AJEHS
African Journal of Environmental Health Sciences
Volume 8, November, 2021
http://www.ehsanonline.org
ISSN: 2476-8030 (Prints)
ISSN: 2714-2930 (Online)
pp 87-98

Antimicrobial Resistance Surveillance in Nigeria: Current Situation and Way Forward: A Review

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Keywords:
Antimicrobial agents, surveillance, resistance, infectious disease, laboratory.

Mots clés:
Agents antimicrobiens, surveillance, résistance, maladie infectieuse, laboratoire

Abstract

Antimicrobial agents are used to prevent, control and treat infectious diseases caused by microorganisms. This survey reviewed the antimicrobial resistance (AMR) situation in Nigeria. An increasing rate of resistance among different microorganisms to various antimicrobial agents was found. The reasons for this include: inappropriate use of antimicrobial drugs in humans, animals and plants, poor infectious disease prevention, control and treatment, poor surveillance, lack of access to clean water, sanitation and hygiene (WASH), poor access to quality and affordable medicines, vaccines and diagnosis, ignorance, poverty and lack of enforcement of legislations. The implications include difficulty in treating infectious diseases, higher risk of disease spreading, reduced efficacy of drugs, long hospital stay, higher cost of treatment as well as greater disability and mortality. To curb antimicrobial resistance and its effects, Nigeria developed her National Action Plan for AMR in 2017 with the Nigeria Centre for Disease Control (NCDC) as the coordinating body. Currently, there exists two tuberculosis national reference laboratories, six zonal laboratories in tertiary hospitals, PCR equipment called Genexpert for molecular-based anti-TB resistance testing in several health centers and an AMR standing committee in tertiary institutions. However, there are no existing surveillance system, laboratory information system and coordinating unit, making AMR surveillance ineffective. As resistance to new antimicrobials emerged and spread, the need for comprehensive resistance surveillance programmes that provide timely information to enable public health interventions and prevent emergence and spread of antimicrobial resistance. Manpower development, public enlightenment, adequate funding, one health approach, collaborative action, building more diagnostic laboratories, effective waste management system as well as greater research and innovation are therefore recommended for improved AMR surveillance.

La Surveillance de la Résistance Antimicrobienne au Nigeria : Situation Actuelle et Voie a Suivre : Une Revue

Résumé

Les agents antimicrobiens sont utilisés pour prévenir, contrôler et traiter les maladies infectieuses causées par des micro-organismes. Cette enquête a examiné la situation de la résistance aux antimicrobiens (le 'RAM'-

antimicrobial resistance) au Nigeria, et un taux croissant de résistance parmi des micro-organismes différents à divers agents antimicrobiens, a été trouvé. Les raisons étant l'utilisation inappropriée de médicaments antimicrobiens chez l'homme, les animaux et les plantes, une prévention, un contrôle et un traitement médiocres des maladies infectieuses, une mauvaise surveillance, le manque d'accès à l'eau potable, à l'assainissement et à l'hygiène (le 'WASH'), un accès limité à des médicaments et vaccins de qualité et abordables, et le diagnostic, l'ignorance, la pauvreté et le manque d'application des législations. Les implications incluent la difficulté de traiter les maladies infectieuses, un risque plus élevé de propagation de la maladie, une efficacité réduite des médicaments, un long séjour à l'hôpital, un coût de traitement plus élevé et une plus grande invalidité et mortalité. Pour freiner la résistance aux antimicrobiens et ses effets, le Nigéria a élaboré son plan d'action national pour la résistance aux antimicrobiens en 2017 avec le 'Nigeria Center for Disease Control' (NCDC) comme organisme de coordination. Actuellement, il existe deux laboratoires nationaux de référence pour la tuberculose, six laboratoires de zone dans les hôpitaux tertiaires, un équipement 'PCR' appelé Genexpert pour les tests de résistance antituberculeuse à base moléculaire dans plusieurs centres de santé et un comité permanent de 'RAM' dans les établissements tertiaires. Cependant, il n'existe pas de système de surveillance, de système d'information de laboratoire et d'unité de coordination, ce qui rend la surveillance de 'RAM' inefficace. À mesure que la résistance aux nouveaux antimicrobiens a émergé et s'est propagée, il est nécessaire de mettre en place des programmes complets de surveillance de la résistance qui fournissent des informations opportunes pour permettre des interventions de santé publique et prévenir l'émergence et la propagation de la résistance aux antimicrobiens. Le développement de la main-d'œuvre, l'information du public, un investissement adéquat, une approche unique en matière de santé, une action collaborative, la construction de plus de laboratoires de diagnostic, un système efficace de gestion des déchets ainsi qu'une plus grande recherche et innovation sont donc recommandés pour une meilleure surveillance de 'RAM'.

