Evolving antimicrobial resistance of extensively drug-resistant Gram-negative severe infections associated with conflict wounds in Ukraine: an observational study

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Summary

Background Conflict can have devastating effects on the development and spread of antimicrobial resistance. In Ukraine, early data post-injury are limited. We aim to explore extensively drug-resistant (XDR) Gram negative phenotypes and genotypes for infections arising early following conflict-associated wounds in Ukraine.

Methods Carbapenem-resistant infections following conflict-associated wounds in Ukraine (February–May 2024) underwent extended antimicrobial susceptibility testing (AST) for 19 antimicrobial agents using 2025 European Committee for Antimicrobial Susceptibility Testing breakpoints. Carbapenemase genes were identified using a novel multiplex molecular resistance assay. Infections arising in the first seven days versus those arising after seven days since injury were compared by logistic regression. Significance was set at $p < 0.05$.

Findings 100 isolates were tested (53, 53.0% *Klebsiella pneumoniae*; 16, 16.0% *other* Enterobacterales; 18, 18.0% *Acinetobacter baumanii* and 13; 13.0% *Pseudomonas aeruginosa*). Gentamicin ($p = 0.0046$) and colistin ($p = 0.049$) resistance were higher in infections arising later. Overall, resistance rates for amikacin (74/100, 74.0%), cefiderocol (44/100, 44.0%) and ceftazidime-avibactam (26/79, 67.1%) were observed. Prevalent resistance genes included NDM + OXA-48-like (24/100, 24.0%), NDM-only (24/100, 24.0%) and KPC (9/100, 9%). Others included OXA 23-like/51-like, IMP and/or mcr1. Earlier infection isolates had a higher burden of carbapenemases/isolate ($p = 0.006$).

Interpretation Extensively drug-resistant infections were observed early post-injury in Ukraine, with some trend to further resistance in those arising later in the patient pathway. A diverse presence of carbapenemase genes amid XDR Gram negative phenotypes highlights the importance of early screening for mechanisms of resistance in this setting.

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Research in context

Evidence before this study

Conflict and catastrophe are increasingly recognised as drivers for the development and spread of antimicrobial resistance (AMR), being recently included in the ratified political statement at the 2024 United Nations High Level Meeting on AMR. Since the outbreak of wider conflict in 2022, Ukraine surveillance data has been severely limited, but reports have suggested an association with highly multidrug-resistant (MDR) Gram negative wound infections. Most information however has been derived from patients receiving care elsewhere in Europe, after contact with multiple healthcare facilities. It remains unclear at which point in the treatment pathway patients are most at risk. We searched PubMED for peer reviewed papers describing Gram negative infections associated with conflict wounds and arising within Ukraine from 01 April 2022 to 31 December 2024 using the terms Ukrain* AND resis* AND infection*. No data was identified for 2024. Two studies were identified that described isolates derived from hospitals in Ukraine from 2022 to 2023 with both reporting high levels of carbapenem resistance. No studies were identified that specifically reported early sampling data from smaller hospitals near the point-of-injury.

Added value of this study

Through a joint Ukraine–UK collaboration, we present phenotypic and molecular resistance characterisation for XDR Gram-negative conflict-wound associated infections identified within Ukraine, early in the treatment pathway. Comparison of isolates derived from initial healthcare treatment facilities during the first seven days post-injury, compared with infections arising later in the treatment pathway, (and after transfer to additional treatment facilities) showed a trend to increasing resistance for infections arising later and significantly so for gentamicin and colistin. A greater burden of carbapenemases among isolates was however seen early post-injury. High levels of agreement between disc diffusion and broth microdilution methods for cefiderocol were observed. Employment of a novel molecular resistance assay affirms an ongoing prevalence of NDM and OXA-type β-lactamase genes but also identifies an increasing scope of alternative genes, including unusual findings of NDM and KPC co-producing *Pseudomonas aeruginosa* and *Acinetobacter baumanii*.

Implications of all the available evidence

Observation of XDR infections arising early post-conflict injury is highly concerning and strongly supports the need for more consistent and representative surveillance to guide treatment options, improve clinical outcomes and reduce the spread of AMR. High levels of concordance between disc diffusion and broth microdilution for cefiderocol is encouraging, with the former offering a more practical option for resource limited settings. Recognition of a broader scope of resistance genotypes than previously reported suggests evolving patterns of resistance in Ukraine. In particular, a considerable portion of phenotypically resistant isolates without an identified carbapenemase genotype, suggests the need for whole genome sequencing to support future surveillance activities.

