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Original Review Article

ANTIMICROBIAL RESISTANCE (AMR): AN IMPENDING CRISIS FOR THE NIGERIAN HEALTHCARE

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ABSTRACT

Antimicrobial resistance (AMR) is a complex challenge posing a significant threat to public health globally. Low-and-middle-income regions have been identified to be facing the greatest impacts of AMR due to various factors. The combined number of deaths reported from cases of maternal and neonatal disorders, tuberculosis, neglected tropical diseases, malaria, respiratory tract infections, and cardiovascular diseases in Nigeria remains lower than AMR-related deaths. The absence of laboratories to conduct sensitivity testing, inappropriate antibiotic prescribing, and extensive agricultural use are some of the factors that have contributed greatly to the rise and spread of antibiotic-resistant infections. There has been a coordinated fight to control the prevalence of AMR since 2017 by the Nigeria Centre for Disease Control; even so, there is a need to harmonize the efforts of other parastatals to address the root cause of AMR within the country. In this study, we described the various factors and the status of antimicrobial resistance in Nigeria and the recommended strategies to improve the situation alongside the national action plan. It is recommended that the government explores research into the use of biotherapeutics products and phages for alternative treatment, host a national platform where Nigerian healthcare professionals and clinical researchers can recommend real-time approaches used at their facilities to control antimicrobial resistance, encourage the use of drug-eluting materials, the Pharmacy Council should develop and implement a field-level monitoring model and disciplinary measures to stop the sales of medicines to non-licensed medicine vendors in communities as well as street drug hawkers.

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INTRODUCTION

Antimicrobials are chemotherapeutic agents that kill or inhibit pathogenic microorganisms [1,2]. AMR occurs when infectious organisms change in some way that reduces or eliminates the effectiveness of antimicrobial agents designed to kill or inhibit their growth and multiplication [3].

Antimicrobial resistance poses a potential risk to the current medicines and future medical progress [4]. AMR is a growing problem globally [2]. Antibiotics' remarkable effectiveness in treating infectious diseases has resulted in their widespread distribution and use [5]. The discovery of penicillin was

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among the most impactful breakthrough made in the 20th century, It provided great relief in infected war wounds treatment and soon into clinical medicine in general [5]. But soon, resistance to Penicillin by bacteria was discovered. The rising prevalence of antimicrobial-resistant pathogens has become well-recognized over the past decade [6]]. Currently, at least one out of the most frequently used antimicrobial agents for therapy faces resistance from about 70% of the bacteria causing nosocomial infections. [3,7,8]. In 2019, infections caused by drug-resistant microorganisms led to an estimated death of 1.27 million people globally. It is predicted that by 2050, about 10 million deaths could occur annually [1]. These deaths could be avoidable to some extent by taking necessary action such as antimicrobial stewardship [1]. Antimicrobial overuse or abuse is a key contributor to AMR [4,8]. The use of antibiotics is typically controlled by factors like extent of training among pharmacists and other healthcare staffs, the patient demand, cultural perceptions and advertising to prescribers by pharmaceutical industry providers, and use in the situation of uncertain diagnosis [4]. Inadequate infection control and lack of potable water and sanitation are some of the challenges of poverty and environmental factors faced by Nigeria [9]; Infections have continued to be the most frequent cause of ailment and mortality across the 36 states of the nation as non-communicable diseases gain prominence [10]. There is an increased rate of antibiotic use in areas of healthcare practices with obstetrics and gynecology accounting for about 72.9% and pediatric medical specialties being 94.6% [11]. There has been reported cases of treatment failure rate in the management of infections like malaria, tuberculosis, respiratory tract infections, diarrhoea diseases, and HIV/AIDS due to antimicrobial resistance [10,12]. There is deficiency in the population's understanding and awareness of AMR in Nigeria, and this correlates with the pattern of use of available over-the-counter antimicrobials [9,13]. Patients, farmers and the general population contribute greatly to the use of antimicrobials and its misuse, especially in addressing real or presumed infections by acquiring antimicrobials without prescriptions or via unlicensed sources. [10]. The attention given to AMR by the public health, agricultural, and environmental sectors vary, which includes resources allocated to combat AMR in Nigeria [14,10]. Antibiotics classes like cephalosporin, chloramphenicol, tetracyclines, penicillins, aminoglycosides and cotrimoxazole have been faced with vast *Escherichia coli* resistance in Nigeria [10]. There has been a notable and consistent rise in resistance patterns among *Shigella* and nontyphoidal *Salmonella* [10]. Nigeria ranked 185 out of 203 countries in age-standardized death rate caused by AMR per every 100,000 persons [15]. In line with the 68th World Health Assembly (WHA) action plan, the Nigerian Minister of Health, on the 26th of November 2016, approved the establishment of Nigeria's National AMR Coordinating Body at the Nigeria Centre for Disease Control (NCDC) [10]. The continuous changes in the mode of drug

