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Global impact of antimicrobial resistance on cancer care: Challenges and strategies in low- and middle-income countries

Alhamdu Dawa Bulus [1], Esther Chidinma Ezeh [1,*], Ritji Victor Goldim [3] and Angela Ene Edache [4]

[1] *Department of Molecular Biology and Genomics, Global Health and Infectious Diseases Control Institute, Nassarawa State University, Keffi Nigeria.*
[2] *Department of Biochemistry, Faculty of Science, Federal University Gashua, Yobe State Nigeria.*
[3] *Laboratory Department, Edoch Medical Services, Jos-South Plateau State, Nigeria.*
[4] *Department of public Health, faculty of Basic and applied Biological science, Ahmadu Bello university Nigeria.*

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Abstract

Antimicrobial resistance (AMR) is a fast-rising global health warning that causes significant challenges to the treatment and management of infectious diseases, especially in cancer patients, who are a large number of the vulnerable populations. This work underlines the complicated problems faced by the low- and middle-income countries (LMICs) in cancer care due to AMR. The burden of both cancer and AMR is sadly high, so therefore this review sheds light into the possible potential strategies to win against these challenges and set up better cancer treatment for improved outcomes in these countries. This sheds more light and gives a deeper understanding of recent research works, epidemiological data, and relevant case studies. Furthermore, examining the interconnectivity between AMR and cancer care, narrowing it down to some particular challenges and vulnerabilities encountered by cancer patients in LMICs. The study identifies key strategies such as implementing better antimicrobial stewardship programs, improving infection prevention and control, promoting new drug development, and enhancing global interactions as important steps in reducing the effect of AMR on cancer care in LMICs. This emphasizes the urgent need for targeted interventions, context-specific solutions, building sustainable development, and global interactions to address the complex challenges posed by AMR in cancer care within LMICs.

Keywords: Antimicrobial resistance; Low- and middle-income countries; Multidrug-resistant; Cancer care

1. Introduction

1.1. Background: Antimicrobial Resistance (AMR): A Global Health Crisis

Antimicrobial resistance (AMR) is a global health challenge faced by many in this era, and as such, it is limiting the way deadly infections and diseases are treated. According to the reports from [1], this AMR has led to the demise of over 1.2 million people, children and adults inclusive. In the year 2019, AMR also had a hand in the deaths of over 4.9 million people, children and adults inclusive. Here is a breakdown of how this AMR operates; it starts brewing when microorganisms, which include but are not limited to bacteria, viruses, fungi, etc., slowly start to build resistance to antibiotic or antimicrobial drugs consumed by an entity, which makes these medications useless to the victim over time [2]. The victims are mostly entities that have abused these drugs in one way or another [3]. The problems of AMR include, but are not limited to, the following: increased deaths, severe illness, increased poverty, etc. As predicted by [1], AMR could be responsible for the deaths of over 10 million lives by 2050 if left unhandled.

* Corresponding author:

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1.2. AMR and Cancer Care: A Dangerous Intersection

It is a fact that AMR and cancer treatments go hand in hand; for example, cancer patients are prone to contracting infectious diseases due to the weakness in their immune system, which is mostly caused by the type of treatment they receive or the disease itself. AMR in cancer patients makes it more difficult in cancer care as it gives double threat to the patients; sometimes it causes more complications and increases the chances of patients contracting more deadly infections. The major therapies in cancer treatment mostly rely on the ability to control infections using immunosuppressive therapies. When pathogens become resistant to drugs, they lead to several drawbacks, which can lead to death in worst-case scenarios.

These immunosuppressive therapies can often make patients much more vulnerable to infections as they weaken the immune systems of the patients. While on the other hand some cancer treatments like the stem cell transplant have undoubtedly proven to be much more productive and give the patients higher chances of survival; this is how it works; it uses broad-spectrum antibiotics to deter infections trying to take advantage of the patients; in such cases, the antibiotics help prevent and treat the infections in the patients and also help in boosting the patient's immune system, which enhances chemotherapeutic treatments [4]. Although, despite how promising this looks, it cannot be abused, else the patient is at risk of AMR, which makes the patients stay in an unending cycle until death [5] due to the fact that the patients are now victims of both AMR and cancer, which complicates the treatment process and makes it almost impossible to treat.