Introduction

Antimicrobial resistance (AMR) surveillance has featured as a key global health priority for over a decade.[1] The potential for conflict and catastrophe to accelerate the development of AMR has since become increasingly apparent,[2] recently featuring as an independent consideration in the political statement following the 2024 United Nations General Assembly High-Level Meeting on AMR.[3]

Much of the recent literature in this area has focused on recognition of highly multidrug-resistant (MDR; non-susceptible to at least one agent in three or more antimicrobial categories) or extensively drug-resistant (XDR; non-susceptibility to at least one agent in all but two or fewer antimicrobial categories) Gram-negative organisms (MDRO/XDRO) complicating the healthcare management of patients from Ukraine.[4–8] Prior to the outbreak of wider conflict in 2022, Ukraine had started submitting AMR surveillance data as part of the Central Asian and European Surveillance of Antimicrobial Resistance network, which showed rising resistance patterns among key Gram-negative organisms against beta-lactams.[9] *Klebsiella pneumoniae* and *P. aeruginosa* blood-stream infections for example had reported rates of 64.4 and 78.0% resistance in 2021.[9] Since then, detection and characterisation of these MDR/XDR organisms has often relied on the screening and surveillance programmes in neighbouring European countries, primarily being derived from injured patients who have required transfer between several medical facilities or after long-hospital stays.[4–6,8,10,11] By 2022, data from within Ukraine observed *K. pneumoniae* infections to have >80% resistance across several β-lactam/β-lactamase inhibitor combination agents, as well as cefiderocol.[7] A lack of surveillance data from early in the patient care pathway restricts any understanding of risk factors for acquisition of MDR infections or effective treatments, hampering the development of targeted mitigation and antimicrobial stewardship efforts in a resource challenged setting.

Among the available evidence since 2022, a pattern of increasing resistance against reserve antimicrobial agents has emerged,[5,7] particularly with New Delhi metallo-β-lactamase (NDM) producing organisms.[5,10–12] However, there remain considerable knowledge gaps in the breadth of phenotypic and genotypic resistance patterns of conflict-associated wound infections in Ukraine, particularly during early surgical management following injury. These data are vital in informing early antimicrobial decision making and targeting infection prevention and control (IPC) measures. We therefore aim to update our understanding of the phenotype and genotype of XDR Gram negative infections following conflict-associated wounds in Ukraine during 2024. Additionally, we will compare infection phenotypes from initial infections observed shortly after injury and those later in the course of the patient care pathway, after transfer between medical facilities.

Methods

Samples were identified from patients with clinical signs of infection following conflict-associated wounds sustained in Ukraine by the treating clinicians and subsequently sent for further characterisation at the National Academy of Sciences of Ukraine (NASU) in Kyiv between February and May 2024. Gram-negative organisms that were considered extensively resistant (phenotypically resistant in all but two or less antimicrobial classes) by disc diffusion (DD) were sent for additional testing at Chelsea and Westminster Hospital and North West London Pathology (NWLP), London, UK to provide further insights to the character of prevalent resistance patterns.

Sample type

Sample types included for further testing included those collected from positive blood cultures (23), deep wound and bone (48), or other (29) endotracheal samples. Isolates were derived from infections observed at one of three different healthcare facilities including a regional hospital in Kharkiv or City Hospital in Kryvyi Rih with general surgical services or a major hospital in Kyiv with rehabilitation services and specialist surgical capabilities including management of polytrauma and burns injuries. Prior work in 2022 would broadly classify the first two as a level 2 echelon of care and the last as level 4 as per NATO standards.[13] Sites in Kharkiv and Kryvyi Rih represented the initial healthcare management facility for injured patients and these initial infections were confirmed within seven days of injury. By comparison isolates from Kyiv represent infections arising after seven days since injury and following transfer from ≥one prior facility. All isolates were independent (e.g. isolates from different locations were not derived from the same patient).