resistance account for the increasing rate of multidrug resistance seen in organisms, with the resistant pathogens affecting the patients and the healthcare system clinically and economically [16,17,18]. The Institute for Health Metrics and Evaluation (IHME) reported that there were 263,400 mortalities connected to AMR in Nigeria in 2019, with 64,500 of the mortality directly caused by AMR. The study revealed that in Nigeria, the mortalities arising from tuberculosis, maternal and neonatal disorders, neglected tropical diseases, malaria, cardiovascular diseases, and respiratory tract infections are lower than mortalities caused by AMR [19]. It is estimated that up to \$100 trillion of the global gross domestic product may be lost due to AMR by 2050, and it is believed that the impact would be most felt by low-income nations [20,21]. This may be because poorly developed and developing countries are most affected by resource constraints, with a considerable amount of uneducated and naïve populations which may lead to a medical poverty trap [22,23,24].

The World Health Organization (reported that 4 out of the 15 primary concerned antibiotic-resistant pathogens were identified in Nigeria [20]. In 2019, Ahmad & Khan noted that the population from LMIC may suffer from poverty over time as a result of expensive healthcare services leading to sickness not being treated and ultimately leading to death which will account for the loss of human capital [22]. With the low human development index of Nigeria sitting at 0.521 [25] and about 63% of Nigerians experiencing multidimensional poverty [26], healthcare status may further deteriorate as the majority of Nigeria's population is living below the poverty line [27].

DISCUSSION

Factors Contributing to Antimicrobial Resistance in Nigeria

Inappropriate prescribing of antibiotics by clinicians is a classic example of antibiotic misuse, a prime factor that can lead to AMR [28]. In Nigeria, empiric use of antimicrobials is widespread despite the provisions of the nation's treatment guidelines to prescribe antibiotics only when there is confirmation of systemic infection [27]. Furthermore, AMR resulting from misuse is frequent in developing countries because unlicensed individuals sell and dispense antimicrobials freely in the streets [17].

In animal breeding, antimicrobial agents are frequently used to improve growth and for disease management. This utilization in food-producing animals has led to the occurrence and spread of resistant bacteria [17,29,30]. Another driving factor of AMR in developing countries is the rise in personal income which has significantly increased the consumption of over-the-counter antibiotics [28]. Other drivers of AMR include a lack of population's knowledge of antimicrobials, compliance with guidelines of antimicrobial usage, and the absence of laboratories to conduct sensitivity testing [23,29].

Future Implications of AMR in Nigeria

As of 2016, an estimated 700,000 deaths occurred annually due to infections caused by resistant organisms, with 214,000 of these being deaths from neonatal sepsis. Without intervention, it is estimated that about 10 million deaths may be recorded annually by 2050 [31]. In 2014, the World Health Organization estimated the societal cost of AMR to be around 35 million US dollars. Given Nigeria's domestic debt of approximately 113.43 billion US dollars as of 2023, the potential consequences of AMR could be catastrophic for both the Nigerian economy and its healthcare system [32,33]. According to the GRAM studies, the 2019 estimated AMR associated death was 263,400, with an additional death of 64,500 attributed to AMR-related causes. These figures foretell a challenging future marked by heightened morbidity and mortality, posing a significant threat to the stability of the Nigerian healthcare system unless substantial interventions are implemented promptly [19]. The failure of therapies, prolonged hospital stays, escalated costs of second-line drugs, and overall increased healthcare expenses due to AMR paint a grim picture for Nigeria's future. This trajectory is marked by economic and medical pitfalls, posing significant challenges to the country's well-being. The World Health Organization highlighted that Nigeria's AMR situation partly poses a threat to food security, global health and development [28,34,35].

