Microbes and Infectious Diseases 2024; 5(2): 581-587

Microbes and Infectious Diseases

Journal homepage: https://mid.journals.ekb.eg/

Mini- review article

The role of armed conflict in driving antimicrobial resistance: examining the overlooked links

Bashar Haruna Gulumbe [1], Junaidu Abubakar [2], Zaharadeen Muhammad Yusuf [3], Ibrahim Abdullahi Dalhatu [4] , Ibrahim Lawal [4]

1- Department of Microbiology, Faculty of Science, Federal University Birnin Kebbi, PMB 1157, Kebbi State, Nigeria
2- Department of Biochemistry, Faculty of Science, Federal University Birnin Kebbi, PMB 1157, Kebbi State, Nigeria
3- Department of Biochemistry, College of Natural and Applied Sciences, Al-Qalam University Katsina, Nigeria
4- Department of Microbiology, College of Natural and Applied Sciences, Al-Qalam University Katsina, Nigeria

ARTICLE INFO

Article history:
Received 6 April 2023
Received in revised form 25 April 2023
Accepted 1 May 2023

Keywords:
Antimicrobial resistance
Armed conflict
Antibiotics
AMR drivers
Multidrug resistance

ABSTRACT

Background: Antimicrobial resistance (AMR) poses a significant global health challenge, complicating the treatment of infections caused by bacteria, parasites, viruses, and fungi. Armed conflict is an underexplored and complex contributor to AMR, with numerous interrelated pathways influencing its emergence and dissemination. These mechanisms include the widespread use of antibiotics in conflict zones, inadequate infection control measures, the role of conflict-related injuries, and the breakdown of surveillance and monitoring systems. This study aims to investigate the relationship between armed conflict and AMR and to assess the extent and impact of this link on global health. Case studies, such as the Syrian civil war and the conflicts in Iraq over the past four decades, are utilized to illustrate the association between armed conflict and AMR. Recognizing and addressing this neglected aspect of AMR is essential for developing comprehensive strategies to combat its spread and preserve the efficacy of antimicrobial drugs. Further research is needed to fully understand the intricate relationship between armed conflict and AMR, which will ultimately contribute to the creation of more effective interventions and policy recommendations. This study serves as a critical step in raising awareness and stimulating discussion on the role of armed conflict in the ongoing battle against antimicrobial resistance.

Introduction

Antimicrobial resistance (AMR) has emerged as a critical global health issue, as it renders various infections caused by bacteria, parasites, viruses, and fungi increasingly difficult to treat [1,2]. Antimicrobial resistance arises when microorganisms evolve to resist the effects of antimicrobial drugs such as antibiotics, antivirals, and antifungals. This resistance often stems from the overuse and misuse of these drugs in healthcare and agriculture, leading to increased morbidity, mortality, and healthcare costs [3,4]. Despite growing awareness of this problem, AMR continues to expand, fueled in part by factors that have not received adequate attention. One under-investigated

DOI: 10.21608/MID.2023.204635.1503
* *Corresponding author:* Bashar Haruna Gulumbe
E-mail address: bashar.haruna@fubk.edu.ng

driver of AMR is armed conflict, which can have devastating consequences on healthcare systems, infrastructure, and affected populations [5,6].

Armed conflict often results in the destruction of healthcare facilities, disruption of essential services, and displacement of healthcare professionals and affected populations [6]. These circumstances create environments that are conducive to the spread of infections and the emergence of resistant pathogens [5-7]. Furthermore, limited resources and compromised infection control measures in conflict zones can exacerbate the problem [5]. This includes challenges in maintaining proper sanitation and hygiene practices, as well as overcrowded living conditions for displaced populations, which facilitate the transmission of antibiotic-resistant bacteria. Additionally, conflict-related injuries and the resulting high rates of trauma and infection often necessitate the use of broad-spectrum antibiotics for wound management, contributing to the development of resistance [5,8]. The breakdown of surveillance and monitoring systems in conflict settings also plays a significant role in the rise of AMR. The lack of reliable data collection and reporting mechanisms makes it difficult to track and respond to the emergence of resistant strains, posing a challenge for both local and global AMR surveillance efforts [7,8]. Despite the complex interplay between armed conflict and AMR, these interlinks are underexplored. To our knowledge, there are a few studies that look at the relationship between conflict and AMR [5,6,8]. The neglect of this important driver of AMR necessitates its deeper examination understanding, as it has the potential to significantly impact global health security. There are also concerns AMR may continue to spread in conflict-hit regions such as Ukraine [7].