Introduction

Antimicrobials are medicines used to prevent and treat infectious diseases caused by microorganisms either by killing them outrightly or stopping their growth. These microorganisms include bacteria, fungi, viruses, protozoa and parasites. They are found in humans, plants, animals and the environmental media (soils, air, and water). The antimicrobials are grouped based on the microbes they act primarily on, into antibiotics for the treating of bacterial infections, antifungal for fungal infections, antiviral for viral infection, antiparasitics and antiprotozoals for parasitic and protozoan infections respectively. Antimicrobials therefore include a wide range of chemical and natural compounds including organic acids, copper alloy surfaces and various plant parts (bark, roots, leaves, soils) which are used as disinfectants to kill a wide range of microbes on non-living surfaces, and antiseptics which are applied to living tissues to reduce infection during surgery (Kalemba, 2003; Cowan, 1999).

Humans have been battling with infectious diseases caused by various pathogens right from time immemorial, and some of these diseases are life- threatening. The use of antimicrobials in combating infectious diseases has been common practice, and came into limelight in the 19th century through the work of renowned microbiologists, Louis Pasteur and Jules Francois who observed the antagonism between some microorganisms,

and highlighted the merits of controlling these interactions in medicine (Kingston, 2008). The golden period of antibiotic era was between 1945 and 1970 when a number of structurally diverse and highly effective agents were discovered, developed and employed extensively in the prevention and treatment of microbial infections and diseases (Ventola, 2015).

Prior to modern civilization and technological era, these agents proved very effective and their prescription and administration were solely the responsibility of trained medical professionals. Hogerzeit *et al.,* (1992) confirmed this assertion through a rational drug use survey conducted in twelve (12) developing countries in which Nigeria was found to have the highest average number of drug prescription (3.8% drug/ encounter) and third highest antibiotic prescription at 48%, while 68% of adults used antibiotics following a doctor's prescription. These antibiotics have been used successfully to treat infections for many years and have greatly reduced morbidity and mortality (Carlet *et al.,* 2011). However, in the past few decades, there has been a surge in the production and use of antibiotics and other antimicrobials which are now sold in unregistered and unlicensed premises by non-pharmacists and taken without prescription. In most cases, these drugs are taken without detection of systemic infections and are used against the standard guideline in Nigeria.

This results in overuse or underuse of various antimicrobial agents, and as a consequence of widespread and precarious usage, there has been an accelerated emergence of antimicrobial resistant pathogens which pose serious threats to global public health. Recent evidence by Ashley *et al*., (2011) suggests that the gains achieved through antibiotics are threatened by the development of antimicrobial resistance in hospital and community settings.

The use and misuse of antimicrobial agent also occurs in livestock and farms. Various antimicrobial drugs are employed in the treatment of infectious diseases of farm animals, and in most cases without prescription. Furthermore, a combination of two to three agents can be used to handle an infection, and there have been cases of wrong use, where antibiotics are used to treat viral or fungi infection. Using antibiotics in farm animal can promote antimicrobial resistance, and drug resistant organisms in meat and crops which can in turn, spread and transfer diseases that affect animals and crops to humans (WHO, 2020; Mclintosh, 2018). Globally, drug resistance causes an estimated 700,000 deaths each year, and if the current trend continues, it is projected that by 2050, AMR could result in over 10 million deaths per year (Chukwu *et al.,* 2020). AMR has been declared a global health and development threat.

Therefore, the World Health Organization adopted a Global Action Plan on antimicrobial resistance and urged member countries to develop their National Action Plan within two years ending in May, 2017 (NCDC, 2017).