Disc diffusion phenotypic testing of XDROs

Identification of species were confirmed on receipt at NWLP by matrix-assisted laser desorption/ionization-time-of-flight (MALDI-TOF). Phenotypic testing was initially conducted by DD method and interpreted for each organism as per European Committee on Antimicrobial Susceptibility Testing (EUCAST) breakpoint guidelines.[13] Each organism underwent initial screening for DD susceptibility with ampicillin (10 μg), piperacillin-tazobactam (36 μg), cefotaxime (30 μg), ciprofloxacin (5 μg), gentamicin (10 μg), temocillin (30 μg), ceftriaxone (30 μg), ertapenem (10 μg), cotrimoxazole (25 μg), amikacin (30 μg), ceftazidime (10 μg), co-amoxiclav (30 μg), ceftazidime-avibactam (14 μg), fosfomycin (200 μg), tigecycline (15 μg), aztreonam (30 μg), cefiderocol (30 μg) and meropenem (10 μg).

Microbroth dilution susceptibility testing

All samples subsequently underwent screening for *in vitro* colistin susceptibility by broth microdilution (BMD) as per EUCAST guidelines.[14–16] Additionally, all cefiderocol results by DD methodology were repeated by BMD as per EUCAST guidelines and interpreted using 2025 EUCAST breakpoints,[14,16] except for *A. baumanii* isolates where CLSI M100 ED35:2025 guidelines were employed instead.

Molecular resistance testing of XDROs

A novel CRE reference polymerase chain reaction (PCR) molecular resistance assay for use on the AusDiagnostics Highplex or Ultraplex 3 system was performed to identify the scope and prevalence of commonly recognised beta-lactamase resistance genes (AusDiagnostics, Sydney, Australia). Pure bacterial colonies were harvested directly from purity culture plates as per manufacturer instructions. The assay has >90 gene targets which included verona integron mediated metallo-β-lactamase (VIM 1–7, 11, 19, 36–40), pan-imipenemase metallo- β-lactamase (IMP 1, 4–7, 10, 13, 26, 29, 34, 40, 42), separate IMP 14 and IMP 8, *Serratia marcescens* enzyme carbapenamase, mobilised colistin resistance gene (mcr1), β-lactamase DIM-1, *K. pneumoniae* carbapenamase (all types), KPC mutation associated with ceftazidime-avibactam resistance (D179Y), NDM 1–8, Seoul imipenemase metallo-β-lactamase 1, German imipenemase metallo- β-lactamase 1, imipenemase resistance gene (IMI 1, 2, 4, 7, 8), Sao Paulo metallo-β-lactamase 1, French imipenemase (FRI 1–4), Guiana extended spectrum β-lactamase, PER β-lactamase, OXA-23 like β-lactamases (OXA 23, 49, 73, 134, 146, 165–171, 225), OXA 24/40-like β-lactamases, β-lactamase OXA 48 group (OXA 48, 181, 204, 232, 244–245, 484), OXA 51 like β-lactamases from Acinetobacter spp. (OXA-51, 66, 69, 87, 89, 106–109, 242, 387, 404), carbapenem-hydrolysing oxacillinase (blaOXA-58) gene (OXA 58, 97), β-lactamase VEB-1.

Statistical analysis

Descriptive statistics were used to assess organism, AST phenotype and genotype prevalence. Susceptibility was determined using the 2025 EUCAST breakpoint guidelines,[14] except for *A. baumanii* with cefiderocol where EUCAST breakpoints are not available and CLSI M100 ED35:2025 guidelines were employed instead. Colistin susceptibilities were reported, acknowledging these isolates may have resistance mechanisms that are not detectable phenotypically and results must be interpreted with caution, noting clinical evidence for use as monotherapy is lacking. Agreement for susceptible and resistant results by DD and BMD were reported for cefiderocol. Clinical data, including outcomes and prior antimicrobial exposure were not reliably available and so not included in analyses. Variations in antimicrobial susceptibility rates and molecular results for samples derived from infections observed in the early post-injury phase (within 7 days of injury while still within initial admission healthcare facilities) versus those observed later (after 7 days since injury and having transferred from at least one other healthcare facility) were compared for each individual antimicrobial agent using binary logistic regression with odds ratios and 95% confidence intervals reported. Significance was set at $p < 0.05$.

Ethical approval

This work was conducted as part of routine surveillance work using residual samples through a collaboration between the Institute of Molecular Biology and Genetics of the National Academy of Sciences of Ukraine and the Clinical Infection Department of Chelsea and Westminster Hospital, United Kingdom. No patient demographic data or clinical information was included in the analysis.

Role of the funding source

Antimicrobial susceptibility testing and genotyping was funded by the Healthcare Infection Society and Chelsea Infectious Diseases Research (CINDER) Group/CW + Charity. Funders had no role in the study design, data collection, data analysis, interpretation, or writing of the report.