Therefore, this commentary aims to analyse the connection between armed conflict and AMR, emphasizing the importance of considering conflict as a key factor in combating antibiotic resistance. By encouraging further research and discussion on the role of armed conflict in AMR development, we hope to contribute to a more holistic understanding of the factors driving resistance and enable the creation of more effective strategies. Recognizing the impact of armed conflict on AMR highlights the need for peace and stability as integral components of a comprehensive approach to address this global health challenge.

Armed conflicts and healthcare challenges

The catastrophic consequences of armed conflicts extend far beyond the immediate loss of life and displacement, as they significantly disrupt healthcare infrastructure and services. The destruction of healthcare facilities, such as hospitals and clinics, can severely limit the availability of essential medical care and treatment for those in conflict-affected areas [9]. In many cases, these facilities are targeted intentionally, further exacerbating the crisis and leaving affected populations without access to adequate healthcare services [9]. This systematic degradation of healthcare infrastructure hinders the ability to effectively respond to both acute and chronic health needs, leading to increased morbidity and mortality among conflict-affected communities.

Moreover, armed conflicts present a myriad of challenges to healthcare professionals, who often face dangerous working conditions and limited resources [6]. Disruption of healthcare services, combined with the displacement of medical personnel, can result in significant gaps in the provision of care, including the management of infectious diseases, the treatment of injuries, and the delivery of preventive services such as vaccination campaigns [6]. In addition, the ability of healthcare professionals to adhere to best practices in infection control is often compromised, leading to increased transmission of pathogens and the emergence of antibiotic resistance [6]. Consequently, the healthcare challenges posed by armed conflicts not only undermine the immediate response to health needs but also have lasting implications for global health security and the fight against antimicrobial resistance.

Key mechanisms linking armed conflicts to AMR

Armed conflicts contribute to the development and spread of AMR through various interconnected mechanisms including the widespread use of antibiotics in conflict zones, inadequate infection control measures, the role of conflict-related injuries, and the breakdown of surveillance and monitoring systems [5,8].

The widespread use of antibiotics in conflict zones is a significant driver of AMR. One contributing factor is the prevalent practice of self-medication, driven by limited access to healthcare facilities and professionals. Additionally, the over-the-counter availability of antibiotics in many conflict-affected regions exacerbates the issue, as

individuals may inappropriately use these drugs without proper guidance from healthcare providers [7]. This unregulated use of antibiotics promotes the emergence and spread of resistant pathogens, posing a grave threat to public health [4]. Inadequate infection control measures in conflict zones are another factor which contributes to the rise of AMR [8]. Limited resources for sanitation and hygiene, such as clean water and functioning sewage systems, make it difficult to implement effective infection prevention and control measures. As a result, the transmission of antibiotic-resistant bacteria can be facilitated, particularly in overcrowded living conditions where displaced populations reside. The lack of proper infection control measures in these settings not only increases the risk of infections but also accelerates the development of AMR by creating environments in which resistant pathogens can thrive.

Similarly, conflict-related injuries play a critical role in driving AMR. High rates of trauma and infection in conflict zones necessitate the use of broad-spectrum antibiotics for wound management and infection prevention. However, the widespread and often indiscriminate use of these antibiotics in such settings can contribute to the emergence and dissemination of resistant bacteria [8]. This issue is further compounded by the limited availability of diagnostic tools to accurately identify the causative pathogens and guide targeted antibiotic treatment, leading to an increased reliance on broad-spectrum antibiotics and a heightened risk of resistance development. In addition, the breakdown of surveillance and monitoring systems in conflict-affected areas hinders efforts to track and respond to the emergence of AMR. The lack of reliable data collection and reporting mechanisms makes it difficult to identify trends and hotspots of antibiotic resistance, hampering the development of targeted interventions. Furthermore, the disruption of healthcare systems in these regions can lead to a reduced capacity to detect and treat resistant infections, allowing resistant pathogens to spread more easily [6,9]. This breakdown of surveillance systems not only poses challenges for local and regional efforts to combat AMR but also has global implications, as resistant pathogens can cross borders and contribute to the worldwide spread of antibiotic resistance.