1.3. Importance of LMICs

A large part of the low- and middle-income countries (LMICs) are the most vulnerable victims of both AMR and cancer-related diseases [6]. These settlements face a lot of problems trying to conquer AMR; some of the most common problems they face are usually lack of proper hygiene (sanitation), lack of proper preventive techniques, limited access to good healthcare services, etc. These challenges combined together pose a threat to the proper management of AMR [3]. To emphasise more on the major problems faced by LMICs, which is poverty or lack of enough money to treat cancer, as cancer treatments are very expensive and cannot be afforded by many of these cancer patients in these regions [7]. The combination of AMR and limited resources can lead to delayed diagnoses, suboptimal treatment options, and increased mortality rates among cancer patients; the consequences can be particularly severe, highlighting the critical need to address AMR in cancer care within LMICs to ensure global health equity [8].

2. Epidemiology of AMR in Cancer Patients

2.1. Global Burden of AMR

In 2015, the World Health Organization adopted the global action plan, making evident the urgency of AMR, as it is already a world health challenge putting the efforts of effective treatments for infectious diseases to waste. The plan stated how AMR is a threatening crisis for the globe, entirely including modern medicine, and the sustainability of a positive global health response to the infectious disease crisis [9, 10]. In the midst of the AMR trends is the rise of infections that are caused by multidrug-resistant (MDR) pathogens, like extended-spectrum beta-lactamase (ESBL), methicillin-resistant Staphylococcus aureus (MRSA), and carbapenem-resistant Enterobacteriaceae (CRE) [11]. The increasing number of deaths in cancer patients with AMR gave rise to multidrug-resistant (MDR) organisms being the major cause of these problems, according to a review by Cattaneo [12]. Recently, estimates reveal that AMR is responsible for over 700,000 deaths annually; these figures could increase massively to 10 million in 2050 if left unattended to [1]. 1.27 million global deaths in 2019 are said to be directly caused by drug-resistant infections, and 4.95 million deaths indirectly as a result of bacterial AMR [13]. The progression of these problems is alarming and underlines the urgent need for a global action to fight against AMR and subside its devastating consequences.

2.2. AMR in LMICs

These LMICs suffer the backlash of AMR as they already have a lot of factors affecting the way they combat cancer, which now gives AMR an upper hand due to resistance to infectious diseases [14]. In LMICs, these factors, such as improper healthcare management and limited access to quality antimicrobials and weak regulatory systems creates a good environment that enhances the rapid development of AMR. The lack of good reporting and documentation systems shows that the true challenge of AMR in cancer patients in these regions is probably not being identified and reported as it should [15].

Cancer patients in LMICs are largely vulnerable to AMR-related complications. Their already weak immune systems make it much easier for them to contract more deadly infections, either by the treatments they are receiving in an

improper facility or by the disease itself. Moreover, prolonged hospital stays, invasive procedures, and the use of medical devices, all of which are more common in cancer care, create additional opportunities for exposure to resistant pathogens [3]. The impact of AMR on cancer care in LMICs extends beyond individual patients. It also strains already overwhelmed healthcare systems, diverts scarce resources, and hinders progress in cancer control efforts.

Specific examples highlight the gravity of the situation. In India, a study of bloodstream infections in cancer patients found that over 70% of isolates were resistant to at least one antibiotic, and 30% were MDR [16]. In sub-Saharan Africa, high rates of AMR have been reported in various cancer-related infections, including pneumonia, urinary tract infections, and surgical site infections [17]. Furthermore, in these regions, the lack of access to second-line or third-line antibiotics means that patients often do not receive effective treatment, further increasing the burden of AMR.

2.3. Risk Factors in LMICs

Several interconnected factors contribute to the higher incidence of AMR in LMICs, creating a complex and challenging landscape for cancer care. These factors can lead to delayed diagnoses, inappropriate antimicrobial use, and inadequate infection prevention and control measures.

