REVIEW ARTICLE
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Armed conflict and the proliferation of antimicrobial resistance: The situation in war-ravaged Afghanistan

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Abstract

Antimicrobial resistance (AMR) constitutes a serious impediment to the attainment of the World Health Organization's Sustainable Development Goals, which seek to ensure and promote healthy living among humans and animals. Studies have identified the vulnerability of conflict-affected populations to exposure to antimicrobial-resistant pathogens. Resource-limited countries like Afghanistan have suffered for long periods from armed conflicts, and this situation is exacerbated by the already poor or dilapidated healthcare delivery services. The country has suffered human and economic losses due to antimicrobial-resistant bacterial infections driven by the prolonged war, as well as a limited number of antimicrobials and frequent under dosage. Most reports point to the overuse of broad-spectrum antibiotics as the main reason for building up resistant strains. There is a need for more efforts toward identifying the major contributors and enlightening the public on the importance of AMR. This review aimed to provide a critical appraisal regarding the current situation of AMR in Afghanistan.

Keywords: Afghanistan, antimicrobial resistance, armed conflict, hospital-acquired infection, public health.

Introduction

Microbes (including bacteria, fungi, and viruses) acquire resistance when exposed to antimicrobial drugs over time and become "Superbugs." The term "Superbug" is used to describe resistant pathogens capable of causing severe illnesses in both humans and animals [1]. Medicines have become ineffective against them and become persisting in the body of the host or suitable environments. The emergence of these resistant pathogens has resulted in increasing the risk of spread to other susceptible hosts [2,3]. Over the years, antimicrobial resistance (AMR) has become a serious public health (PH) concern due to the emergence of new resistance mechanisms and the speed at which the resistance is spread globally [4,5]. This development of resistance is seen to constitute a serious threat to our ability to treat common diseases leading to prolonged illness and death. In addition, AMR exerts an economic burden due to the cost of prolonging hospitalization and drugs [6].

The development of resistance among infectious disease pathogens, including bacteria, viruses, fungi, and protozoa is usually genetic in nature and tends to occur naturally over a long period [7,8]. Nonetheless, the inappropriate use of antimicrobial agents is believed to accelerate the process. The unregulated use of chemotherapeutic agents is a global phenomenon; however, the misuse and overuse of antimicrobials in both humans and animals are more rampant among resource-poor countries [9-11]. Frequent instances of misuse and overuse of antimicrobials are when used for the wrong treatment (e.g., when taken by individuals with viral infections) or as growth promoters in animal breeding. Drug-resistant microbes reside in humans, animals, and suitable environments, including food and water. Their transmission is exacerbated by poor or inadequate sanitary conditions unhygienic handling of food materials.

This review was undertaken to give a general overview of the hazards of AMR and to demonstrate an up-to-date situational report on the status of AMR in war-torn Afghanistan. This is important because AMR is a complex health problem affecting all societies and potentiated by numerous interconnected factors, including poverty, low healthcare delivery services, as well as war and civil unrest [12].

PH Importance of AMR

AMR is emerging in both hospitals and the population as a major PH issue. AMR presents a great challenge to PH worldwide, with several bacterial infections already untreatable. Rising AMR combined

with numerous epidemiological factors that improve the spread of drug-resistant pathogens, and the issue is likely to worsen. Management of resistance to antimicrobials is possible but it will be difficult [13]. AMR is one of the most significant global health challenges the world is experiencing in contemporary times. The consequences of which are basically the same for humans, animals, and even the environment [11,14]. AMR among infectious pathogens is the consequence of misuse of antimicrobials either for chemotherapy, prophylaxis, or as feed additives and growth promoters in animals [15-17]. This results in increased development of resistance, especially among bacterial organisms inhabiting different environments. From a PH point of view, bacterial organisms harboring resistance genes against multiple classes of antimicrobials are of particular interest. Resistance genes, when acquired, can alter the genetic make-up of the bacterial pathogen, making it more virulent; as well as delaying healing and recovery of patients, leading to prolonged hospitalization which comes with a serious economic burden [18,19]. Among the most common bacterial pathogens with broad resistance against multiple antimicrobials are the methicillin-resistant *Staphylococcus aureus* (MRSA), colistin-resistant Enterobacteriaceae, extended-spectrum beta-lactamases (ESBL)-carrying *Escherichia coli*, and vancomycin-resistant *Enterococcus* spp. [5,4,20,21]. Unfortunately, assessing the PH implications of these resistance characteristics is an arduous task. This difficulty in understanding the PH burden of AMR among infectious pathogens can be attributable to the complex epidemiology involving the production and distribution systems of animals and food, due to their crucial role in the transmission of resistance determinants. There are indications that adverse human health consequences as a result of resistant pathogens result from irresponsible usage of antimicrobials [22]. In other words, foodborne transmission is one of the major routes by which resistant bacteria and subsequent resistant genes are acquired. Similarly, AMR is also common among domestic and wildlife, and the potential implications include their role as environmental reservoirs, the zoonotic potential of some enteric bacteria, as well as difficulties during medical treatment [23].