Antimicrobial Resistance

Prescription and use of antimicrobial agents have become so common that some microbes have adapted and started resisting them, resulting in lack of effective treatment for some diseases. Antimicrobial resistance occurs when microorganisms including bacteria, fungi, viruses, protozoa and parasites change over time and no longer respond to drugs that previously treated them effectively by evolving mechanisms that protect them from the effect of antimicrobials (Mclintosh, 2018).

The World Health Organization (2020) described antimicrobial resistance as a phenomenon where microorganisms acquire genes that enable them withstand the effects of antimicrobial agents, thereby threatening the success or medical intervention at all levels of healthcare. It also creates a set of specific challenges for clinical, therapeutic and public health intervention with local, national and global dimensions.

Antimicrobials work by interfering with one or more processes vital to the growth, survival and reproduction of invading microorganisms. Resistance of microorganisms to these agents occurs naturally over time, usually through genetic changes which may be triggered by the host immune response, metabolic processes and environmental factors.

In their separate works, Davies (1994) and Nikaido (1994) revealed that resistance to antimicrobial agents occurs typically as a result of four (4) main mechanisms namely; enzymatic inactivation of the drugs, alteration of target sites, reduced cellular uptake and extrusion by efflux.

These processes make the microorganisms acquire adaptive features which equip them to survive and multiply, thereby dominating the less resistance species. The emergence of antibacterial resistance is therefore determined by a complex interaction of environmental, epidemiological, clinical and behavioural factors (Coast and Smith, 2003). Antimicrobial resistance is a global public health problem which threatens the successful treatment of an ever-increasing range of infections by adding to the high cost of cure, reduced efficacy of medicines, disease severity, and high disability and mortality of otherwise easy to treat infections (NCDC,2017; Mohammed *et al.,* 2018).

Furthermore, it makes the control of some infections harder, thereby causing treatment failure, longer stay in the hospital, increasing economic and social cost of infection, a higher risk of diseases spreading, severe illness and consequently death (Mclintosh, 2018; WHO, 2020). The causes of antimicrobial resistance are grouped into two; microbial behavior and people's behaviour. The processes involved in microbial behaviour according to Nasir *et al.,* (2015) and Mclintosh (2018) include:

- Genetic mutation which occurs during reproduction and gives rise to offsprings with genes that enable them survive in the face of antimicrobial agents.
- Selective pressure which involves newly produced resistant microorganisms surviving, replicating and eventually dominating
- Gene transfer in which microorganisms pick up drug resistant genes from other microbes.
- Phenotypic change which involves the change of some characteristics to acquire resistance to common antimicrobial agents (Mclintosh, 2018; Nasir *etal.,* 2015).

Similarly, people's behaviours which accelerate the emergence and spread of antimicrobial resistance include:

- Misuse (overuse and under-use) of antimicrobial agents and failure to complete a course of treatment.
- Wrong diagnosis and prescription of antimicrobial medicines.
- Poor infection and disease prevention and control in healthcare facilities and farms.
- Lack of access to clean water, sanitation and hygiene (WASH) for both human and animals.
- Poor access to quality and affordable medicines, vaccines and diagnosis.
- Lack of new drugs being developed.
- Inappropriate application of antimicrobial agents in agricultural farms (Mclintosh, 2018; WHO, 2020; NCDC, 2021).

The World Health Organization has observed high rates of resistance against antibiotics frequently used to treat bacterial infections such as urinary tract infection, respiratory tract infections, sepsis, sexually transmitted infections and diarrhoea, worldwide. For example, the rate of resistance to Ciprofloxacin varies from 8.4 to 92.9% for *E.coli* and 4.1% to 79.4% for Klebsiella pneumonia, while resistance to flouroquinolone antibiotic in *E.coli,* methicillin in *Staphylococcus aureus*, penicillin, tetracycline, marcroledes and cephalosprins in N.gonorrhea are widespread. Similarly, antibiotics resistant mycobacterium tuberculosis strains are threatening progress in curtailing the global tuberculosis epidemic with an estimated half a million new cases of riflampicin-resistant TB (RR-TB) identified globally in 2018, of which the vast majority have multi-drug resistant TB (MDR-TB). Similar cases have been observed in viral infections. Resistance has developed to most antivirals especially in immune-compromised patients. All antiretroviral (ARV) drugs including newer cases are at risk of becoming partly or fully inactive because of the emergence of drug- resistant HIV (HIVDR) strains.