- **Antibiotic use**: The unregulated sale of antibiotics, self-medication, and lack of awareness about appropriate antibiotic use are common in many LMICs, further fuelling the AMR crisis [18]. Has agriculture been mentioned? No. The widespread use of antibiotics in agriculture, particularly in livestock production, can also contribute to the emergence of AMR. Resistant bacteria can spread from animals to humans through the food chain or direct contact, posing a significant public health risk.
- **Socioeconomic conditions:** Poverty, overcrowding, and poor sanitation can create environments conducive to the spread of infectious diseases, increasing the need for antimicrobials and the risk of AMR [19]. Patients in LMICs often delay seeking medical attention due to financial constraints, leading to more severe infections that are harder to treat and more likely to be caused by resistant organisms [20].
- **Limited access to quality antimicrobials:** Shortages of quality-assured antibiotics and the prevalence of substandard or falsified medicines can lead to treatment failure and the selection of resistant strains. These medications often contain insufficient amounts of the active ingredient, which can lead to incomplete eradication of bacterial infections and promote the development of resistance [21].

3. Impact of AMR on cancer treatment outcomes

3.1. Chemotherapy-Related Infections

Chemotherapy, a cornerstone of cancer treatment, often weakens the immune system, leaving patients susceptible to a range of infections. In this context, antibiotics play a crucial role in preventing and treating infections, allowing patients to continue their chemotherapy regimens and improving their chances of recovery; however, the management of these infections becomes increasingly complex and challenging, particularly in LMICs where access to effective antibiotics may be limited.

A study by Gudiol [21] found that infections caused by MDR Gram-negative bacteria in neutropenic cancer patients are associated with a significantly higher risk of treatment failure and death.

3.2. Surgical Outcomes

Surgical interventions are frequently required in cancer care, ranging from biopsies for diagnosis to complex tumor resections. Surgical site infections (SSIs) are among the most common postoperative complications, and AMR significantly impacts their management.

The risk of postoperative infections is a major concern; it often requires the use of broad-spectrum or last-resort antibiotics, which may not be readily available or affordable in LMICs.

3.3. Mortality and Morbidity

The impact of AMR on cancer treatment outcomes is evident in the increased mortality and morbidity rates observed among cancer patients, particularly in LMICs. The unavailability of effective antibiotics can lead to treatment failures, septic shock, and multi-organ dysfunction, ultimately resulting in death. Moreover, AMR can also contribute to increased morbidity, as resistant infections often require prolonged and more aggressive treatment, leading to increased

complications and a diminished quality of life for cancer patients. According to a study by Tacconelli [5], AMR is directly responsible for approximately 700,000 deaths annually, with a large proportion of these occurring in cancer patients.

4. Challenges in Managing AMR in Cancer Care in LMICs

The escalating crisis of AMR poses a formidable challenge to cancer care globally, but its impact is particularly devastating in LMICs. These regions grapple with a complex interplay of factors that worsen the difficulties in managing AMR infections in cancer patients.

4.1. Healthcare Infrastructure

The healthcare infrastructure in many LMICs is often characterized by limited resources, inadequate staffing, and a lack of specialized facilities, creating a breeding ground for the spread of AMR, particularly those with specialized training in infectious diseases and oncology. The healthcare facilities lack the necessary diagnostic tools, laboratory capacity, and trained personnel to detect and manage AMR [23]. For instance, a study in sub-Saharan Africa found that only 37% of healthcare facilities had the capability to perform basic microbiological tests, which are essential for identifying resistant pathogens [24].

4.2. Diagnostic and Treatment Challenges

Diagnosing and treating AMR infections in cancer patients presents significant challenges in resource-limited settings. The lack of access to advanced diagnostic tools, such as culture and sensitivity testing and molecular diagnostics can hinder the timely identification of resistant pathogens and the selection of appropriate antimicrobial therapy. Moreover, the high cost and limited availability of newer and more effective antibiotics in LMICs due to supply chain issues and regulatory barriers can restrict treatment options for cancer patients with resistant infections. Many healthcare facilities in these regions have a limited formulary, and the antibiotics that are available may be of poor quality or counterfeit [21].

4.3. Economic and Social Barriers

Economic constraints, lack of education, self-medication, and limited awareness about AMR pose additional barriers to its effective management in cancer care in LMICs. The high cost of cancer treatment, coupled with the added expenses associated with managing AMR infections, can be financially devastating for patients and their families [25]. Traditional beliefs and practices, stigma associated with certain diseases, and limited health literacy can influence healthcare-seeking behaviour and adherence to treatment.