Results

100 isolates were identified and sent for further analysis. Of these, 69/100 (69.0%) were Enterobacterales of which 53/69 were identified as *K. pneumoniae*, 11/69 as *Escherichia coli*, 2/69 as *Enterobacter hormachei*, 2/69 as *Proteus mirabilis* and 1/69 as *Providencia stuartii*. The remaining samples were lactose non-fermenters including 18/100 (18.0%) *A. baumanii* and 13/100 (13.0%) *P. aeruginosa*. Agreement between MALDI-TOF methods was 94.0%. Where disagreements were observed this was typically between species of *Klebsiella* or *Enterobacter* with *Klebsiella aerogenes* identified by API being alternatively identified by MALDI-TOF as *K. pneumoniae* or *E. hormachei* and *Klebsiella oxytoca* being identified as *K. pneumoniae*. In addition, 6/100 isolates (6%), showed additional growth of Gram-positive species including coagulase negative Staphylococci (1/6 *S. haemolyticus*, 1/6 *S. epidermidis)* and *Enterococcus faecalis* (4/6), of unclear significance. 37/100 (100%) were derived from primary infections following initial admission (<seven days since injury) and 63/100 (63%) from later (>seven days since injury) in the patient care pathway after transfer between medical facilities. There were no missing data for antimicrobial susceptibilities.

AST phenotypes

All 100 samples underwent DD AST for 18 antimicrobial agents. Three samples (two *P.* mirabilis and one *P. aeruginosa* isolates) did not meet the XDR criteria. Of the remaining 97 isolates, meropenem susceptibility was 9/67 (13.4%) for Enterobacterales, 0/18 (0%) for *A. baumanii* and 1/12 (8.3%) for *P. aeruginosa* samples by DD (Fig. 1; a complete breakdown of species-meropenem susceptibility-genotype is provided in Supplementary Figure S1). Co-amoxiclav, ceftriaxone and ceftazidime susceptibility were each 1.5% (1/67) across all Enterobacterales. Ciprofloxacin susceptibility was 0% for all organisms tested. Gentamicin and amikacin susceptibility ranged from 1/12 (8.3%) for XDR *P. aeruginosa* for both agents, to 3/18 (16.7%) and 2/18 (11.1%) respectively for *A. baumanii* and 9/67 (13.4%) and 20/67 (29.9%) respectively for XDR Enterobacterales. For tigecycline, 10/11 (90.9%) *E. coli* isolates tested as susceptible. Overall, 56/67 (83.6%) XDR Enterobacterales were susceptible using the same EUCAST breakpoints, however there is limited data around non-*E. coli* species and only where higher doses are employed.[14] Susceptibility to ceftazidime-avibactam was 25/67 (37.3%) for XDR Enterobacterales and 1/12 (8.3%) among XDR *P. aeruginosa* while colistin susceptibility ranged from 66.6% (8/12) for XDR *P. aeruginosa* to 77.8% (14/18) for *A. baumanii* and 64.2% (43/67) among XDR Enterobacterales. The mean disc zone size for fosfomycin was 19.5 mm (IQR 14–23).

Comparison of cefiderocol testing by disc diffusion and microbroth dilution methods

For cefiderocol, susceptibility by BMD was 50.7% (34/67) for XDR Enterobacterales, 61.1% (11/18) for *A. baumanii* and 91.7% (11/12) for XDR *P. aeruginosa*. In total, 10/100 (10.0%, 9 Enterobacterales, 1 *P. aeruginosa*) were observed to be within the ATU for their respective organisms when tested by DD. Of these, 10/10 were susceptible by BMD methods. Agreement between disc diffusion and microbroth dilution was 99.0%, with a mismatch for one *P. aeruginosa* sample reported as susceptible by DD (24 mm) but resistant by BMD methods (MIC >16).