Furthermore, there is an increased resistance to Artemisinin-based combination therapies (ACTs)

which are first line treatments for uncomplicated Fulciparum malaria. The emergence of drug-resistant parasites poses one of the greatest threats to malaria control, and results in increased malaria morbidity and mortality. Similar cases have been observed in fungal infections. Drug-resistant *Candida auris*, one of the most invasive fungi infection is widespread, with increasing resistant to fluconazola, amphotericin B, voriconazole and caspofungi (WHO, 2020).

Based on the complexity of the problems arising from antimicrobial resistance, the World Health Organization in its 68th World Health Assembly in May 2015, adopted the Global Action Plan for antimicrobial resistance control in collaboration with the Food and Agricultural Organization (FAO) and the World Organization for Animal Health (OIE), and mandated member countries to establish their national action plans within two years, ending in 2017. Other actions taken by WHO to combat AMR include:

- Establishment of Tripartite Joint Secretariat on AMR to promote best practices and reduce the level of AMR and slow its development.
- Declaration of World Antimicrobial Awareness week (WAAW) in 2015 as a global campaign held annually to create awareness of antimicrobial resistance, and encourage best practices among the general public health workers and policy makers.
- Launching of the Global Antimicrobial Resistance and Use Surveillance System (GLASS) in 2015 to fill knowledge gap and strategies at all levels.
- Development of Global Research and Development Priority Setting for AMR in 2017 to update pathogen priority list to guide research and development into new antimicrobials, diagnosis and vaccines.
- Initiation of Global Antibiotics Research and Development Partnership (GARDP) to develop and deliver five (5) new treatments that target drug-resistant bacteria identified by WHO as posing the greatest threat in 2015.

These steps aim at achieving continuity of successful treatment and prevention of infectious diseases with effective and safe medicines that are quality assured, used responsibly, and accessible to all who need them (NCDC, 2017).

Current Situation of Antimicrobial Surveillance in Nigeria

Public health surveillance according to Nasir *et al.,* (2015) is a continuous systematic collection, analysis and interpretation of health-related data needed for planning, implementation and evaluation of public health issues. The essence of AMR surveillance is to track changes in microbial populations; permit the early detection of resistant strains of public health importance and to support the prompt notification and investigation of outbreaks (WHO, 2021). In the World Health Organization's global strategy for AMR curtailment, establishment and support of microbiology laboratories were identified as the fundamental priority in guiding and assessing intervention efforts. Enhanced results would only be obtained when surveillance is linked to monitoring of antimicrobial use and practice. The WHO guideline encompasses the following steps:

- Creating awareness and training in good laboratory practice to follow global standard operating procedures, quality control and quality assurance.
- Standard practice on AMR testing must be strictly adhered to in the laboratory.
- Result must be interpreted using international guidelines.
- Standard documentation of procedures and timely dissemination of result into the surveillance must be followed.
- Networking of laboratories within states and across the country to build capacity of testing laboratories through technology transfer, training and inter-laboratory comparison of result (WHO, 2011).

Furthermore, environmental surveillance has been considered as one of the important factors in

AMR surveillance. In their work on the need to include environmental surveillance in AMR efforts, Patricia *et al.,* (2019) revealed that environmental surveillance could contribute towards the protection of human, animal and ecosystem, and enumerated five (5) objectives achievable through the following steps:

- To address the risk of transmission of already antibiotic-resistant bacteria to humans via the environment.
- To address the risk for accelerating the evolution of antibiotic resistance in pathogens through pollution with selective agents and bacteria of human and animal origin.
- To address the risks antibiotics pose, for aquatic and terrestrial ecosystem health, including the effects on ecosystem functions and services.
- To identify the population-level resistance prevalence.
- To identify population-level antibiotic use.