5. Strategies to Combat AMR in Cancer Patients in LMICs.

The escalating threat of AMR in cancer care, particularly within LMICs, necessitates a multifaceted and proactive approach to safeguard the efficacy of antimicrobial treatments and improve patient outcomes. This involves a strategic blend of strengthening healthcare systems, implementing robust antimicrobial stewardship programs, exploring innovative approaches, and fostering policy changes and education initiatives.

5.1. Strengthening Healthcare Systems

The foundation for combating AMR in cancer care lies in bolstering healthcare infrastructure and systems in LMICs. This entails a multi-pronged approach that addresses various aspects of healthcare delivery. Upgrading healthcare facilities, ensuring adequate staffing, and providing essential medical equipment and supplies are crucial steps in improving infection prevention and control measures. This includes establishing isolation facilities, investing in sterilization equipment, investing in diagnostic laboratories, training healthcare professionals, and ensuring the availability of essential medicines [23].

Strengthening laboratory infrastructure and expanding access to diagnostic tools, such as culture and sensitivity testing and molecular diagnostics, can enable the timely identification of resistant pathogens and guide appropriate antimicrobial therapy [9].

5.2. Antimicrobial Stewardship Programs

Antimicrobial stewardship programs (ASPs) play a pivotal role in optimizing antimicrobial use and reducing AMR rates among cancer patients. ASPs have been shown to be effective in reducing inappropriate antimicrobial use, improving

patient outcomes, and minimizing the emergence of resistance [26]. Key components of successful ASPs in LMICs include:

- **Context-Specific Guidelines:** Developing and adapting guidelines to the local context, considering the prevalence of resistant pathogens and available diagnostic and treatment resources [27].
- **Multidisciplinary Collaboration:** Engaging a team of healthcare professionals, including physicians, pharmacists, microbiologists, and infection control specialists, to ensure a comprehensive approach to antimicrobial stewardship.
- **Education and Training:** Providing ongoing education and training to healthcare professionals about AMR, appropriate antimicrobial use, and the importance of stewardship [28].
- **Monitoring and Feedback:** Implementing systems to monitor antimicrobial use and provide feedback to prescribers, enabling them to identify areas for improvement and optimize their prescribing practices.
- **Patient Education:** Engaging patients and their families in the stewardship process, providing them with information about AMR and the importance of responsible antimicrobial use.

5.3. Innovative approaches

In addition to strengthening healthcare systems and implementing ASPs, exploring innovative approaches is crucial for combating AMR in cancer patients in LMICs. These approaches can complement existing strategies and offer new avenues for prevention, diagnosis, and treatment. Rapid diagnostic tests (RDTs) have the potential to revolutionize the management of infections in LMICs. These tests can accurately identify the causative pathogen and its susceptibility to antibiotics, enabling timely and targeted treatment decisions [29].

Alternative therapies, like phage therapy and probiotics, are also being investigated as potential tools for combating AMR. Phage therapy involves the use of bacteriophages (viruses that infect bacteria) to target resistant bacteria [30]. They have shown promise in treating infections caused by MDR pathogens. Vaccine development is another crucial area of research. Vaccines can prevent infections altogether, thereby reducing the need for antibiotics and limiting the selective pressure that drives the development of resistance [31].

5.4. Policy and Education

Policy changes, awareness campaigns, and educational interventions are essential for addressing the root causes of AMR and promoting responsible antimicrobial use in LMICs. Education and awareness campaigns targeted at healthcare professionals, patients, and the public are vital for promoting responsible antibiotic use and preventing the spread of the resistance. These campaigns should focus on key messages, such as the importance of completing the full course of antibiotics, avoiding self-medication, and seeking medical advice before using antibiotics [32]. Educational interventions should be culturally sensitive and tailored to the specific needs and literacy levels of the target audience.

6. Case Studies and Success Stories

6.1. Successful Interventions in LMICs

While the challenges posed by AMR in cancer care within LMICs are substantial, there are glimmers of hope in the form of successful interventions and programs that have demonstrated the potential to mitigate this threat. These case studies and success stories offer valuable insights and lessons that can be adapted and applied to other LMICs, paving the way for a more hopeful future in the fight against AMR.

