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Antibiotic resistance in times of war and conflict

PERSPECTIVES

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Antimicrobial resistance increases during times of war and conflict. The rise in armed conflicts worldwide highlights the need to improve preparedness within the Norwegian health service to manage patients evacuated from abroad who are carriers of multidrug-resistant organisms.

Although the close association between armed conflict and antimicrobial resistance is well established, it has attracted little attention. The development and transmission of resistance accelerate when health services collapse and basic infection prevention is impaired. Patients evacuated to Norway from war-torn Ukraine created unforeseen challenges in managing antimicrobial resistance in Norwegian hospitals.

In a world characterised by increasing armed conflicts, military build-up and geopolitical instability, Norway should strengthen its preparedness to treat patients who are carriers of multidrug-resistant organisms. The protracted conflicts in the Middle East, Sudan and Ukraine illustrate how resistant organisms can spread following acute humanitarian crises, including to countries far from the conflict zone.

War creates ideal conditions for antimicrobial resistance

The war in Ukraine provides an example of how health care is organised during armed conflicts. Injured patients are transported to basic emergency units and reception centres near the front line, where they receive rapid, life-saving treatment and are stabilised. There is often a severe lack of effective infection prevention and microbiological sampling equipment. Patients are subsequently transferred to a larger unit and then to a local hospital, and many undergo surgery at one or more of these facilities. The most complex cases are referred to tertiary hospitals or university clinics for repeated operations and reconstructive procedures.

By the time patients reach a hospital with microbiological expertise, they may have passed through three or four different healthcare institutions. Throughout this pathway they will often have received broad-spectrum antibiotics, which select for resistant bacteria. Moreover, most treatment facilities operate beyond capacity and with inadequate infection prevention. Consequently, there are ample opportunities for resistant bacteria to be transmitted between patients and healthcare personnel, and within the clinical environment at each institution (1).

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Healthcare settings in war zones thus become incubators for resistant organisms, which can then spread beyond the conflict area (2). Ukrainian colleagues at the public health centre in Ukraine report that patients with war-related injuries requiring surgery accumulate resistant organisms. The longer they remain in hospital, the more types of organisms they acquire (3).

High levels of resistance even before the invasion

The prevalence of antimicrobial resistance was already high in Ukraine before the armed conflict began in 2014 and the Russian invasion in 2022. The European Centre for Disease Prevention and Control (ECDC) reported that 64 % of invasive *Klebsiella pneumoniae* isolates were carbapenem-resistant in 2021 (4). The widespread presence of resistant organisms, particularly in healthcare facilities, creates a poor baseline for responding effectively in a full-scale war scenario.

Iraq is another example of a country that previously had a relatively well-functioning health service, but with high antibiotic consumption and a high prevalence of antimicrobial resistance (5). Since the 1980s, successive conflicts have progressively destroyed Iraq's healthcare infrastructure. Hospitals nationwide face shortages of qualified personnel, inadequate infection prevention, lack of microbiological testing and limited access to appropriate antibiotics (5). All of these factors combined have contributed to a high prevalence of resistant organisms (5).

Lack of data from war and conflict zones

The absence of surveillance data is a fundamental challenge for all healthcare activities in war and conflict zones. Although several reports describe widespread resistance in these areas, they are almost exclusively isolated studies that do not provide a comprehensive overview of the situation. According to the World Health Organization (WHO), the prevalence of antimicrobial resistance is highest in countries with low surveillance coverage, and there is a strong inverse relationship between the quality of resistance surveillance and the reported median levels of antimicrobial resistance (6).

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Basic information is lacking in the areas most severely affected, as life-saving frontline care must take priority in acute situations. Conducting systematic surveillance in conflict zones is extremely challenging, and even in countries that report data, information is often limited to incomplete reports from the larger hospitals. In the most conflict-torn regions, almost no sampling or antimicrobial resistance testing is performed.

Mobility increases the risk of resistance

Widespread antibiotic resistance has been reported in refugee camps in various parts of the world (7). Health services are often overwhelmed by the influx of patients with war-related injuries, which is compounded by the departure of healthcare personnel. Patients with chronic conditions, such as diabetes, chronic obstructive pulmonary disease and renal failure, often lack access to qualified care for infections and resort to improvised medicine outlets and advisers with no training. Unstable supply chains and concerns about medicine shortages lead to stockpiling and widespread misuse. Antibiotic resistance has risen rapidly among Syrian refugees in Lebanon, as confirmed by the refugees themselves (8).