Different types of environmental surveillance could be among the best, most likely ways of evaluating the different avenues the environment contributes to human, animal and environmental health risks. Such surveillance should be carried beyond soil, water and ambient air, since the environment is not limited to these media.

However, a conceptual framework to systematically clarify the why, what and where questions is currently lacking (Patricia *et al.,* 2019). Similarly, in the studies carried out, to establish the possible role of the natural environment in the transmission of clinically relevant AMR bacteria to humans, AMR bacteria were detected at exposure-relevant sites such as drinking water, recreational areas, ambient air, shellfish and fresh produce, as well as in environmental compartments which include wildlife, water, soil and air/dust and also in contamination sources like wastewater and manure (Patricia *et al.,* 2015). The abundance of AMR bacteria at these sites is an indication of danger to humans. Therefore, intervention strategies targeted at these sources could mitigate emission of AMR bacteria to the environment, and consequently humans and animals.

In response and in compliance to the World Health Organization's call, Nigeria developed her National Action Plan (NAP) on antimicrobial resistance in January, 2017 with the Nigeria Centre for Disease Control and Prevention (NCDC) as the coordinating entity. This was achieved through a one Health approach and enrollment in the Global Antimicrobial Resistance Surveillance System (GLASS). According to the Nigeria Level Country Report (2018), work commenced immediately with NCDC identifying the stakeholders and forming a technical working group comprising the National AMR Technical Working Group (AMR-TWG) and the AMR National Steering Committee (NSC) with membership drawn from the Federal Ministries of Health, Agriculture and Rural Development and Environment. The target was on developing an outline of a roadmap for antimicrobial resistance, and situation analysis with the support of a coordinator from the global antibacterial resistance partnership. The situation analysis and action plan were published in May, 2017.

According to the report, a significant amount of work is currently being undertaken by various divisions in terms of education and public awareness. This is not only for the public but also for health workers within households, public places, business environments and schools, on hand hygiene, Water Sanitation and Hygiene (WASH) aspect, and how to access health facilities and information on mother and child health. These are considered as important aspects of AMR, and are currently funded and provided by National Primary Healthcare Development Agency (NPHCDA), Family Health Division, National Environmental Standard Regulation and Enforcement Agency (NESREA), National Agency for Food and Drug Administration and Control (NAFDAC), UNICEF and Federal Ministry of Health. Similarly, significant activities are put in place within various divisions to improve hand hygiene practice and WASH in health facilities within

communities to facilitate disease prevention and control. However, Infection Prevention and Control (IPC) programmes have not been regarded as a substantial programme except for mother and child health. Hence inadequate funding to strengthen the programmes and provide vaccines to prevent communicable diseases as well as misuse of antibiotics and other antimicrobials have been a limiting factor. According to Nigerian legislation, antibiotics should only be dispensed on prescription, but a combination of factors ranging from a shortage of licensed prescribers, pharmacies and access to quality medicines in some areas to proliferation of under-regulated patent medicine vendors, drug markets and hawkers suggest that Nigeria suffers from severe access problem and irrational drug use.

Furthermore, the WHO global strategy for antibacterial curtailment identifies interdisciplinary collaboration and laboratory-based surveillance as top priorities for handling AMR. These applies in Nigeria as multiple stakeholders are involved in AMR surveillance with various development partners which include United States Center for Disease Control (USCDC), Global Fund, World Bank, Japanese International Cooperation Agency (JICA), Pepfar, and Laboratory provider groups such as NPHCDA, Hospital division, Federal Ministry of Health, Military, TB/HIV laboratories, veterinary laboratories, NCDC, Nigerian National Institute of Pharmaceutical Research and Development (NIPRID) and the private sector. The implication is the existence of several diagnostic laboratories in different cities, communities and villages, even in the rural areas. However, not all the laboratories are equipped according to international standards. In their work, Nasir *et al.,* (2015) identified the presence of few accredited medium equipped medical and pathology laboratory services in both public and private sectors which generate key information on bacterial isolates and their antibacterial resistance patterns.

