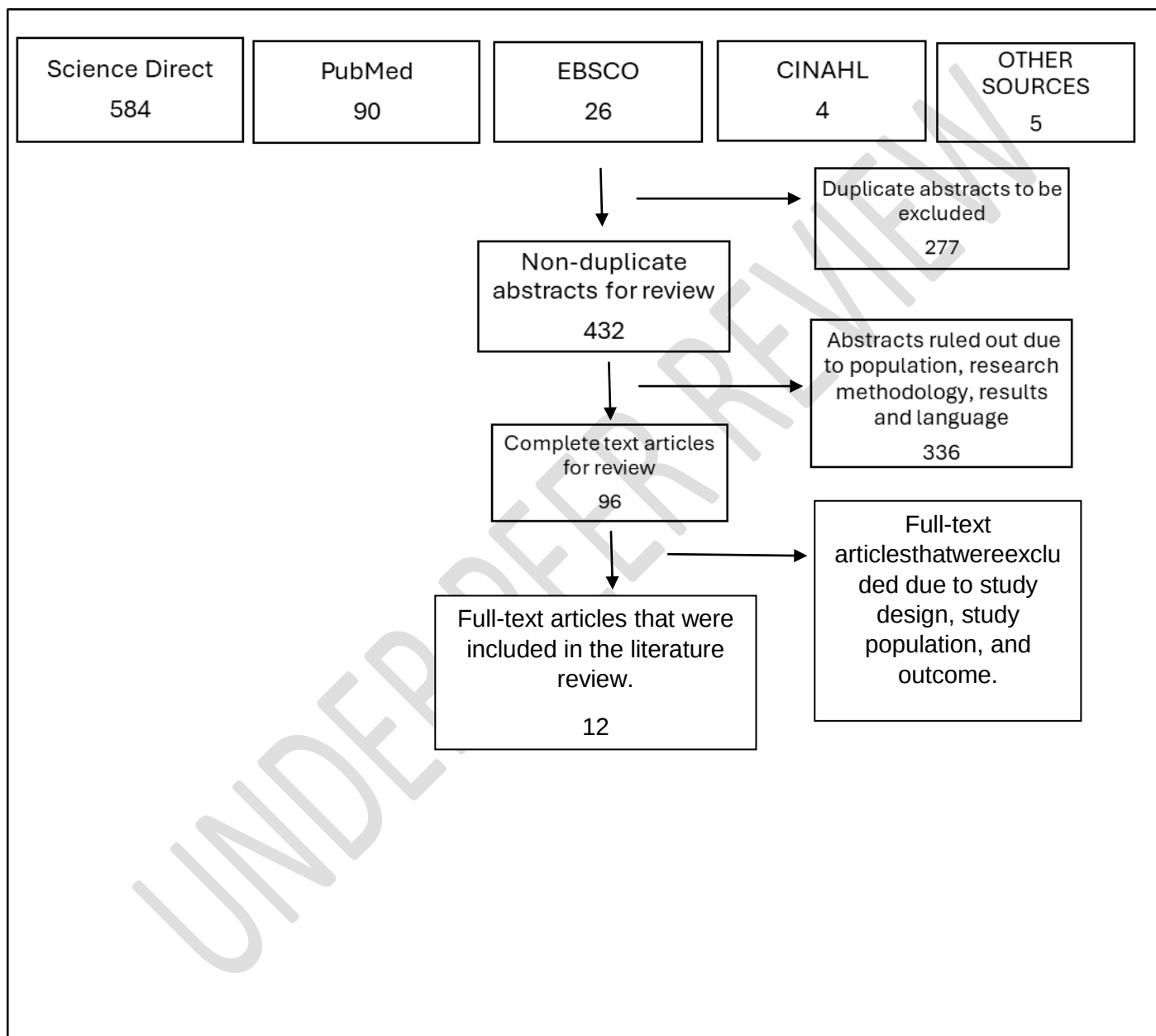


Fig. 2: Data retrieval and inclusion depicted in the PRISMA Flowchart

Among these twelve studies, five studies were conducted in water bodies in different regions in Nigeria, and three research studies were carried out in the United Kingdom examining the application of WASH interventions in diverse settings such as farms, schools, communities, and healthcare facilities, assessing their impact on infection prevention and control and the subsequent reduction in antimicrobial resistance. Another four studies consisted of policy documents outlining the Nigeria and United Kingdom's national action plans for addressing antimicrobial resistance, emphasizing the significance of integrating WASH practices into antimicrobial resistance control and prevention efforts.