> ***«Patients with chronic conditions often resort to improvised medicine outlets and advisers with no training. Antibiotic resistance has risen rapidly among Syrian refugees in Lebanon»***

Refugees are particularly vulnerable to disease when living in impoverished conditions, characterised by overcrowding, no access to clean water, poor sanitation and inadequate or insufficient food. Basic healthcare services are often lacking and vaccination programmes are discontinued.

Sudan is considered to have the world's most severe ongoing humanitarian crisis, with 14.5 million refugees and 25 million people affected by famine (9). Studies indicate a high prevalence of antibiotic resistance in several such regions.

Norway is also impacted

Healthy people arriving in Norway from conflict zones can be carriers of resistant organisms. To date, this has not posed a significant challenge for the Norwegian health service. When civil war broke out in Syria in 2011, no cases of methicillin-resistant *Staphylococcus aureus* (MRSA) were reported to the Norwegian Surveillance System for Communicable Diseases (MSIS) where Syria was the probable country of infection. A gradual increase was subsequently observed as refugees from the conflict zone began arriving in Norway.

In 2016, when the largest number of people from Syria were granted residence in Norway (12,700), 84 % were asylum seekers or mandate refugees (10). In the same year, 142 MRSA cases with Syria as the country of infection were reported to MSIS, representing only 5 % of all MRSA cases in 2016 (2504) and far fewer than the 577 cases with Norway as the probable country of infection (11). No corresponding increase was observed for other resistant organisms monitored in MSIS, and no special infection control recommendations were needed for the health service.

The high prevalence of antimicrobial resistance in refugee camps in the Middle East did not lead to resistance challenges in Norway. This is because the vast majority of refugees were healthy and had no immediate need for medical care upon arrival. These findings support evidence that carriage of resistant organisms is lost over time following relocation to areas with a low resistance prevalence and limited antibiotic use (12).

Where should preparedness be implemented in Norway?

The situation is markedly different when patients are transferred directly from healthcare facilities abroad. The European Medevac system was established just a few months after Russia's full-scale invasion of Ukraine in February 2022, and Norway received its first medically evacuated patients in June that year. This rapidly led to a record number of cases of carbapenemase-producing organisms (CPO) in MSIS. CPO encompasses *E. coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Acinetobacter baumannii* and other Gram-negative bacteria resistant to carbapenems, often with concomitant resistance to other key antibiotic classes.

In June 2022, 63 cases of CPO were reported, which is more than three times the highest monthly total previously recorded (18 cases). Cases of MRSA, vancomycin-resistant enterococci (VRE) and the resistant yeast *Candida auris* were also identified among these patients, but the increase was most pronounced for CPO. A substantial proportion of CPO isolates were resistant to all antibiotics recommended in Norwegian guidelines, leading to the use of agents with which clinicians in Norway have limited experience. In some instances, treatment was delayed because appropriate antibiotics were unavailable domestically and had to be imported under a special exemption.

Following initial experiences with Medevac patients, national recommendations were introduced for extended screening for resistant microbes and rapid isolation of patients transferred directly from hospitals abroad to Norwegian facilities. In 2023, 38 % of all CPO cases in MSIS were reported as acquired in Ukraine, which remains the most frequently identified country of infection (11). The number of CPO cases in Norway has risen substantially in recent years. While the increase cannot be attributed solely to Medevac patients, this group clearly illustrates how severe war injuries and healthcare provision in conflict zones can drive antimicrobial resistance and facilitate cross-border transmission. Norwegian real-time surveillance systems were instrumental in detecting early signals of rising resistance and in enabling implementation of infection control measures to bring the situation under control.

> ***«Norwegian real-time surveillance systems were instrumental in detecting early signals of rising resistance and in enabling implementation of infection control measures»***

A global blind spot

International forums concerned with antimicrobial resistance often lack a clear focus on conflict zones. Norway is well positioned to help shift this perspective. Conflict zones must be considered if the drivers of global resistance are to be properly understood and managed. The most important measure to reduce war-related antimicrobial resistance is to strengthen the healthcare provision in these regions. Preventing infections and limiting the spread of resistant organisms requires sufficient staffing and infection control equipment. Accurate diagnostics are also essential to ensure patients receive the correct antibiotic treatment and timely access to surgical interventions.

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