AMR and the Environment

Another major cause of AMR is the environment which represents a key component of AMR and according to the World Health Organization (WHO). Environmental contamination can occur either as a result of poor manufacturing practices, the improper disposal of unused medication, human and animal excretion, or the inadequate disposal of human and animal carcasses [24]. Despite the seeming crucial role the environment plays in the persistence and continued spread of AMR bacteria, the environmental dimension has received comparatively less focus than AMR studies in humans and animals [25]. The two most important determinants in environmental AMR are water and soil, which may serve as prime localities for AMR development and spread, particularly among resource-limited countries or countries ravaged by war leading to the destruction of basic amenities such as adequate water supply, hygiene, and sanitation. Investigations have provided empirical evidence indicating that antimicrobial compounds released into the environment, in combination with other naturally occurring bacterial communities, are among the major drivers of bacterial evolution and the emergence of more resistant strains. The WHO has identified both drinking and recreational water to harbor resistant organisms, and that contacts with wastewater from industries and livestock farms where antimicrobials are used, often lead to colonization with drug-resistant organisms.

Emergence and Spread of AMR

Antimicrobials are an important part of the drugs used to guarantee health, including humans and livestock. The widespread use, abuse, and overuse of antimicrobials in humans and animals have raised concerns about the production of resistant bacteria that could pose a risk to animals and humans [26]. AMR has been identified as a global health issue and deemed the greatest health threat of the 21th century by major health organizations. The improper medicinal use and the non-prescribed use of antimicrobials in animals are definitely considered to be one of the causes of resistance growth in the human field [10,27].

The increased emergence and global spread of AMR pathogens are driven by globalization, and international travel for either recreational or medical tourism [28]. Hospitals globally are battling with the unprecedented crises occasioned by the speed at which multidrug-resistant (MDR) pathogens are emerging [29]. Strains of ESBL- producing Enterobacteriaceae, MDR *Acinetobacter* spp., MRSA and *Staphylococcus pseudintermedius*, highly virulent *Clostridium difficile*, and vancomycin-resistant enterococci are being frequently reported in many hospitals and other healthcare institutions [30]. Studies have demonstrated a strong correlation between the emergence of AMR and selective pressure on pathogenic microbes as a result of the unregulated use of antimicrobial agents [31]. This phenomenon is described as a genetic mutation, where genes coding for targets, or proteins activating the antimicrobial confer resistance. When these pathogens are exposed to antimicrobial agents, the sensitive ones die, leaving the resistant ones to grow and multiply. This scenario is further potentiated when the drugs are used repeatedly and inappropriately. Therefore, the WHO is advocating for the adoption of appropriate antimicrobial stewardship principles, which will guide the choice of drugs, dosage, and duration of treatment whenever indicated. Other important factors responsible for the

emergence of resistance include microbial characteristics and social factors such as self-medication and non-compliance with recommended treatment which tend to enhance the transmission of resistant organisms, poor infection control in hospital settings, as well as poor environmental hygiene and sanitation.

AMR and Armed Conflicts

PH services in conflict or post-conflict areas typically face the threat of when and how to transition effectively from support to consolidation and growth programming [32]. Ample evidence abounds, indicating the low quality of healthcare delivery services among resource-limited countries [33]. The deficiencies in healthcare quality are mostly attributed to the lack of required knowledge, underutilization of available resources, and technological backwardness [34]. However, a great majority of the time, breakdown in health services and crippling of diagnostic laboratories are the result of conflicts and war, which are frequently associated with many low- and middle-income countries. Armed conflicts present a serious challenge with respect to disease surveillance, including AMR surveillance and control. Surveillance and monitoring of AMR in a population requires a holistic approach involving all stakeholders. Unfortunately, war and conflict undermine these activities, thereby giving room for increased spread as a result of the disruption of health systems. Situations of war affect the fight against AMR by destabilizing health personnel as well as the supply and availability of essential medical supplies, thereby making interventions impossible. The lack of medical supplies promotes the rise of falsified or adulterated drugs and an increase in the number of expired or soon to be expired drugs. Similarly, conflicts, especially long-term conflicts, result in displacement of people and increased concentration in camps and other refugee settlements, thereby increasing the spread and dissemination.

War and armed conflicts cause severe injuries and wounds that require regular care, especially because wounds are almost always contaminated during the war. Unfortunately, because of the non-existent healthcare services, people resort to self-medication with antimicrobials, including the availability of over-the-counter antimicrobials, further increasing resistance. Self-medication, however, also directly relates to the lack of access to healthcare and access to the right antimicrobials in conflict. Noteworthy is the fact that the increase in antimicrobial-resistant pathogens in war-torn countries should bother the rest of the world, especially because these microbes can easily cross borders and spread as migrants move from one country to the other in search of solace [12].

