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Unravelling the linkages between conflict and antimicrobial resistance

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The compounded impacts of conflicts, natural disasters and climate change increasingly fuel the development and spread of drug-resistant organisms while weakening mitigation efforts through failed governance and health system disruptions. The impacts of conflict drive pathways of exposure to toxic remnants of war and environmental contaminants in settings of forced displacement and broken infrastructure. Tackling antimicrobial resistance in these settings demands context-specific, sustainable interventions that take a transdisciplinary approach.

Setting AMR within Humanitarian Contexts

Over the last three decades, there has been a rise in the number and complexity of armed conflicts and related forced displacement, with the additional, often simultaneous, impact of disasters and climate change¹. These further degrade health and eco-systems in fragile and conflict-affected settings contribute to environmental degradation and toxic waste production, stifling the potential for antimicrobial resistance (AMR) detection, mitigation and control². These include negative impacts on water and sanitation³, diagnosis and surveillance, infection prevention and control and antimicrobial stewardship, all essential components of AMR control. Such degraded environmental conditions, rising temperatures and changing disease patterns due to climate change and natural disasters can fuel social and political tensions that can lead to conflicts. Alongside this, the humanitarian system is grappling with multiple crises amid funding shortfalls to key areas e.g. WASH⁴, vaccination⁵, enhancing healthcare service capacity, impacting on protracted crises, which, in turn, affect the ability of health systems and responses to address AMR effectively. As of 2024, 33 countries globally are affected by armed conflict and 110 million people are forcibly displaced globally (33.5 million as refugees (UNHCR/UNRWA) and 72.5 million are internally displaced people (IDPs)), numbers which are growing every year¹. Arguably, these factors are increasing in scale and complexity and require high-level political support, global commitment and institutional investment to tackle them through evidence-based decision-making and tailored policies to address AMR in these settings. They also necessitate ground-up, contextualised evidence and sustainable approaches to address local concerns meaningfully.

Addressing AMR in settings affected by armed conflict and disasters requires targeted, evidence-driven, ground-up approaches which tackle the myriad drivers of AMR within these environments. For example, the breakdown of water and sanitation systems may lead to increased risks of infections, e.g. diarrhoeal illnesses, skin conditions, which can lead to over prescribing of antibiotics or inability to appropriately clean wounds, leading to further infections. Poor access to antibiotics through poor healthcare access or interrupted supply chains may lead to AMR through inappropriate use or overuse, particularly where there are poorly enforced policies or in acute armed conflicts where such measures are not respected. Such factors are compounded where there is inadequate or lack of diagnostic infrastructure for detection and epidemiological surveillance and limited capacity to interrupt to halt the spread through improved infection control^{2,6}. Additionally, the voices of affected communities—service users and providers—must be centred in these discussions as they arguably hold both knowledge of the local contextual drivers and are integral to the solutions^{7,8}. Engaging these communities enables a deeper understanding of the issues and helps in crafting customised solutions that effectively tackle local contributing factors. For example, if access to healthcare in general, and essential antimicrobials in particular, for refugees and migrants, is interrupted, it may contribute to behaviours which may lead to overuse, misuse, hoarding of antimicrobials or omission, which could lead to harm⁹. In other settings, the response to humanitarian crisis e.g. mobile clinics with a lack of diagnostics support, can potentially contribute to antimicrobial overprescribing or ineffective antibiotic choices. Additionally, there can be widespread concerns about counterfeit, substandard or poor-quality antibiotics with inadequate governance or quality control further exacerbating the issue.

Evidence from affected populations can also inform the responsibilities of wider transdisciplinary collaborators—including health practitioners, engineers, water, sanitation and hygiene (WASH/WATSAN) specialists, anthropologists, environmentalists, sociologists, politicians, and economists, among others—to prevent and tackle AMR in the particular contexts in which they exist¹⁰. This includes those who have been forcibly displaced into tented settlements, urban or peri-urban informal settlements and slums or who are living among host communities. This approach must also recognise the interconnectedness of human-animal-environment within the One Health framework in armed conflict settings, ensuring a comprehensive strategy against AMR¹¹.