3.2 NIGERIA'S WATER, SANITATION AND HYGIENE RESULTS

Research conducted by Titilawoet *al.* in 2015, which focused on the river waters of Osun State in Southwestern Nigeria, revealed the significant prevalence of *Escherichia coli* strains showing antimicrobial resistance through phenotypic testing. Significantly, these bacteria exhibited high levels of resistance to commonly employed antibiotics such as amoxicillin, ampicillin, cefuroxime, sulphamethoxazole, and tetracycline across all the surveyed locations. This resistance pattern is likely influenced by factors such as domestic, industrial, and medical waste discharge, surface runoff, and various human activities in the surrounding rivers. The existence of bacteria resistant to antimicrobials in surface waters represents a notable public health issue since it heightens the potential for transmission to humans when they consume contaminated water. Consequently, this amplifies the broader spread and endurance of antimicrobial resistance in both the community and the ecosystem, thus creating potential health risks.

Similarly, a study carried out by Yusuf-Omoloyeet *al.*, 2023 employed a cross-sectional approach to examine clinical, ready-to-eat (RTE) food, and water samples. Various water sources in Southwest Nigeria, including surface water (36 samples), groundwater from boreholes (39 samples), and well water (75 samples), were collected from each of these six selected zones. Within this study, it was observed that 73.4% of the 64 Vancomycin-resistant Enterococci (VRE) strains analyzed carried at least one of the three clinically significant van genes (vanA, vanB, or vanC), which are known to confer high-level resistance to vancomycin and teicoplanin.

In the same vein, Fakayode and Ogunjobi in 2018, conducted another study in Osun State, Nigeria, to assess the physical, chemical, and microbiological quality of water from fourteen water supply schemes provided and commissioned by the government. Antibiotic susceptibility patterns of bacteria isolated from these sources were also examined. Pathogenic bacteria like *Acinetobacter*, *Pseudomonas*, *Enterobacter*, *Escherichia*, *Klebsiella*, and *Pseudomonas* were found in both the source and drinking water. All the isolates displayed varying degrees of resistance to antibiotics while most of the strains (over 280) showed resistance to at least one antibiotic, and over 250 were resistant to three to eight antibiotics. The presence of pathogens and antibiotic-resistant bacteria in all types of water samples highlights the possible public health hazards for community members depending on these water schemes for drinking water.

Furthermore, another study by Okafor *et al.*, 2022 whose objective was to investigate the drug resistance patterns of *Pseudomonas aeruginosa*, which forms biofilms, in the aquatic environment of Ebonyi state, Southeastern Nigeria examined 272 water

samples and standard microbiological techniques were used for the bacteriological analysis. Among these samples, 223 *Pseudomonas aeruginosa* isolates were confirmed, with a notably high occurrence rate of 85.11%. These biofilm-forming isolates displayed resistance to several antibiotics, including imipenem (39%), ceftazidime (68%), ciprofloxacin (69%), ofloxacin (70%), ertapenem (84%), cefepime (85%), ticarcillin (89%), amikacin (90%), gentamicin (91%), and cefotaxime (93%).

Likewise, another study by Adekambiet *et al.*, 2019, reported that 56 isolates were recovered from hospital wastewater (HWW), with 31 of them identified as coagulase-negative staphylococci (CoNS), comprising *S. epidermidis* (22) and *S. saprophyticus* (9). Among the CoNS, a significant 77.4% exhibited resistance to oxacillin, while approximately a quarter displayed resistance to tetracycline and erythromycin (25.8% each). Furthermore, 16.1% demonstrated resistance to vancomycin and ciprofloxacin, 45% showed resistance to sulfamethoxazole-trimethoprim, with 12% resistant to linezolid, 41% to clindamycin, and 32% to chloramphenicol. This research highlights that hospital wastewater is a potential reservoir of the methicillin-resistance gene (*mecA*) and underscores the necessity for proper treatment of HWW before disposal to mitigate the risk of introducing antibiotic-resistant bacteria and their genes into the environment, which could pose a public health threat.