The Situation in Afghanistan

For over three decades, Afghanistan has faced health effects of war, including those attributable to population displacement, health and social care deterioration, and increased risks of disease transmission [33]. Globally, the annual deaths attributable to antimicrobial-resistant infections are projected to rise from the current 700,000 to 10 million by 2050 if immediate intervention is not made [35]. It is believed that AMR poses a profound threat to human and animal health. However, relevant surveillance data are not available from of the problem difficult. As the conflicts in Afghanistan persist, a serious danger lurks in the form of the increasing rate of AMR among bacterial pathogens. In many instances, medical doctors grappling with treating soldiers injured from the war are beginning to observe that many of their patients were developing almost incurable, MDR infections in their wounds that are not responsive to the routinely used antimicrobials. This means injured personnel undergo prolonged hospitalization, requiring the administration of higher doses of antimicrobials, and combination therapy that comes with most parts of the world, including Afghanistan, which makes understanding the burden severe side effects. On the other hand, civilians have much fewer resources and access to healthcare with no other alternatives. Afghan citizens continue to die from the ongoing war; the emergence of drug resistance will mean even more deaths. A typical situation that highlights the devastating impact of AMR is the emergence of MDR *Acinetobacter baumannii* in Afghanistan. The syndrome was nicknamed "Iraqibacter" because it was first reported among Iraqi soldiers [36]. Initially, the bug was being reported among aged patients and those with chronic infection, but later, doctors started to notice its occurrence among young, healthy soldiers with blast wounds. As a result, carbapenems and colistin, which are highly efficacious in treating MDR bacterial infections, were employed. In addition to *A. baumannii*, other bacterial pathogens with high resistance were also frequently isolated, including *Pseudomonas aeruginosa, Klebsiella pneumoniae*, as well as *S. aureus* [37,38]. Much later, the use of these drugs became so common that the government had to restrict it because patients were developing more infections. Many of the factors that played a role in the development of these health crises are the results of the prolonged war and other political conflicts in Afghanistan. These include smuggling of drugs and other chemotherapeutic agents across porous borders, poor knowledge and awareness of the public on the health implications of drug resistance (including among professionals and PH workers), as well as ravaged economic state (National Action Plan on AMR [NAP-AMR]/Afghanistan). Unregulated use of antimicrobials is very common among Afghans, including professionals prescribing drugs without proper diagnosis. Other factors identified by the NAP-AMR report are proliferation and distribution of low standard cheap drugs in the markets, as well as poor standards in the transportation of these drugs.

Having identified AMR as a serious health impediment, the Ministry of PH Afghanistan is

advocating for urgent standardization of guidelines regarding antimicrobial prescription and usage, regulating the use of antimicrobials in hospital settings, and controlling the sale of over-the-counter medications without proper prescription.

Overcoming the Challenge

To successfully mitigate the impact of the ongoing armed conflict on the development and spread of AMR in Afghanistan, considerable efforts must be made to identify the specific roles of the conflict in the emergence of AMR and device mechanisms to surmount the underlying issues. With the global fight against AMR and the willingness of the international community to tackle AMR from a global perspective and to strengthen local capacity, the work of the Afghan government and PH sector has been cut out. It has become necessary for the Afghan government to adopt these internationally recognized modalities aimed at controlling the AMR and then modifying it if necessary to address the peculiar situation of Afghanistan. Fortunately, the NAP-AMR 2017-2021 [39] has already set out to effectively combat AMR in Afghanistan, which at the same time will contribute to the global efforts to tackle this PH threat. In collaboration with relevant stakeholders, the program has developed strategies and policies to achieve the aim. These include creating awareness better understanding of the health and economic hazards associated with AMR, ensuring regulated prescription and use of antimicrobials in humans and animals, undertaking active surveillance of AMR in the country, and promoting investment and research and development [40]. It adds to the aforementioned, and there is also the need to highlight the complex interactions and causative pathways that come into play, leading to the emergence and spread of AMR occasioned by the ongoing armed conflicts. Other important recommendations put forward by the plan include engaging stakeholders in the health industry, enriching medical curricula, and training of health professionals, as well as improving diagnostic capacity.

Conclusion

AMR is a serious problem in armed conflict; unfortunately, there is no practical solution at sight at the moment. This emphasizes the need for countries prone to conflicts to have an established and functional health system that ensures regulated circulation and use of antimicrobials. This is very important because AMR can easily be prevented when basic healthcare needed for the treatment of wounds and infections are adequate. Moreover, as a humanitarian response, improving laboratory diagnostic capabilities, and active surveillance of AMR are paramount. Similarly, infection control measures such as water and environmental hygiene and sanitation interventions will go a long way in promoting healthcare services.

Authors' Contributions

MAA and BG: Collected the literature and conducted its critical review. MAA, QS, AAA, and BG: Participated in the drafting and revision of the manuscript. All authors read and approved the final manuscript.

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Competing Interests

The authors declare that they have no competing interests.

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