In alignment with international standards and assessment methods proposed by WHO and GLASS, NCDC through collaboration with the various laboratory providers is gathering grants from the various partners to establish a national reference laboratory for AMR surveillance. At present, the National Tuberculosis and Leprosy Control Programme in Zaria is supposedly fulfilling the role of coordinating AMR at the national level. There are two (2) TB national reference laboratories and six (6) zonal laboratories which perform sensitivity tests. Recently a nested PCR equipment called Genexpert® was introduced to detect rifampicin resistance, which has aided availability of molecular-based anti-TB resistance testing in several healthcare facilities in Nigeria (WHO, 2014). Similarly, microbiology and infectious disease laboratories within the National Institute of Pharmaceutical Research and Development, established as HIV new drug development and pharmacovigilance laboratories (funded by Pepfar and government budget) are able to provide microbiology and AMR testing, as well as conduct surveillance for malaria, tuberculosis, HIV and upper respiratory tract infections using their onsite clinics. In addition, the Medical Laboratory Science Council of Nigeria (MLSCN), also funded by the Federal Ministry of Health is involved in registering laboratories and medical laboratory Scientists for specific training with the aim of standardizing laboratory susceptibility testing via guidelines and standard operating procedures, as well as the training of laboratory scientists to apply these testing standards (Nigeria AMR Country Level Report, 2018).

Furthermore, the National Primary Healthcare Development Agency has established pilot programmes/projects in three (3) States which it intends to extend to five (5) states. Also the Nigeria State Health Investment Project Programme has an extensive Monitoring and Evaluation (M&E) framework covering sixteen (16) domains, some of which include antibiotic availability and use, compliance to treatment protocol, hygiene compliance, laboratory availability and use of diagnostic tests and waste management compliance indicators. The essence is to gather AMR specific and non-specific information from the three states as a sentinel source of primary healthcare data. However, 3 out of 36 states in Nigeria give only 8.3% coverage which will make an infinitesimal impact on AMR surveillance, considering the

population of Nigeria. There is therefore the need to expedite action to extend the programme to more states to achieve substantial results.

In Nigeria, provision of healthcare and other health-related services and research are carried out by the three levels of government (Federal, State and Local Government Councils), individuals, agencies and Non-Governmental Organizations (NGOs). This had made healthcare services more accessible to the masses and has expanded the level of monitoring and research. For instance, in their separate works on antimicrobial use and resistance in Nigeria, Ghebremedhin *et al.,* (2009) reported the emergence of community-associated methicillin resistance *Staphylococcus aureus* in South-West Nigeria. Also, Okesola and Oni (2009) discovered high antibiotics resistance rate among common gram-negative and gram-positive bacteria isolates in various clinical specimens in a tertiary hospital in Nigeria. Similarly, in a national survey on antimicrobial resistance awareness in Nigeria, Chukwu *et al.,* (2020) revealed that 70.3% of Nigerians procured antibiotic from pharmacy stores, 14.2% from chemist stores and 2.1% from hawkers. As regards the knowledge of AMR, 56.5% agreed to be aware while 76.6% believed they were powerless to stop the spread of AMR. Further studies on the knowledge and practice in the use of antibiotics among a group of students in the University in Nigeria carried out by Igbenebu (2013) revealed a high rate of consumption within the group, who admitted obtaining their antibiotics from unofficial sources, and were not able to complete their course of antibiotics therapy when they felt better. Additional research on AMR surveillance system in Nigeria by Mohammed *et al.,* (2018) revealed non-existence of a surveillance system, and the group proposed three models which could be modified and adopted by the government for establishing a national AMR surveillance system for the country. The models include:

a. Sentinel survey which involves selecting a sentinel site, preferably a teaching hospital from every zone, appointment of a focal committed person as the head, capacity building for staff and provision of testing materials and incentives to motivate staff.
b. Trans-border surveillance for antimicrobial resistance with the site at the major international airports in the country for testing patients travelling abroad in conjunction with the health portal using rectal swap specimen.
c. Periodic survey (active surveillance system) which involves carrying out purposive sampling with community-based and hospital-based populations being the target population.

