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Response to the Antimicrobial Resistance Problem among Developing Countries

Kavulavu Briton Matata*

Graduate student, KEMRI Graduate School, Nairobi, Kenya

***Corresponding author:** Kavulavu Briton Matata, Graduate student, KEMRI Graduate School, Nairobi, Kenya

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ABSTRACT

It would be easy to presume infectious diseases are no longer a significant public threat compared to non-communicable conditions. However, statistics say otherwise, with these ailments still featuring in the top 10 death etiologies. Africa, which constitutes the bulk of the developing world, reports disproportionately high morbidity and mortality rates related to infectious diseases. Sadly, with many factors promoting the high prevalence of infectious diseases, the threat of antimicrobial resistance (AMR) has emerged as a life-threatening issue in managing these diseases. This review article aimed to scale the problem of AMR in Africa compared to the rest of the world and summarize strategies used in its mitigation as well as the challenges encountered with the implementation of AMR prevention strategies. As per the findings herein, AMR is an underestimated public health emergency needing urgent attention among African countries. Weak laboratory systems, failure to adhere to efficient antimicrobial use guidelines, and unregulated antimicrobial agents access are the primary promotive factors behind te AMR problem. It is outstanding that whereas Kenya has made significant steps in implementing NAPs on AMR, there is still a need for more attention, especially with the observation that funding for AMR activities is mainly from donor funds.

Keywords: Antimicrobial Resistance; Prevention; NAPs; Antimicrobial Agents

Introduction

It would be easy to presume infectious diseases are no longer a significant public threat compared to non-communicable conditions. However, statistics say otherwise, with these ailments still featuring in the top 10 death etiologies [1,2]. Africa constitutes the bulk of the developing world, and the prevalence of infection-related deaths hits as high as 69%. Enteric infections have been observed to cause disproportionately high mortality and morbidity rates in sub-Saharan Africa [1]. Adding to the discussion on the significant burden of infectious diseases in SSA, (Godman, et al. [3]) postulate that HIV/AIDS, Malaria, and TB alone account for up to 1.2 million deaths in this region. This alarming rate is potentially aggravated by the rapidly increasing population in SSA, migration to urban areas to seek jobs, bulging of informal settlements, and poor water and sanitation infrastructures. Sadly, with many factors promoting the high prevalence of infectious diseases, the threat of antimicrobial resistance (AMR) has emerged as a life-threatening issue in managing these diseases. By definition, antimicrobial resistance is a term used to denote the ability of a condition-causing micro-organism, be it a virus, bacteria, protozoa, or fungus – to gain genes wither through imitation or gene transfer that enable it to survive a concentration of an antimicrobial agent that was previously effective for its treatment. Consequently, clinically attainable concentrations of an antimicrobial agent end up being ineffective in managing the microbe [4]. This review article aimed to scale the problem of AMR in Africa compared to the rest of the world and summarize strategies used in its mitigation as well as the challenges encountered with the implementation of AMR prevention strategies.

Antimicrobial Resistance as an Underestimated Emergency

Globally, AMR is receiving attention at the level of a pandemic. (Murray, et al. [5]) discuss that up to 1.27 million deaths in 2019 were related to resistant bacteria. This mortality rate, notably, was significantly clustered in Africa since western SSA accounted for the bulk of the deaths while Australasia reported the least rates [5]. In writing the prevalence and clinical implications of AMR in Ethiopia, (Berhe, et al. [6]) reported 8 to 20% vancomycin resistance among clinical isolates. In the assessment, E. coli, K. pneumoniae and P. aeruginosa, major Gram-negative pathogens, were resistant to most commonly used antibiotics. Among children in SSA, a meta-analysis by (Williams, et al. [7]) observed significant extended-spectrum β-lactamase production among gram-negative organisms causing neonatal sepsis and a high reported prevalence of non-susceptibility among the gram-positive pathogens associated with infections in the neonatal period. For instance, non-susceptibility to ampicillin was above 60% among isolates of Klebsiella, S. aureus, E. coli, and Salmonella [7]. The AMR problem is becoming more significant with each new research study. One study by (Bernabe, et al. [8]) noted that bacteria isolated in the clinical specimen in West Africa were significantly resistant to cephalosporins, ampicillin, cotrimoxazole, gentamicin and amoxicillin/clavulanate. It was observable in the analysis that hospitalized patients suffered higher AMR rates [8]. Let alone the disease burden of AMR, the socioeconomic effects of the pandemic are also notable and palpable among economies. (Kariuki, et al. [9]) observed that the eastern part of SSA, of which Kenya is part, records up to 1.3 million deaths related to infections, of which about a quarter are connected to resistance. It has been rightly approximated that a death rate of 21.4 (16.3-28.1) may be related to AMR in eastern SSA [9].