- **South Africa**: South Africa has made significant strides in addressing AMR in healthcare settings, particularly through its focus on infection prevention and control (IPC) and surveillance. The National Institute for Communicable Diseases (NICD) plays a pivotal role in monitoring the emergence and spread of AMR, providing valuable data to inform policy and practice. One successful intervention is the implementation of the National IPC Strategic Framework, which outlines a comprehensive approach to preventing and controlling healthcare-associated infections (HAIs). This framework emphasises the importance of hand hygiene, environmental cleaning, and the appropriate use of personal protective equipment. It also promotes the use of surveillance data to identify and address high-risk areas for HAIs. A study conducted at a major cancer center in South Africa found that the implementation of a comprehensive IPC program led to a significant decrease in the rate of bloodstream infections and pneumonia among cancer patients [33].
- **Kenya's Diagnostic Advancements**: In Kenya, the Aga Khan University Hospital in Nairobi implemented rapid diagnostic tools to identify resistant infections in cancer patients quickly. The introduction of molecular diagnostic techniques, such as polymerase chain reaction (PCR), allowed for the early detection of resistant

pathogens, enabling timely and appropriate treatment. This intervention reduced the mortality rate associated with AMR infections in cancer patients by 15% over two years [34].

- **Thailand National Strategic Plan and Antimicrobial Stewardship**: Thailand has emerged as a leader in combating AMR, thanks in part to its comprehensive National Strategic Plan on Antimicrobial Resistance 2017-2021 [35]. This plan outlines an approach that includes strengthening surveillance systems using the One Health approach, promoting rational antibiotic use to prevent AMR in humans and pets, and investing in research and development by strengthening the government mechanisms. A pharmacist-enhanced antimicrobial stewardship program in Thailand led to a significant reduction in inappropriate antibiotic prescribing, de-escalation of therapy, and shorter hospital stays. This study showcased the potential of pharmacists in driving antimicrobial stewardship initiatives and improving patient outcomes.
- **Brazil's Public Health Campaigns**: Brazil has launched several public health campaigns to raise awareness of AMR among cancer patients and the public. The Brazilian National Health Surveillance Agency (ANVISA)-led initiatives to educate patients about the dangers of overusing antibiotics, particularly in cancer treatment settings. These campaigns, combined with stricter regulations on antibiotic prescriptions, resulted in a significant decrease in the misuse of antibiotics among cancer patients, contributing to a slower rise in AMR cases [36].
- **Peru Community-Based Interventions and Education:** Peru has adopted a community-based approach to tackling AMR, recognizing the importance of engaging and empowering communities in the fight against this global threat. A study conducted in rural Peru found that participation in an educational program on AMR led to a significant reduction in self-medication with antibiotics and an increase in appropriate healthcare-seeking behavior [37]. The Ministry of Health has implemented a series of educational campaigns and interventions aimed at raising awareness about AMR and promoting responsible antibiotic use. These initiatives have been particularly successful in rural and underserved areas, where access to healthcare and information may be limited.
- **China:** A national antimicrobial stewardship campaign implemented in China resulted in a substantial decrease in antibiotic consumption and procurement expenditure, as well as a reduction in the incidence of methicillin-resistant *Staphylococcus aureus* (MRSA) and carbapenem-resistant *Pseudomonas aeruginosa* isolates. The major elements of the plan were: to launch new initiatives against antibacterial agents and diagnostic techniques; to conduct antibiotic sales with prescriptions in pharmacies countrywide and for veterinary use in half of the provinces; to optimize the surveillance system and establish an evaluation system for antibacterial consumption and resistance in both healthcare and animal sectors, as well as to establish AMR reference laboratories and bacterial strain banks; to implement an antimicrobial stewardship program in all hospitals; to withdraw antibiotics as animal growth promoters; to provide AMR education to medical staff, veterinarians, animal producers, students, and the public; and to set up a yearly antibiotics alert week [38].

6.2. Lessons learned

These case studies and success stories offer valuable lessons that can be applied to other LMICs battling the challenges of AMR in cancer care.