Many more research works on AMR surveillance have been done and are still ongoing by NCDC, individuals, institutions, organizations and agencies in the country. The Nigeria AMR Country Level Report indicated that the NPHCDA primary healthcare programme appears to be sufficiently funded for the states where activities are active from additional grants and funds provided by World Bank and other development partners.

However, despite all these efforts and the existence of antibacterial standing committees in several tertiary institutions, Nigeria has no existing surveillance system to coordinate the various activities and measure the magnitude of antimicrobial resistance and its associated threat to public health. Nasir *et al.,* (2015) pointed out that existing national and state-based antibacterial surveillance activities are often voluntary, and operate without systematic oversight and functional leadership at the national level.

Challenges to Antimicrobial Surveillance in Nigeria

One of the major challenges to effective antimicrobial surveillance in Nigeria is inadequate funding.

Although, the World Bank and various other development partners have provided substantial funds to sponsor AMR activities, the funds are not adequate to extend the programme to other states, provide equipment as well as install necessary facilities and infrastructure such as testing laboratories and laboratory information system. Funds are also needed for capacity building and effective coordination of activities in the different states and regions.

Another limiting factor is inadequate of public health policies, laws and regulations guiding drug procurement, administration and usage, as well as the inability to enforce existing laws. Prescription monitoring is poor with the result that drugs including those antimicrobial in nature, are purchased from unofficial sources such as market hawkers, drug vendors and unauthorized patent medicine dealers. This results in chaotic drug distribution system which account for antimicrobial abuse and misuse, and consequently increase rate of resistance by microorganisms. The existing legislations are not implemented as some regulatory bodies do not have the capital to carry out the work for which they were set up. An attempt to amend the obsolete Pharmacists Council of Nigeria (PCN) Act Decree 91 of 1992 which became the Act of the National Assembly, 2004 was frustrated by the presidency as reported in Nigeria National Action Plan for Antimicrobial Resistance 2017-2022. The amendment, if carried out would have brought sanity into drug distribution by reducing access, and also curb the menace of putting drugs in the custody of trained professionals thereby making it illegal for an untrained person to carry or distribute drugs.

AMR surveillance is also hampered by inadequate coordination among the different health providers. All levels of government according to the Nigeria AMR Country Level Report (2018) have responsibilities for healthcare provision as a concurrent function within their constitution. Similarly, various agencies, Non-Governmental Organisations (NGOs) and individuals are involved in provision of healthcare services in different regions, countries and states. Hence, policies at the Federal level are not necessarily implemented at the sub-national levels except when interested. Also, there is a legislation to ensure that federal grants to the states cannot be earmarked in any way, not even for health, medicines or specific health-related programmes. This limits the ability of the Federal Government to ensure the implementation and resourcing of any health plan at the State or Local Government levels. Coordination of programmes and activities of the different sectors involved in provision of health care services will ensure effective monitoring, evaluation and surveillance of antimicrobial use and resistance.

Furthermore, there are inadequate research centres, microbiology and PHC antimicrobial testing laboratories, while the existing ones are not adequately equipped. Also, there is no laboratory information system to collate data from different laboratory results for policy making, evaluation and implementation. Similarly, only two national reference laboratories exist which cannot effectively monitor antimicrobial resistance as well as other infections, considering the population and area coverage of Nigeria. Moreover, there is no inter-laboratory framework and network for collaborative surveillance of AMR among the existing laboratories. These seriously hampered the efforts to track emerging and re-emerging resistance challenges, identify, characterize and contain new antibiotic threats, and to systematically compare and evaluate the value of national resistance containment activities (CDC, 2009). Establishment of effective research centres and laboratories will go a long way to identify drug-resistance organisms, the level of resistance and how best to prevent and treat infections and diseases associated with microbial resistance.

Another limiting factor is people's ignorance of the meaning, causes, health and economic impacts of antimicrobial resistance. Majority of the population are unaware of the problems arising from abuse and misuse of antimicrobials, hence these drugs are indiscriminately prescribed, administered and consumed. The implications are increasing rate of resistance to commonly used antibiotics, difficulty in the treatment of infectious diseases and higher rates of morbidity and mortality.