Additionally, another research by Alhaji *et al.*, 2019, conducted in the North-central geopolitical zone of Nigeria, known for its abundance of rivers, streams, and dams which ultimately flow into the Atlantic Ocean through the River Niger showed antimicrobial resistance patterns in fishponds. The study, conducted between January 2018 and December 2019, followed a cross-sectional approach and targeted fish farm proprietors in both urban and rural areas as participants. Eligibility criteria required participants to be farmers primarily involved in fish farming as a primary source of income. Questionnaires were administered to farm owners, and a total of 151 fish farms were selected, with a fish sample or water sample from the fishpond collected from each farm. The results of the research are noteworthy, revealing that a substantial majority of farmers (94%) practiced self-prescribing antibiotics, and an equally high percentage (94.9%) administered these antimicrobial agents on their fish farms without seeking advice from veterinarians. Significantly, the study highlights the possible health hazards linked to the consumption of fish and fish products contaminated with antimicrobial residues and contact with tainted fish and related items. These pathways are significant sources of antimicrobial residues and the potential development of resistance in humans.

Correspondingly, in 2018, the Nigerian Federal Ministry of Health launched a National Action Plan (NAP), a 13-year strategy designed to revitalize the country's WASH sector. The National Action Plan (NAP) seeks to attain comprehensive and secure access to sustainable WASH services by 2030, in alignment with the objectives of the Sustainable Development Goals. This effort demonstrates the government's commitment to rectifying the significant shortcomings in the WASH sector and guaranteeing that every Nigerian can access fundamental water and sanitation services.

Moreover, until 2022, there was an absence of a comprehensive nationwide framework for WASH in Healthcare Facilities (HCFs) to provide guidance and coherence in WASH service delivery and the allocation of roles and responsibilities within HCF in Nigeria. The National Guidelines on Water, Sanitation, and Hygiene in Healthcare Facilities, issued by the Federal Ministry of Health in Nigeria, were

designed to offer direction, standardization, and enhancement of WASH services by various stakeholders at all levels. This aimed to address the existing WASH-related challenges in HCFs across Nigeria.

3.3 THE UNITED KINGDOM'S WATER, SANITATION AND HYGIENE RESULTS

All three investigations assessing the impact of WASH interventions on antimicrobial resistance in the United Kingdom yielded positive outcomes. In a study conducted by Pinto *et al.*, in 2023, systematically gathered and summarized evidence about biosecurity measures and water, sanitation, and hygiene interventions implemented on farms, specifically targeting the potential reduction of infections and antibiotic resistance in animal agricultural settings. Their findings revealed the feasibility of significantly decreasing a wide array of clinically significant antibiotic resistance genes, including those associated with tetracycline, sulfonamide, macrolide, vancomycin, and mobile genetic elements, by percentages ranging from 21% to 99%.

Likewise, Cullet and Bhullar 2022, emphasized the significant connection between antimicrobial resistance in the environment and Water, Sanitation, and Hygiene which is closely related to the provision of healthy hygiene standards, sufficient sanitation, and access to clean water. WASH has a strong connection to environmental concerns since poor sanitation greatly increases water pollution and public health problems while also compromising the quality of the drinking water supply. The study confirmed that water is directly involved in both AMR and WASH, which are both intimately related to public health (Cullet and Bhullar, 2022).

In a similar vein, Storr *et al.*, in 2021 summarized the vital role of WASH in healthcare settings, emphasizing that a hospital cannot maintain a safe and hygienic environment or provide clean care without access to water. Also highlighted was the importance of cleaning staff within the healthcare workforce and identified this group as a priority for training, given their critical role in overall health service delivery.

Between 2011 and 2021, the now-defunct Department for International Development (DFID) established and successfully met ambitious global objectives for its WASH initiatives. From 2011 to 2015, DFID committed to ensuring that 60 million individuals gained access to safe drinking water, basic sanitation, or hygiene education, and they not only fulfilled this commitment but exceeded it, aiding 62.9 million people. DFID renewed this commitment for the 2015-2020 timeframe and succeeded in reaching 62.6 million people (Independent Commission for Aid Impact, 2022).

DISCUSSION AND SIGNIFICANCE

This literature review summarises the effect of WASH on combatting the spread of AMR using studies carried out in Nigeria and the United Kingdom.