Economically, studies continue to link AMR to increased length of hospital stay, which culminates in increased healthcare costs and decreases labor supply for nation-building [10,11]. The global economic burden of AMR will be as high as US$ 100 trillion in the next 30 years if the present trend persists. As (Ferri, et al. [12]) reported, the current cost of AMR is about 2 billion euros in Europe and about 55 billion US$ in the USA. In the absence of accurate approximations of the cost of AMR in the SSA region, (Kariuki, et al. [9]) report that the economic losses due to the AMR pandemic may be the highest globally. Of course, the costs will continue to rise if no interventions prevent the trend.

Why is AMR so Significant in the Developing World?

Health systems capacity, clinical care policies and guidelines, and infrastructure may be blamed for the continued propagation of AMR. To effectively tackle the problem of AMR, there is a significant need for antimicrobial stewardship guidelines, proper diagnostic procedures to check antimicrobial susceptibility, and consideration of alternative options to resist drugs. In high-income countries where the burden of infectious diseases is only modest, resistant bacteria are detected by proper diagnosis and treated using effective second-line agents [12]. However, the situation is different in SSA, even with the highest global prevalence of infectious diseases. Often, antimicrobial susceptibility testing may be missing. Even when AST is done, and resistant strains are identified, it may be difficult to avail high-quality second-line antimicrobial agents among such patients [12,9]. Besides, African countries, including Kenya, are still struggling to protect their populations from the infiltration of the market by low-quality and ineffective antibiotics supplying sub-optimal doses [13]. Difficulties in performing quality ASTR tests constitute a significant challenge in developing countries, especially Kenya. Diagnostic systems in the developed world are generally efficient and well-equipped to undertake ASTs. In a case, for example, Project ICARE in the USA, (Steward, et al. [14]) concluded that up to 75% of laboratories assessed could correctly report MIC values and zone sizes for resistant Serratia marcescens. Further, up to 42% of laboratories could detect extended-spectrum beta-lactamase-producing bacteria, showing highly effective diagnostic systems. On the contrary, developing nations like Kenya only have scanty laboratories that can undertake culture and sensitivity tests for bacteria. For example, (Odhiambo, et al. [15]) report that most hospitals in Kenya lack the capacity for AMR testing.

This being the case, most clinicians are compelled to treat infections based on empirical clinical judgment using broad-spectrum antibiotics. In many other cases, patients resort to self-medication because laboratory tests in microbiology take excessively long turnaround times [1]. Although efforts have been made to implement quality assurance systems such as SLIPTA, there is still a need for more AMR testing gaps [16]. Thus, limited and low-quality microbiology diagnostic services remain significant AMR promoters. In several studies, failure to treat based on accurate diagnosis has been affirmed to be a potent promoter of AMR [17,18]. Unregulated antimicrobial access and use in the developing world are among the key promoters of AMR. Whereas genetic methods of acquiring and transferring resistant genes among pathogens are the primary cause of AMR at the molecular level [19], its acceleration is believed by researchers to be purely a function of human error. Failure or observe antimicrobial stewardship guidelines in SSA, primarily through inappropriate use and overdose of antimicrobial agents for humans, animals and plants, is a significant propagator of AMR [20,21]. Inappropriate prescription of antibiotics without sufficient justification. Unnecessarily long treatment courses, self-medication, and failure to complete prescriptions are common trends in SSA that promote AMR [25-24]. One study observed that antibiotic consumption globally increased by 46% between 2000 and 2018 [25]. According to the WHO, antibiotic consumption in

Burundi and Tanzania, which might reflect the situation in East Africa, is 4.4 and 27.29 daily defined doses as of 2018 [26]. Reducing excessive antimicrobial use might be connected to a reduction in the AMR acceleration rate [27] (Figure 1).