Current Approaches to Curtail Antimicrobial Resistance (AMR).

Alternative treatment like the bacteriophage therapy are being developed in order to contain the continuous rise in AMR, and to preserve the effectiveness of the currently available classes of antibiotics [36,37]. Discovery of novel antibiotics via structural modification of existing drugs, screening small-molecule libraries, or exploring unique environments are some of the strategies that have been proposed for curtailing antibiotic resistance [37]. Furthermore, efforts are focused on improving the efficacy of existing antibiotics by stimulating metabolism or developing novel delivery systems like the small molecule antibiotics, hence, serving as alternatives to conventional antibiotics such as bacteriophages, anti-biofilm drugs, probiotics, nanomaterials, vaccines, and antibody therapies are being developed [37]. Alongside these efforts, antibiotic and antimicrobial stewardship play a crucial role, while the concept of antibiotic-resistant breakers is also being explored [38,39]. Antibiotic-resistant breakers use adjuvant-like compounds to increase the effectiveness of current antibiotics by combatting the resistance mechanisms employed against them. Antibiotic-resistant breakers can be co-administered with or conjugated with failing antibiotics [40]. Antibiotic and antimicrobial stewardship (AMS) refers to steps taken for the optimal selection, dosing, and antimicrobial treatment duration aiming for the best clinical outcome with

the least side effects on the patients and the least possible impact on subsequent resistance [41,42].

Nigeria's National Action Plan on Antimicrobial Resistance.

The NCDC has positioned itself to lead the drive in responding to antimicrobial resistance since 2016 with the development of the National Action Plan (NAP) implemented from 2017 to 2022. The NAP aligns with the WHO Global Action Plan on AMR and addresses five key pillars. These pillars encompass;

- I. Increasing rate of awareness and building the capacity of health workers and the public about AMR,
- II. Establishing a 'One Health' surveillance system,
- III. Strengthening infection prevention and control alongside biosecurity measures,
- IV. Promoting the rational use of antimicrobials and ensuring access to quality medications,
- V. Conducting research into alternatives to antimicrobials, new diagnostics, and therapeutics.

To ensure a comprehensive approach, a National Technical Working Group (TWG) on antimicrobial resistance, as well as a National Steering Committee, oversee antimicrobial-related activities across all sectors in the country [32,33,44,45].

Strategies to Combat AMR In Nigeria

Five (5) key focused strategies in Nigeria to prevent, reduce, and slow the evolution of resistant organisms and their impact on healthcare while ensuring optimal use and improving access to effective safe, and quality-assured antimicrobials for continued successful management of infections [44,45]. These include:

- I. Improving awareness and knowledge of AMR and related topics [45,47].
- II. Building a "One Health" AMR Surveillance System [49].
- III. Intensifying infection prevention and control in the tripartite sectors [50].
- IV. Promoting rational access to antibiotics and antimicrobial stewardship in Nigeria [50].
- V. Investing in AMR research and development [44,45].

CONCLUSIONS

Antimicrobial resistance is a challenge attributed to multiple factors globally. Over time, AMR has created a dent in the efforts to achieve efficiency in treatment outcomes, and even worse in low-income countries like Nigeria. Antimicrobial resistance, if not controlled, will eventually multiply the proliferation of morbidity and mortality across all age groups, thereby impacting the nation's workforce negatively. This will consequently contribute to the further breakdown of its economy. Therefore, there is an urgent need for policymakers to make conscious efforts toward the development of a strategic plan for effectively monitoring the quality of field-level implementation of the national action plan regarding

antibiotic stewardship programs to tackle AMR across the nation.

RECOMMENDATIONS

To control antimicrobial resistance, Good antimicrobial use and prescription policies need to be put in place. AMS is also a key factor that should be established and promoted.

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CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest

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