4.1 HOW DOES WASH AFFECT ANTIMICROBIAL RESISTANCE?

This review has revealed that WASH plays a very significant role in the control of antimicrobial resistance especially in the studies conducted in the United Kingdom because all the studies reviewed from Nigeria showed antimicrobial resistance patterns from microbial isolates obtained from water bodies from healthcare facilities, fish farm, drinking water but did not address the significance of incorporating WASH

into AMR containment efforts. Studies by Titilawoet *et al.*, 2015, Fakayode and Ogunjobi, 2018, Okafor *et al.*, 2022, Adekambiet *et al.*, 2019 and Alhaji *et al.*, 2021 all revealed that bacteria such as *Acinetobacter*, *Staphylococcus*, *Pseudomonas*, *Enterobacter*, *Escherichia*, and *Klebsiella* all demonstrated resistance to vancomycin and ciprofloxacin, sulfamethoxazole-trimethoprim, methicillin, clindamycin, chloramphenicol, amoxicillin/clavulanic acid, tobramycin, oxacillin, and aztreonam. This paints a gloomy picture of the AMR effect in Nigeria as most of these antimicrobials are last-resort drugs that are initiated when there are medication failures. With the dearth in the discovery of new antimicrobials and a poor and almost non-existent antimicrobial stewardship program in Nigerian healthcare institutions as exemplified by Fadareet *et al.*, 2019, the continued proliferation of AMR in Nigeria calls for urgent public health attention.

The Nigerian Federal Ministry of Health launched a National Action Plan (NAP) and The National Guidelines on Water, Sanitation, and Hygiene in Healthcare Facilities published by the Nigeria Federal Ministry of Health in Nigeria, aiming to mitigate the state emergency that the lack of WASH services created, including inadequate infrastructure, a shortage of trained personnel, insufficient investment, and a lack of effective regulatory oversight, failed to address the link between AMR and WASH through research conducted and published by the Pinto *et al.*, 2023, Cullet and Bhullar, 2022, Maina *et al.* 2019, Zeitoun *et al.*, 2021, Storr *et al.* in 2021, World Health Organization, Agriculture Organization of the United Nations and World Organisation for Animal Health, 2022 all emphasizing the importance of combatting AMR through WASH in healthcare facilities, farms, schools. WASH facilities and interventions in Nigeria are concentrated on areas that experience water-borne diseases like cholera and do not address the issue of AMR. Sixty million Nigerians lack access to basic drinking water, eighty million lack access to improved sanitation, and over one hundred and sixty million lack access to even basic handwashing facilities because of these problems (Nigeria Center for Disease Control and Prevention, 2022). In rural areas, the situation is particularly dire, where about one-third of households still practice open defecation, barely half have access to better sanitation, and thirty-nine percent of households lack a basic water supply. Due to their bearing the burden of long-distance water collection, women and girls suffer disproportionately, which has negative impacts on their well-being, attendance at school, and risk of gender-based violence. By reducing the amount of time spent collecting water, reducing the prevalence of disease, and fostering a safer and healthier learning environment, improved access to WASH services will have a positive impact on education.

The United Kingdom plays an important role in supporting the World Health Organization (WHO) and various other global health initiatives. Additionally, it actively participates in international policy discussions aimed at enhancing Infection Prevention and Control (IPC) within forums like the G7 and G20. UK Aid's support for health system strengthening, along with its efforts in areas like nutrition and WASH, also contributes to bolstering IPC practices and reducing the reliance on antibiotics in partner countries abroad.

To fulfill these objectives, the UK established substantial bilateral WASH initiatives between 2017-2022 in numerous countries, including the Democratic Republic of the Congo, Ethiopia, Malawi, Mozambique, Nigeria, Tanzania, Zambia, and Zimbabwe. Additionally, the UK partnered with the United Nations Children's Fund (UNICEF)

through a £57.3 million initiative to provide sustainable WASH services to 3.8 million individuals in ten countries as part of the Sanitation, Water, and Hygiene for the Rural Poor program.

Within the United Kingdom itself, a rigorous system of regulation and monitoring ensures that citizens can have confidence in the safety of their drinking water and the proper management and treatment of sewage waste. The only exceptions to this are households, particularly in rural areas, that depend on private water sources and local waste management solutions like septic tanks. In such instances, regular monitoring is essential to ensure appropriate management and to promptly address any emerging risks (Department of Health and Social Care, 2019).