Other drivers of AMR in the context of conflict include the destruction of health infrastructure, fragmentation of the health system, exodus or death of healthcare workers, lack of training for remaining health workers, overcrowding and displacement, lack of availability of antibiotics, increased use of prosthetic materials, and insufficient resources [6]. The shortage of trained personnel and the spread of infections in overcrowded and unsanitary conditions can also contribute to the spread of AMR. The lack of resources, including funding for healthcare and access to essential medicines, can also make it difficult to control and manage AMR in conflict-affected areas. Addressing these factors is critical for reducing the risk of AMR and promoting global health security. However, a deeper understanding of these mechanisms is essential for the development of targeted strategies to mitigate the rise of AMR in conflict-affected areas.

An armed conflict and its impact on AMR: A vase study of Iraq and Syria

The Syrian civil war and the series of conflicts in Iraq over the last four decades, including the Iran-Iraq war (1980–1988), the First Gulf War in 1991, the UN economic sanctions, the US invasion and occupation (2003–2011), and the ISIS conflict (2014–2017), serve as pertinent case studies to illustrate the complex relationship between armed conflict and AMR. Both countries have experienced widespread devastation of their healthcare infrastructure, with numerous hospitals and medical facilities being destroyed or rendered non-functional. The violence has forced millions of Syrians and Iraqis to flee their homes, resulting in overcrowded refugee camps and internally displaced persons (IDPs) settlements [10,11]. These camps often lack adequate sanitation facilities, clean water, and access to healthcare services [10,11], creating a conducive environment for the spread of infectious diseases and the development of AMR.

The AMR challenges observed during and after the Syrian and Iraqi conflicts highlight the consequences of warfare on public health. In both conflict-affected regions, the widespread and unregulated use of antibiotics, driven by the scarcity of healthcare professionals and the over-the-counter availability of drugs, has contributed to the rise of resistant pathogens. For instance, during the Iran-Iraq war, resistant Gram-negative pathogens emerged among Iraqi soldiers, with declining susceptibility to antibiotics commonly used at the time [12]. Similarly, the US invasion and occupation of Iraq in 2003 led to the emergence and spread of AMR, as documented by US military medicine

research and humanitarian organizations such as Médecins Sans Frontières [13]. The breakdown of surveillance and monitoring systems in both countries has further complicated efforts to identify and respond to the emergence of AMR [5]. Additionally, the compromised infection control measures, including poor sanitation and hygiene practices in IDP camps and refugee settlements, have facilitated the transmission of resistant bacteria [5]. As bombings, unsafe living conditions, and destruction of public infrastructure became commonplace in both countries, these factors overlapped with a catastrophic worsening of AMR, potentially resulting from a broader ecology of war that has been decades in the making [14].

The multidrug resistance issue in Iraq has been linked to *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, and *Acinetobacter. baumannii*, which presents a difficulty for both military and civilian medical workers [12]. With evidence of regional and global transmission, the resistance of these four bacteria was worsened in healthcare facilities including burn and field hospitals [15]. Even though *A. baumannii* was not known to exist in Iraq in the 1980s, Iranian researchers found resistant strains among Iranian soldiers who had returned from the front lines of the war in Iraq to a hospital in Shiraz [16]. In Iranian hospitals throughout the Iran-Iraq conflict, there has been an increase in the spread of Gram-negative infections with decreased antibiotic susceptibility, and the advent of resistant *Acinetobacter* is a part of that trend [16]. In a hospital in East Mosul, a city severely affected by the ISIS conflict, 90% of patients with a microbiologically verified infection had been infected with a multidrug-resistant bacterium, according to an MSF report from 2019 [13]. The same four germs that surfaced during the American invasion were also common throughout the battle with ISIS, and additional resistance to other classes of agents was noted. For instance, a Ramadi study found that while *S. aureus* and *P. aeruginosa* were among the most prevalent isolates in wounds, *S. aureus* had become more and more resistant to vancomycin, and *P. aeruginosa* had become more and more resistant to imipenem [17].