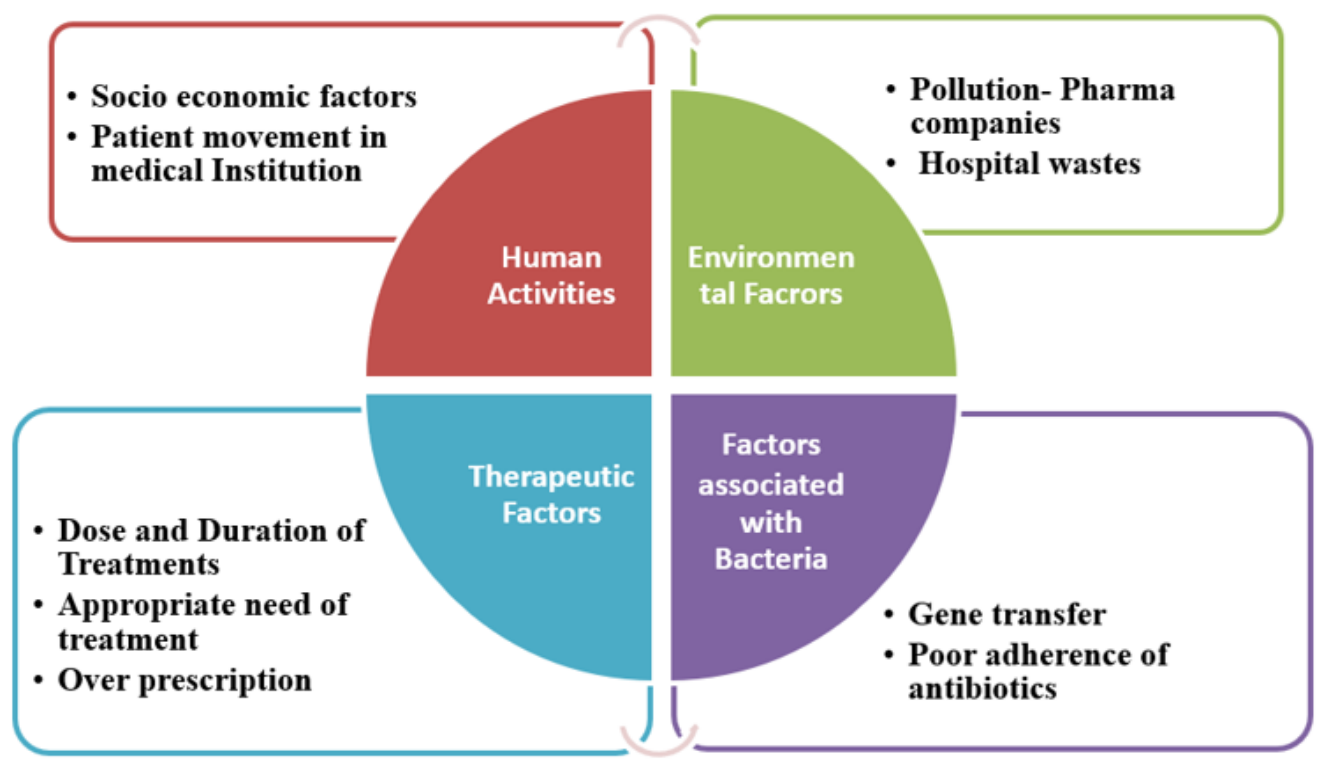

Figure 1: Factors responsible for AMR adopted from (Nishanth [38]).

Proposed Responses to the AMR Problem in the Developing World

Without effective laboratory systems, empirical treatment cannot be fully devilized. However, there is a need to ensure that the practice of empirical treatment is streamlined by implementing updated national guidelines that consider local susceptibility patterns as revealed by epidemiological surveys in the country [6]. The provision of culture and drug susceptibility testing facilities in diagnostic laboratories and the establishment of a solid antimicrobial stewardship program should be a top priority [6]. This would at least limit blind treatment and introduce some aspects of evidence-based practice. Nonetheless, strengthening laboratory capacity remains the most effective response to the AMR problem since the only accurate way to treat infections without risk of resistance is based on AST data from high-quality testing systems [28]. Implementing proper antibiotic stewardship guidelines might effectively regulate the pandemic's progression. Thus, educating populations on the effective use of antibiotics while stressing about using them only based on prescriptions and insisting on completing doses remains an essential strategy for controlling the AMR menace [28]. It has been demonstrated that reducing improper antibiotic usage directly correlates to a lowering in AMR development; nevertheless, this alone would not be sufficient to address the worldwide AMR crisis [27]. As a result, the One Health strategy is required to manage the rapid appearance and transmission of antimicrobial-resistant bacteria and mutations in the environment, animals, and human population [29]. The global action plan on AMR also recommends a One Health approach [9]. Thus, establishing One Health clubs and consortiums concerned with awareness of AMR and collaborative approaches to better antibiotic use has been a common trend in Kenya over the last few years.