Other limitations to antimicrobial resistance surveillance identified by Nasir *et al.,* (2015) and Frean *et al.,* (2012) include limited quality assurance and control protocols, inadequate essential laboratory reagents and consumables, limited access to basic health services coupled with shortage of essential medicines including antibiotics, poor bacterial surveillance systems and strategies

as well as weak data collection and documentation for reference purposes.

Recommendations

Antimicrobial resistance is a complex issue that threatens public health globally. Though many projects have been put in place, yet the efforts are not yielding the required results. The following recommendations are proffered to curb the increasing microbial resistance and associated health problems.

1. Public Enlightenment Campaign

Most Nigerians are ignorant of the meaning, occurrence and causes of antimicrobial resistance and its health implications. Therefore, elaborate campaign through workshops, seminars, social media, the use of fliers and medical outreach to communities, schools, churches and commercial centres is needed to inform the masses of the dangers of indiscriminate prescription, administration and use of antimicrobial drugs.

2. Funding

Adequate budgetary provisions should be earmarked for procurement of facilities, infrastructure, equipment, and training of health professionals for effective healthcare delivery.

3. Collaborative Action

Since antimicrobial resistance requires multidisciplinary approach, the One-Health approach which brings multiple sectors and professionals together to design and implement programmes, policies, regulations and research to attain better public health services as proposed by World Health Organization (WHO, 2020) is recommended.

4. Innovations and Research

There is a great need for the establishment and equipment of more research centres for greater innovations and research in the development of new antimicrobial drugs, vaccine production, data collection, analysis, monitoring and evaluation to improve healthcare services.

5. Establishment of Laboratory Information System and Medical Diagnostic Laboratories

More microbiology and medical science laboratories and laboratory information system need to be put in place for effective data collection, collation, analysis and result comparison for building information into a single database for AMR surveillance, prevention, control and management.

6. Capacity Building and Manpower Development:

Considering the enormous population of Nigeria, there is a great need for training and re-training of personnel in different sectors of public health. This is in a bid to complement the existing workforce already overwhelmed by increasing health issues and pandemics such as COVID-19, and to enhance their productivity based on the fact that knowledge is strength. It is a fact that an educated and literate population is potentially a productive population.

7. Effective Waste Management System

Improper disposal of wastes and dumpsites provide breeding places for pests, parasites, vectors and pathogens, and are consequently sources of infectious and non-infectious disease transmission. A holistic waste management system is therefore advocated to make the environment sanitary, pristine and sustainable, thereby reducing the spread of infectious diseases, consumption of antimicrobials and associated antimicrobial resistance complications.

8. Implementation of One Health and Water, Sanitation and Hygiene (WASH) Concept

Due the complexity of antimicrobial resistance, implementation of One Health and WASH approaches which focus on human, animal, plant and environmental health through multi-sectoral and multidisciplinary collaboration is recommended to checkmate the emergence and re-emergence of infectious diseases, their spread and antimicrobial resistance occurrence.

Conclusion

Antimicrobial resistance is a global challenge arising mainly from inappropriate use of antimicrobial drugs overtime, which causes genetic changes in pathogens, and the emergence of antimicrobial resistance species. It occurs in humans, animals and plants, and leads to difficulty in treatment of infectious diseases, longer stay in hospital, morbidity and in severe cases mortality. Antimicrobial resistance can be controlled by effective monitoring and surveillance. In Nigeria, several public health care programmes and facilities have been put in place for microbial resistance surveillance.

However, the existing facilities, manpower, and infrastructure are found to be inadequate. Effective antimicrobial surveillance requires a collaborative approach involving multi-sectorial and multidisciplinary actions. Concerted efforts and improvement are therefore needed in the areas of disease epidemiology and surveillance, laboratory diagnosis, data collection, analysis and documentation, monitoring of antimicrobial administration and usage as well as environmental sanitation to achieve the aim and objectives of establishing the Action Plan for Antimicrobial Resistance in Nigeria.

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Umeh, S.I., Uwakwe, F.E., Onyimah, E. O., and Opara, M.C.
© *African Journal of Environmental Health Sciences*
Volume 8, November, 2021
ISSN: 2476-8030 (Prints)
ISSN: 2714-2930 (Online)
pp 87-98