Due to the chronic lack of healthcare professionals, the precarious state of medical facilities, and the nature of wounds among civilians and combatants, it is likely that the ISIS conflict exacerbated drug resistance [5]. The tactics employed during the conflict made it difficult to distinguish between civilians and combatants, leading to thousands of wounded people seeking care in areas with few resources.

Although reliable data on the exact nature of AMR in Syria in the context of conflict is scarce, the few published studies available tend to utilize inconsistent methodologies, and small sample sizes and are often limited to one or a few centres with unclear sample processing procedures [6,18]. However, the limited data suggests high AMR rates; for instance, one study found 66% of *A. baumannii* to be carbapenem-resistant, while another reported 61% of *Staphylococcus aureus* isolates as methicillin-resistant aureus (MRSA) [19]. Moreover, **Mahfoud et al.** [20] documented high resistance rates to common antipseudomonal antibiotics among *P. aeruginosa* isolates from hospitalized Syrian patients at three key tertiary care hospitals in Aleppo, with resistance rates of 73% for ceftazidime, 46% for piperacillin–tazobactam, 41% for meropenem, and 11% for colistin. Notably, data on tuberculosis revealed 62.5% of tested clinical *Mycobacterium tuberculosis* isolates from previously treated patients as multidrug-resistant (MDR) strains, as previously reported [18].

Similarly, there is an increasing body of evidence indicating high antimicrobial resistance (AMR) rates among Syrian refugees [18]. This encompasses both AMR colonization [21] and infections due to resistant bacteria [22,23]. Drug-resistant bacteria have been particularly isolated from displaced patients injured in armed conflict, with colonization possibly taking place during medical evacuation flights or in compromised medical infrastructure characterized by low hygiene standards and unregulated antimicrobial use [24]. In Lebanon, an extremely drug-resistant *M. tuberculosis* strain was recently identified in a Syrian refugee [23]. In separate studies, elevated AMR rates have also been observed among healthy refugee populations, including children in Germany [25], Netherlands [26] and Swiss [26]. One recent study on Syrian asylum seekers arriving in Italy revealed the presence of uncommon microorganisms, some of which were potential pathogens and carriers of AMR [27]. Additionally, a longitudinal retrospective study found a high prevalence of methicillin-resistant MRSA among asylum seekers and refugees arriving in Finland from active conflict zones, including Syrian territories [28]. These concerning findings highlight not only the role of conflict as a driving force behind

AMR but also the need for further research to better understand the complex interplay involved.

Conclusion

The pressing issue of AMR emergence and proliferation in conflict-affected areas necessitates prompt and comprehensive attention. The exacerbation of AMR in conflict settings can be attributed to a multitude of factors, including the decline in healthcare infrastructure, loss of healthcare professionals, insufficient training, overcrowding and displacement, restricted antibiotic availability, antibiotic misuse, and limited resources. Additionally, war-associated traumas, such as those resulting from heavy weaponry and explosive devices, coupled with the increased usage of prosthetic materials, further aggravate the situation. A crucial aspect of addressing AMR in conflict settings involves tackling the root causes of conflicts themselves, encompassing the underlying political, social, and economic factors. By mitigating these conflict drivers, conditions that contribute to AMR can be alleviated. Concurrently, it is vital to ensure that medical facilities in conflict-stricken areas are equipped with the necessary resources and capacity for effective care provision. The implementation of these measures will aid in curbing the spread of AMR and improving access to essential medical services in conflict-affected regions, ultimately strengthening global health security.

Acknowledgements

The authors would like to express their gratitude to the researchers whose scholarly work has been referenced in the development of this mini-review article.

Source of funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Ethical approval: Not applicable

Conflicts of interest : None.

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