AMR poses a severe danger to improvements in public health and, if ignored, might reverse years of progress. The development of resistance in bacteria to medications including amoxicillin (an antibiotic), clotrimazole (an antifungal), and oseltamivir (an antiviral), because of suboptimal prescription and self-medication, leads to the spread of AMR (Sreeja *et al.*, 2017, Sulis *et al.*, 2020). Nosocomial diseases are more likely to occur in hospitals because of the constant influx of patients, medical personnel, visitors, and deceased patients (Uddin *et al.*, 2021). Even though hospitals take precautions and set up infection control systems, they are overburdened during pandemics and/or wars (Vinodhini and Bhoomadevi, 2016). The world's life expectancy has increased thanks to antibiotics' assistance in preventing and treating infections. Patients recovering from major surgeries like organ transplants and cardiac surgery, as well as those getting chemotherapy, and those with long-term conditions including diabetes mellitus and end-stage renal failure, benefit from infection prevention (Ventola, 2015). In low- to middle-income countries with poor sanitation, antimicrobials reduce food-borne illnesses and diseases linked to poverty (Rossoliniet *al.*, 2014).

The global spread of antibiotic resistance poses a threat to the lives of numerous people. Human health, medical treatment, life expectancy, and food production are all threatened by AMR (Zhou *et al.*, 2022). AMR usually develops in microorganisms that are likely to spread across the population, such as those that cause infections that are sexually transmitted, pneumonia, diarrhoea, and tuberculosis (Ndiokubwayo *et al.*, 2013). Due to AMR, the price of preventing, reducing, and managing infectious diseases has gone up. AMR causes early mortality, lengthy hospital stays, and absenteeism (Aslam *et al.*, 2018). AMR also raises healthcare spending by necessitating additional critical care units to prevent the spread of disease, more expensive and potentially toxic antibiotics, and longer consultation times with medical professionals. Additionally, AMR might increase hospital operating costs by forcing the closure of some wards due to hospital-acquired infections brought on by resistant pathogens. Furthermore, the development of resistant bacteria in hospitals may cause the postponement of elective procedures, resulting in the wastage of hospital resources and a decline in profitability (Pulingam, 2022).

4.2 MINIMISING ANTIMICROBIAL CONTAMINATION IN NIGERIA; WASH, THE MISSING LINK

Despite the national action plans, the usage of antibiotics and resistance to them is still rising and spreading. Infections caused by bad hygiene and sanitation encourage the use of many antibiotics. According to studies, hand washing can

prevent up to 25% of diarrheal incidents and lower the risk of respiratory infections by 6-44 percent (Essack, 2021). Many antibiotic prescriptions, which are frequently inappropriate, are for acute diarrheal conditions and respiratory tract infections (Kotwaniet *al.*, 2017). Thus, improving sanitation is crucial for reducing antimicrobial resistance. Numerous potentials for the transmission of infections, particularly those involving drug-resistant microorganisms, exist in the family, schools, and other settings of daily life. The Global Hygiene Council recently highlighted the importance of hands and contact surfaces in the home and other communal settings as reservoirs of potentially harmful microorganisms (Maillard *et al.*, 2020).