- **Context-Specific Solutions:** Interventions must be tailored to the specific context and resources of each setting, considering the prevalence of resistant pathogens, available infrastructure, and cultural factors.
- **Multidisciplinary Collaboration:** Engaging a diverse team of healthcare professionals from various fields, hospitals can develop comprehensive strategies that address AMR from multiple angles, leading to better outcomes for cancer patients. Also, foster collaboration between government agencies, healthcare providers, academia, and civil society to ensure a coordinated and effective response.
- **Education and Training:** Providing ongoing education and training to healthcare professionals and the public about AMR, appropriate antimicrobial use, and infection prevention and control is essential for fostering behavioral change and promoting responsible practices.
- **Monitoring and Evaluation:** Implementing robust surveillance systems and monitoring antimicrobial use and resistance patterns can provide valuable data to inform policy decisions and guide interventions.
- **Policy and advocacy:** Strong political commitment and supportive policies are crucial for driving change and ensuring the sustainability of AMR control efforts.
- **Innovation and Technology:** Exploring innovative approaches, such as rapid diagnostics, alternative therapies, and vaccine development, can offer new avenues for combating AMR and improving cancer care.

7. Future Directions and Research Needs

7.1. Gaps in Current Research

While significant progress has been made in understanding the impact of AMR on cancer care, several gaps in current research need to be addressed to develop more targeted and effective interventions in LMICs.

- **Epidemiology of AMR in cancer patients**: While there is considerable data on AMR in general populations, specific data on its prevalence, impact, and risk factors in cancer patients in LMICs is sparse [39]. Understanding these dynamics is essential for developing targeted interventions.
- **Impact Assessment:** Further research is needed to quantify the specific impact of AMR on cancer treatment outcomes in LMICs, including mortality, morbidity, and economic burden. The financial burden of treating resistant infections, particularly in resource-limited settings, is not well documented. Studies that quantify these costs could provide the necessary data to advocate for increased funding and resources to combat AMR in these regions [6].
- **Innovative Approaches:** Exploring and evaluating novel strategies, such as rapid diagnostics, alternative therapies, and vaccine development, can offer new avenues for combating AMR and improving cancer treatment outcomes in LMICs.
- **AMR and cancer microbiome**: The interaction between AMR and the cancer microbiome is another under-researched area. Emerging evidence suggests that the microbiome plays a significant role in both cancer progression and response to therapy. However, the impact of resistant bacterial strains on the microbiome and, consequently, on cancer treatment outcomes remains poorly understood [40].

7.2. Collaborative Efforts

Addressing the global challenge of AMR in cancer care requires concerted international collaboration in research, funding, and implementation of effective strategies. This involves fostering partnerships between high-income countries (HICs) and LMICs to facilitate the exchange of knowledge, expertise, and resources and supporting capacity-building initiatives in LMICs to strengthen their healthcare systems and research capabilities [41].

7.3. Long-Term Goals

The long-term vision for AMR management in cancer care, particularly in LMICs, focuses on sustainability, development of new therapeutics, global health equity, personalized medicine, responsible antimicrobial use, global collaboration, and the preservation of effective antimicrobial treatments for future generations. By pursuing these future directions and research needs, we can strive towards a world where AMR no longer poses a significant threat to cancer patients, particularly in LMICs.

8. Conclusion

The evidence under review indicates that AMR affects cancer patients in the sense that it complicates the management of infections related to cancer treatment, particularly patients from LMICs. These regions rely on antibiotics to practice stewardship and infection control; they are less effective in areas with limited infection prevention and with minimal stakeholder compliance in enforcing antimicrobial stewardship programs. Unfortunately, there are also socioeconomic factors that become a major barrier in cancer care, thus leading to untimely and inadequate infection treatment, mortality, and cost implications. It can also be seen that there are problems that LMICs have to endure to deal with these problems, including limited availability of modern procedures, weak health systems, financial constraints, etc.

In conclusion, based on the available evidence so far, it paramount for the development of both innovative and time-sensitive interventions for tackling AMR in the context of cancer care in LMICs. There is a need for the integration of policymakers as well as other stakeholders, such as the health care providers and the international organizations, to scale up the health systems and improve on the diagnostic tools in addition to implementing efficient ASPs. As a final addition, investing more in the research to find new antibiotics and other options that can counteract the resistance factors is paramount.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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