In the much anticipated zero draft¹² of the political declaration on AMR, we see the initial framings, which aim to solidify AMR's place in the global agenda in the lead-up to the United Nations High-Level Meeting (UNHLM) in September 2024. In the first iteration, while there is a commendable focus on access, there was a notable omission of the specific

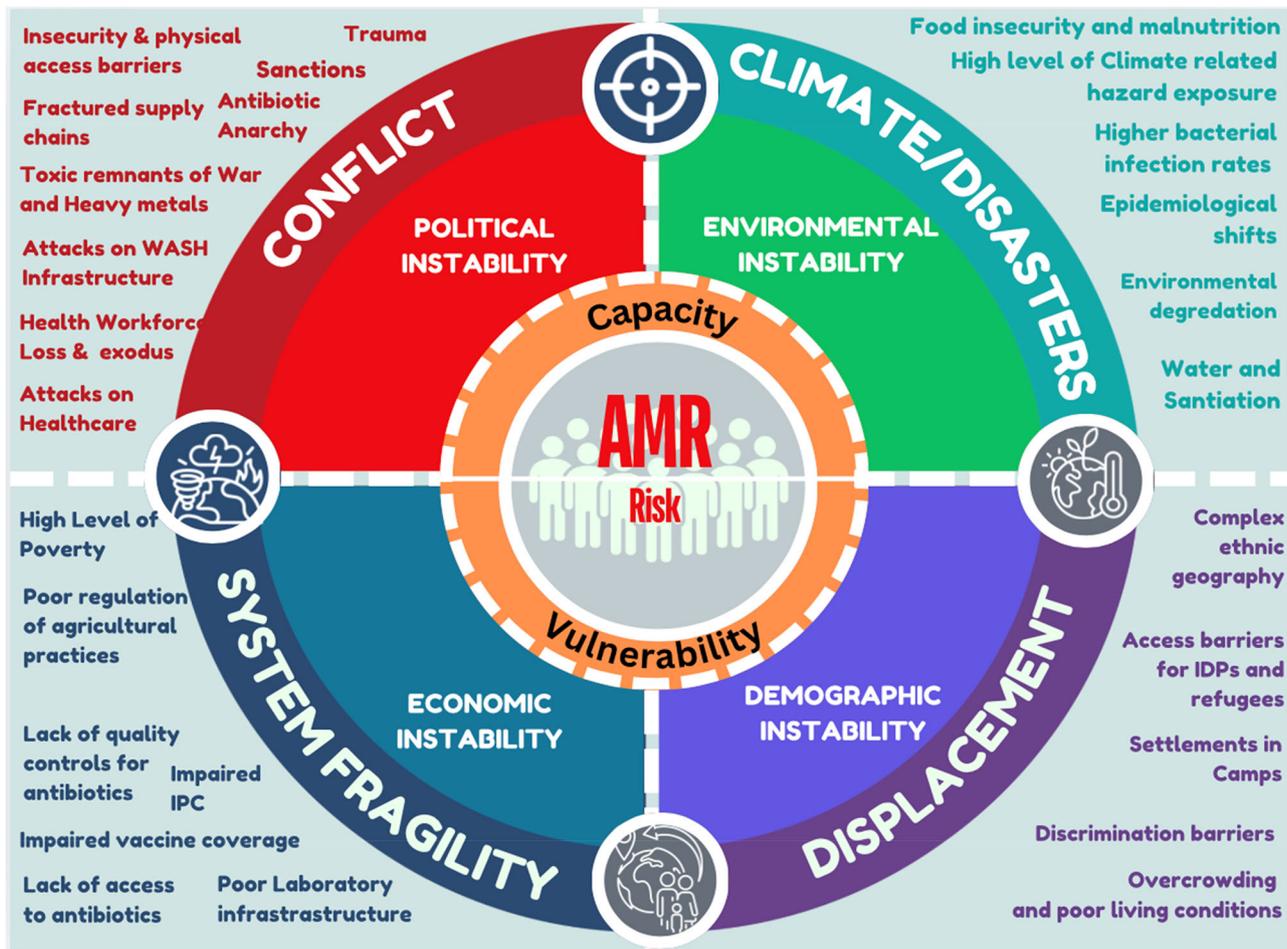


Fig. 1 | Conceptual representation of drivers of AMR within complex humanitarian crises. At the core, there is health system capacity and population vulnerability. The inner circle represents the various exposures which often co-exist in

complex humanitarian contexts and the outer layer depicts the different dimensions of complex humanitarian crises that can often co-exist.

challenges areas affected by armed conflict or complex humanitarian crises face. Additionally, in the final political declaration, global targets put forward lack sufficient data to substantiate their effectiveness, relevance, and transformative potential in humanitarian settings. Failing to address the unique ecosystems of armed conflict and humanitarian crisis through tailored, transdisciplinary collaborations that extend beyond human health will fail to tackle AMR in these settings¹³. Beyond this, it is vital to explore the direct and indirect impacts of armed conflict and their role in unmasking or catalysing the emergence of AMR through various contributing factors.