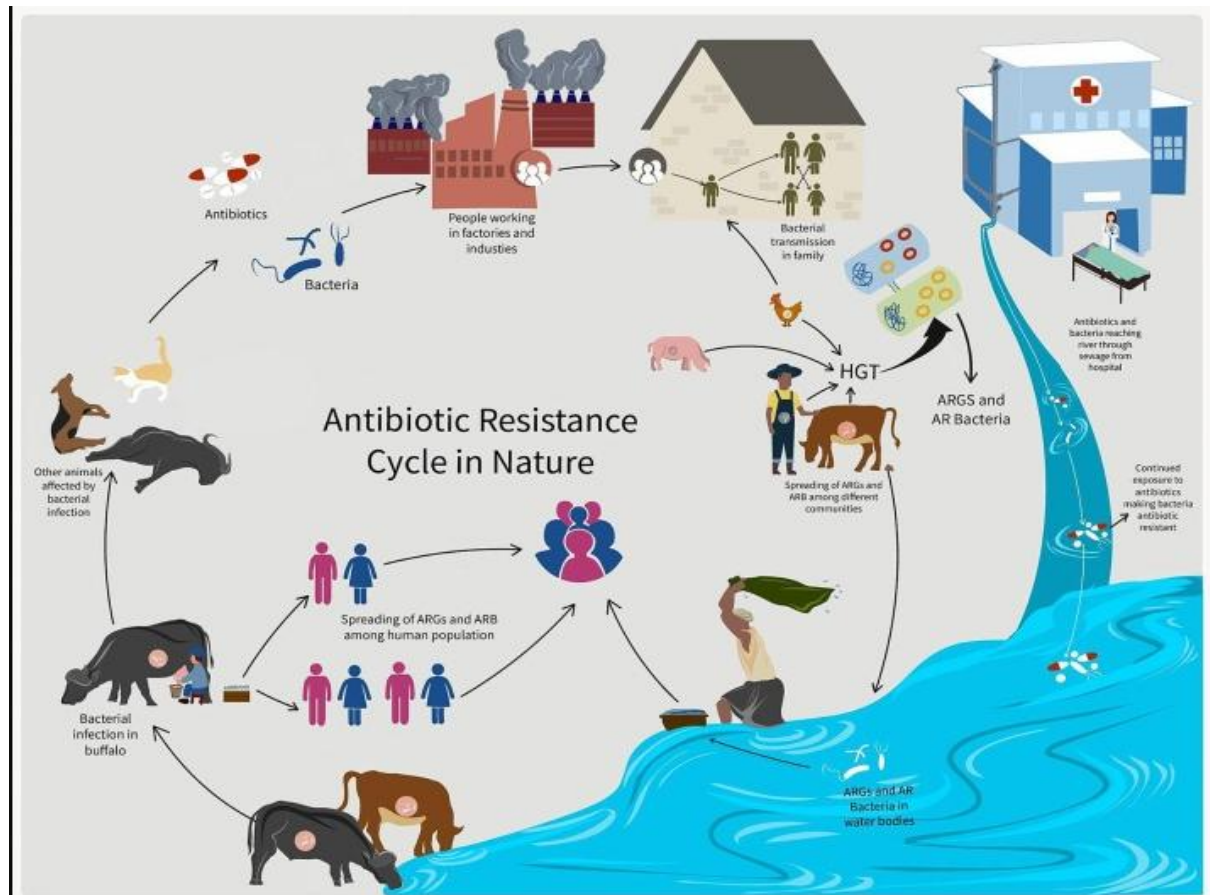


Fig 3 Water, sanitation and hygiene influences on Antimicrobial resistance (Kavya *et al.*, 2023)

Previous studies suggest that poor WASH perpetuates gender inequities, hence investments in WASH are not gender-neutral (Caruso *et al.*, 2015). For instance, there are dangers of infection, harm, and sexual harassment for women who fetch water. Concerningly, the absence of WASH in rural healthcare facilities, many of which are involved in child-birthing, puts women at risk of infection and maternal mortality. Worldwide, diseases that occur right after birth claim one million new mothers and babies every year (WaterAid, 2021). Only 44% of hospitals in East Asia and the Pacific had clean sinks with water, soap, and equipment for drying hands in the delivery rooms, according to a survey by Mannava *et al.*, 2019. Infection rates, AMR, and gender disparities can be lowered by investing in WASH. It has not yet been fully examined how WASH interventions are conceptualized to stop AMR from spreading. Most research and development initiatives are geared toward enhancing human access to clean water, hygienic conditions, and sanitation, as well as lowering diarrhoea morbidity, which primarily affects children in LMICs (Pinto *et al.*, 2023). The application of community-level hygiene initiatives that have been beneficial in reducing the prevalence of COVID-19 can serve as a lesson for nations and public health organizations. In addition to preventing the spread of other illnesses, such as those that are resistant to treatment, these efforts in water, sanitation, and hygiene also help to reduce the usage of antibiotics, which reduces the selection pressure for resistance. To reduce antibiotic resistance, both within the community and globally, infection prevention is crucial (Essack, 2021).