Kenya's Implementation of the Global Action Plan on AMR

Following reports of alarming rates of AMR among the community and hospital-acquired pathogens as well as livestock and plants, 194 member states of the WHO adopted the global action plan on AMR, intending to streamline strategies to fight the problem [30]. Based on the GAP framework, every country

was supposed to develop a national action plan to successfully treat and prevent infections using safe, effective and high-quality antibiotics used responsibly. These action plans' key objectives were to increase AME awareness, promote surveillance and research, reduce infection incidence, optimize antimicrobial agents utilization, and sustainably invest in controlling AMR. Collaboration between the World Health Organization, the Food and Agriculture Organization (FAO) and the Office International des Epizooties (OIE) was symbolic of the One Health approach [30]. Whereas the global response towards developing NAPs has been rapid, only 14 African countries had developed NAPs by 2017, and only nine were monitoring antimicrobial usage within their jurisdictions [9]. Kenya is among those that developed a NAP and committed to its implementation. The first Kenyan NAP on AMR expires in 2022. According to (Kariuki, et al. [9]), Kenya is among the countries effectively implementing the NAP on AMR. The Fleming Fund has significantly assisted the execution of NAPs in Kenya by promoting awareness, guaranteeing an expanded antibiotic stewardship blueprint to optimize antimicrobial use, increasing AMR and antimicrobial use monitoring, monitoring, and data exchange, and implementing infection prevention and control strategies [31].

Challenges Encountered in the Implementation of NAP on AMR

Being a developing country, the classical challenges are natural. Several setbacks still limit the effective implementation of the NAP on AMR. Government commitment to supporting AMR wars through funding is still limited, but this may be understandable owing to the prevailing economic times. The situation is similar to many other countries in the developing world where resources are a significant challenge. Other challenges include a lack of political commitment to the framework, ineffective intersectoral coordination [32], weak health systems, lack of surveillance data [9], and lack of quality assurance systems. Also, the limited availability of microbiology experts and lack of technical staff for diagnosis has been observed as a significant challenge [32,33]. Discussing the role of political commitment, Goldberg et al. posit that NAPs on AMR may not succeed without a demonstrated political commitment from the government. The absence of this commitment limits the possible gains of these NAPs [34]. Whereas African governments in 2001 had committed to spending at least 15% of their budgets on health, spending on health declined significantly between 2002 and 2014, mainly secondary to public debt and lack of commitment [35]. Sadly, between 20 and 40% of health budgets are wasted through systemic inefficiencies, misarranged priorities and corruption in African governments, as is the case in Kenya [36].

Conclusion and Recommendation

It stands out from this review that AMR remains a significant roadblock hindering efforts to manage infectious diseases in developing countries like Kenya effectively. This review focused on exploring the prevalence of AMR in developing and comparing the rates with what is observed in developed countries. This revealed that AMR is an underestimated public health emergency needing urgent attention among African countries. This review also set out to consider the reasons AMR is most significant in the developing world. Notably, weak laboratory systems, failure to adhere to efficient antimicrobial use guidelines, and unregulated antimicrobial access are the primary promotive factors. Whereas Kenya has made significant steps in implementing NAPs on AMR, there is still a need for more attention, especially with the observation that funding for AMR activities is mainly from donor funds. To improve the fight against AMR in Kenya and other developing nations, there is a need to increase government commitment to this course. In line with the suggestions of the WHO on maintaining the sustainability of AMR prevention policies [37], it is recommended that Kenya strengthens governance, prioritizes the implementation of the NAP, mobilizes resources for effective action, and creates effective sustenance systems geared towards AMR. The finance of these AMR programs as part of public health expenditure must be considered [38]. Governments must also include the business sector in resource mobilization. Establishing a coordinating team of specialist groups and representatives from other industries is also critical. The coordination team would be crucial in determining national priorities, synchronizing the operations of various NAPs, mobilizing resources, and engaging politicians.

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