It is in this space that the breakdown of health care and essential infrastructure, including water and sanitation infrastructure, electricity and roads, coupled the loss or exodus of health workers, alongside ongoing violence and insecurity, can impede top-down approaches, such as policies and regulations relevant to AMR¹⁴. Health system governance in these areas is also disrupted, leading to poor enforcement of antimicrobial policies, weak infection control practices, substandard antimicrobials and their injudicious use in human, environmental and agricultural practices¹⁰. For example, poor stewardship of antimicrobial use in animal husbandry or dairy, poor animal welfare, improper carcass disposal and related environmental or water contamination can all exacerbate AMR or propagate its

entry into the human food chain¹¹. Additionally, surveillance is also hampered by inadequate microbiology capacity, data capture and reporting mechanisms, impacting on availability of essential data with proper regulatory and ethical oversight. As a result, the generation and consequences of AMR cannot be fully understood from one specific epistemological viewpoint, as they are inextricably linked to broader access challenges and their determinants, which is particularly evident in these settings. The interplay of such factors is summarised in Fig. 1.

Unseen dynamics of AMR amidst armed conflict

Drawing on recent examples where the reality of AMR, exacerbated by armed conflict, can result in excess morbidity and mortality and become a global health security threat beyond country borders, we can begin to explore the theories of how AMR in such settings evolve and the challenges faced in tackling them. For Ukraine, the Russian invasion in 2014 and escalation in February 2022 has led to increasing concerns around the degree and extent of AMR among both civilians and combatants¹⁵. The armed conflict has acted as a catalyst for pre-existing high rates of AMR with damage to infrastructure, loss of workforce, traumatic wounds, heavy metal contamination from toxic remnants of war¹⁶, overwhelmed health system

and widespread antibiotic misuse exacerbating underlying contributors¹⁵. Pre-escalation data from 2019 suggests that there were 8000 deaths directly attributable to AMR, and it was a contributor to a further 31,500 deaths¹⁷. A report by the US Centre for Disease Control and Prevention (CDC) from 2022 found high rates of hospital-acquired infections with 30 of 50 isolates (60%) affected by a carbapenem-resistant organism¹⁸, far higher than Europe-wide estimates. As of late June 2024, there have been 11,284 civilian deaths and 22,594 injuries, with 1,878 verified attacks on healthcare¹⁹. This has occurred alongside extensive environmental damage resulting in toxic remnants²⁰ and interruption of water and sanitation²¹ provision particularly in healthcare facilities - all of which are associated with AMR²². However, unlike other conflict-affected countries, there has been rapid investment in addressing AMR in Ukraine; in August 2023, a WHO program to support the implementation of Ukraine's Antibiotic Resistance Plan in which they planned support for laboratory capacity and AMR surveillance²³. This included the donation of surveillance equipment to ten laboratories and consumables to a further eleven (which had the equipment)²³. Furthermore, advanced surgical care has ensured that wounds in both civilian and military sectors are properly debrided and managed. However, even these measures have not stopped the growing threat of AMR within Ukraine and the spillover impact on the wider European environment. Multisectoral measures are essential as a means of combating AMR for both the sake of clinical care and also for mitigating spread²⁴.

The military intervention in Gaza presents new and devastating challenges for the population, humanitarian responses and the spread of AMR. Even prior to the current intensification of the hostilities by Israel as well as the destruction of vital infrastructures, this area, which has been under blockade since 2007, faced existing concerns about AMR²⁵. As such, the AMR epidemic in Gaza could lead to almost untreatable infections in a context where, pre-October 2023, there was already grave concern about AMR, adding further suffering to the population. Data before the current armed conflict showed that around 70% of isolates in Al-Awda Hospital's surgical reconstruction project were multidrug-resistant²⁶. This Médecins Sans Frontières (MSF) supported project found in 2022 around 65% *Staphylococcus aureus* isolates were Methicillin-Resistant (MRSA). Resistance mechanisms included 30% Extended-Spectrum-Beta-Lactamases (ESBL) in Gram-negative isolates, with almost 25% carbapenem-resistant *Enterobacteriaceae* (CRE)²⁶. These data from MSF laboratories provided a glimpse of the extent of AMR for patients with traumatic injuries, but the current destruction and cessation of function of all microbiology laboratories and the need to prioritise immediate life-saving conditions impedes all such efforts. Alongside other humanitarian supplies, consumables and therapeutics (including antimicrobials, antiseptics, laboratory and personal protective equipment), which are essential to preventing and managing such infections, are interrupted²⁷.

The current armed conflict exacerbates existing factors which influence AMR. For example, water and sewage were already severely degraded by the blockade, prior armed conflicts and the damage to aquifers, leading to high levels of nitrates and salinity²⁸. Shomar et al.²⁹ gathered random samples ($n = 345$) from two of the largest public hospitals in Gaza in 2021 (Al-Shifa and European Gaza Hospital) and found that 34% were contaminated; notably, 22% of identified *Enterobacteriaceae* were ESBLs, and 11% carried the NDM (new Delhi metallo-beta-lactamase) gene which confers carbapenem resistance²⁹. According to the latest UNOCHA data, nearly 70% of all WASH facilities have been damaged or destroyed³⁰. At the same time, local surveys in Rafah show that in 93% of all shelter locations, people were exposed to solid waste and sewage water. Hundreds of thousands of tons of garbage spread throughout Gaza, often with dozens of large informal waste dumps amidst or near makeshift displacement camps and populated areas