CONCLUSION and RECOMMENDATIONS

The relationship between WASH with AMR is a significant concern, encompassing health, water quality, and sanitation. This connection between AMR and WASH has long been recognized, with the COVID-19 pandemic highlighting the direct relationship between health, the environment, and development patterns. The pandemic has also emphasized the interdependence of global health and the importance of preparedness for health crises. AMR is a global issue, and addressing it necessitates collective action since resistance in one country can have worldwide repercussions. Misuse of antibiotics or inadequate WASH practices in one country can adversely affect the health of other nations.

Promoting the development and provision of WASH infrastructure across various settings in Nigeria, including communities, healthcare facilities, industries, schools, farms, and marketplaces, is crucial in combating AMR. This approach will not only prevent the transmission of infections and diseases but will also curb the spread of resistance genes and break the chain of AMR development via water sources. Furthermore, policymakers need to incorporate WASH considerations into NAPS. This inclusion ensures the regulation and compliance of WASH projects and initiatives supported by local and international partners, including the United Kingdom government, World Bank Group, UNICEF, Water Aid, and other non-governmental organizations. By reducing the number of infections, investments in WASH directly decrease the demand for antibiotics and, consequently, the development of resistance. Additionally, improved WASH practices limit the spread of resistant infections, reducing illness rates and the opportunity for resistant infections to become prevalent (United Nations Children's Fund, 2015).

In Nigeria, there hasn't been sufficient focus on the connection between WASH and efforts to combat the spread of AMR. Though Nigeria has its challenges to the implementation of WASH with its current struggling economy and a healthcare budget that is about 5.75 percent, significantly lower than the African Union recommendation at the Abuja Declaration of 15 percent of annual budgets for African countries, the potential of incorporating WASH measures into AMR containment strategies, which has proven effective and cost-efficient in countries like the United Kingdom, the United States, and BRICS nations, hasn't been fully harnessed. This literature review aims to serve as a wake-up call to government officials at the local, state, and national levels, policymakers, service providers, funding partners, medical and healthcare workers, and community leaders in Nigeria, urging these stakeholders to invest in WASH infrastructure nationwide like eradicating open defecation practices, promoting the proper and continuous utilization of toilet facilities, and establishing handwashing stations with soap at strategic places. Additionally, there's a need for extensive health promotion campaigns through various media channels, including radio, television, and social media, to raise awareness about antimicrobial resistance and its perilous implications for the Nigerian population. Methods for altering sanitation practices and promoting hygiene behaviours, such as Community-Led Total Sanitation (CLTS), Community Health Club (CHC), and Sanitation Marketing (SanMark), can also be introduced in communities to stimulate social change, foster self-awareness, encourage collective action, and underscore the importance of incorporating leadership and innovation into strategies aimed at containing AMR. Emphasis should also be placed on educating the public about the vital role of water, sanitation, and hygiene in daily life. Lastly, it is essential to invest in research and initiatives exploring the relationship between WASH and AMR to avert the potential crisis posed by unchecked AMR spread in Nigeria and globally.

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APPENDIXES

APPENDIX 1: Medical Subject Heading (Mesh)terms for literature search

ANTIMICROBIAL RESISTANCE	WASH	GEOGRAPHIC REGION
AMR, antimicrobial, resistance, antibiotic, disease burden, morbidity, mortality, antibiotic resistance, antifungal resistance, antiviral resistance, Infection prevention, multiple drug resistance, antimicrobial stewardship,	water, sanitation, hygiene, wastewater, WASH,	United Kingdom, Nigeria, United States of America, BRICS, Sub-Saharan Africa

APPENDIX 2: Boolean search for different research articles

BOOLEAN WORD	BOOLEAN KEYWORDS FOR SEARCH
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AND	Antimicrobial resistance and Nigeria Antimicrobial resistance and United Kingdom AMR and Nigeria and WASH AMR and United Kingdom and WASH Antimicrobial Resistance and Nigeria and Water Antibiotic Resistance and United Kingdom and Water Antibiotic Resistance and United Kingdom and sanitation Antibiotic Resistance and Nigeria and sanitation Antimicrobial Resistance and Nigeria and Water and Northern Nigeria Antimicrobial Resistance and Nigeria and Water and Eastern Nigeria Antimicrobial Resistance and Nigeria and Water and Western Nigeria
OR	Antimicrobial or antibiotic Antimicrobial or antifungal Antimicrobial or antiviral WASH or water quality WASH or wastewater