consisting of household, medical and industrial waste³¹. Both sewage and solid waste dumps are adding another vector for contamination³². Beyond wastewater contamination and solid waste vectors and pathways, it is estimated that more than 39 million tonnes of debris have been generated by the explosives used on Gaza (an area of 365Km²), leading to extensive environmental and infrastructure destruction^{33,34} something which is also associated with AMR. Toxic contamination with heavy metals from remnants of war and the destruction of buildings have increasingly been shown to support the co-selection of resistance^{35,36}. All of these factors contribute to multiple pathways and selective pressures through which AMR can develop and spread.

Beyond the biomedical approach

The complex drivers of AMR in settings like Ukraine and Gaza and other countries marred by armed conflict, including Syria^{37,38}, Afghanistan³⁸, Sudan³⁹, South Sudan³⁸, and Yemen^{38,39}, among others, emphasise the need for multidisciplinary approaches. Much has been written about the need to strengthen laboratories and improve access to quality antimicrobials and equitable access to health services; however, without tackling the wider determinants of AMR in armed conflict and disasters and embedding these in the affected contexts, efforts to tackle AMR will stall. This requires both high-level and local commitment to address the causes and consequences of armed conflict and displacement, without which the threat of AMR will continue both for the affected countries and elsewhere, given global increases in forced displacement. Such solutions must be contextualised, multisectoral, and appropriate to the contexts, noting that they face differing drivers, are in different stages of armed conflict, and are impacted in different ways^{2,12,38}. Bringing different disciplines and sectors together—something that WHO One Health, WASH, and AMR teams have aimed to do in their initiatives—to discuss the particular needs in armed conflict and humanitarian crises remains essential⁴⁰. This must occur alongside both top-down and ground-up approaches, with the May 2024 zero draft of the Political Declaration¹² needing to explicitly consider the unique challenges in which armed conflict and settings of complex disasters exist³⁷. In addition to those highlighted, this includes blockades, high rates of malnutrition, inadequate vaccination coverage, and the poor general health of the population, which can predispose to infections, e.g. diabetes or cancer and ongoing violence or insecurity.

Ukraine, Gaza and other armed conflict-affected contexts also demonstrate the need for a more robust understanding of the experiences of affected populations themselves, how they interact with health systems, and how they view antimicrobials and potential resistance. There may be both common and unique factors in these settings that need to be considered in any proposed policies or actions⁸. There exists in many settings the access/excess paradox when it comes to antimicrobials. Through his anthropological work exploring the consequences of AMR in armed conflict settings, Dewachi describes an 'antibiotic anarchy'³⁹, whereby patients' and clinicians' behaviour around antimicrobials are altered by both armed conflict and non-conflict factors and are influenced by restricted supplies, poor trust in the quality of antimicrobials (including the prevalence of counterfeit or expired medications) lack of diagnostics and the apparent failure to respond to infections; this can lead to first-line use of last resort antibiotics, further contributing to the disarray. Patients may stockpile antimicrobials, overuse or underuse them, use non-medically approved dosages or durations or purchase over-the-counter treatments (with little accountability or disincentives for pharmacists to challenge this behaviour)³⁹. This needs to consider the increasingly prevalent and perhaps less regulated private sector and its influence on AMR. Centring the often-neglected voices can contribute to transformative changes in how we address AMR in such settings⁸.

Conclusion

To strengthen the evidence base across many of these contributors, transdisciplinary approaches, centring conflict-affected populations and service providers and exploring the contextual factors contributing to AMR in armed conflicts or complex disasters, is essential. This can be driven forward by partnerships between humanitarian actors, funders and academics across disciplines. It is critical that we look at both the immediate and the long-range impact of armed conflict and recognise the threat of AMR that stays well after the armed conflict has formally ceased. Additionally, the impact of forced displacement as a consequence of armed conflict, along with natural disasters and climate change that are likely to exacerbate the development and proliferation of drug-resistant organisms, needs to be viewed in a holistic manner. There is also an imperative for rapid investment in the laboratory capacity of conflict-affected countries, which is essential for adequate surveillance, noting significant gaps in the EMRO region where data for clinical and policy decision-making remains sparse. One step towards addressing evidence gaps, representation and awareness of AMR in armed conflict settings and complex humanitarian disasters has been to bring together experts from a plurality of disciplines to share expertise and influence the existing discourse on this topic. Working closely with policy makers, such networks, which sit outside of formal governance structures, are essential for both theoretical framing and practical recommendations to tackle AMR in armed conflict settings.

Data availability

No datasets were generated or analysed during the current study.

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Competing interests

The authors declare no competing interests.

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