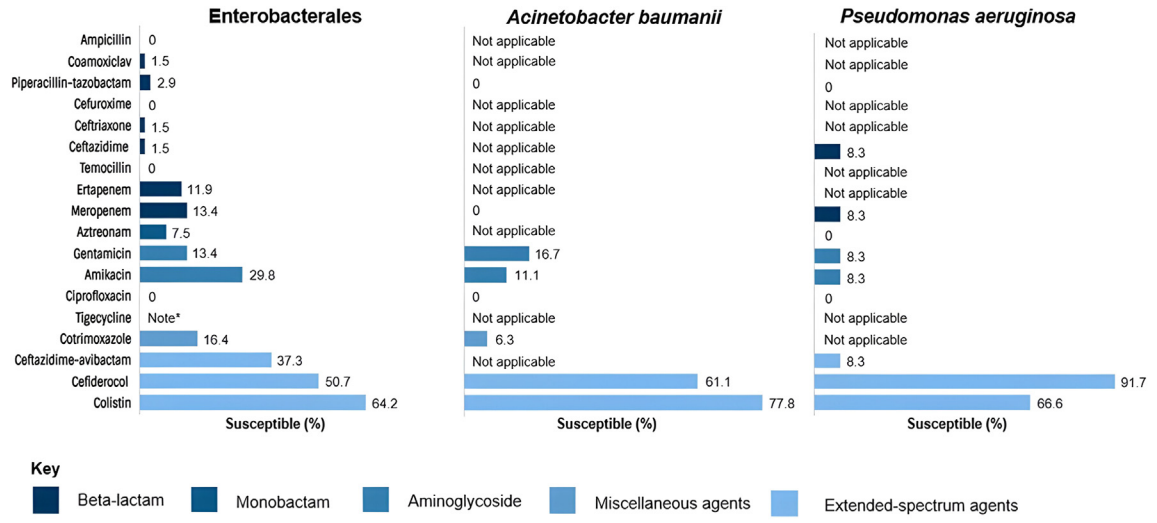

Fig. 1: **Antimicrobial susceptibility testing of severe Gram-negative infections associated with conflict-related injuries within Ukraine, 2024**. Antimicrobial tested and reported as per European Committee on Antimicrobial Susceptibility Testing (EUCAST) 2025 breakpoint guidelines, except for *A. baumanii* with cefiderocol where EUCAST guidelines are not available and so CLSI M100 ED35:2025 guidance was used. For colistin, EUCAST breakpoints are provided as a best fit, acknowledging these isolates may have resistance mechanisms that are not detectable phenotypically and noting that clinical evidence for use as monotherapy is lacking. Colistin susceptibility results presented here should be interpreted with caution. For tigecycline, 10/11 (90.9%) *E. coli* isolates tested as susceptible. Testing was conducted using disc diffusion methodology except for cefiderocol which underwent both disc diffusion and broth microdilution testing and colistin which was undertaken by broth microdilution as per EUCAST guidelines.

Molecular resistance testing results

All isolates were included in the molecular resistance testing analysis. Of the 10/100 samples that tested susceptible to meropenem, 6/10 were associated with detection of a resistance gene (3/6 NDM, 1/6 IMP, 1/6 mcr1 and 1/6 OXA-48-like). Of those isolates that were meropenem susceptible and had no gene detected, 4/4 were phenotypically resistant to third-generation cephalosporins, aztreonam and piperacillin-tazobactam. The most prevalent detected resistance genes included 24/100 (24%) of isolates with both NDM and OXA-48-like carbapenemases and 24/100 (24%) with NDM only (Fig. 2). Identified molecular resistance mechanism distribution among Gram-negative species were as follows, Enterobacterales (*n*): NDM + OXA-48-like (19), NDM (16), KPC (10), OXA-48-like (3), KPC + NDM (2), IMP (2), KPC + OXA-48-like (1), NDM + OXA 51-like (1), mcr1 (1), IMP + NDM (1), IMP + KPC (1), not detected (12); *A. baumanii*: NDM (5), OXA 23-like + OXA 51-like (3), IMP + OXA 51-like (2), OXA-48-like (2), NDM + OXA 23-like + OXA 51-like (1), IMP + KPC + OXA 51-like (1), OXA 23-like + OXA 51-like + OXA 48-like (1), not detected (3). *P.* aeruginosa; NDM (4), NDM + KPC (1), NDM + IMP (1), NDM + OXA-48-like (1), IMP (1 meeting XDR criteria, 1 not meeting XDR criteria), not detected (4) (Fig. 2).

Comparison of AST and molecular results across locations

Organisms resistant to each tested agent were identified at all three locations. There were no significant differences for most AST results (Supplementary Data, Table 1). Where significant results were detected, these trended for greater resistance in samples from infections observed later in the patient care pathway, including with WHO AWaRe classification of access for gentamicin (odds ratio 4.56, 95% CI 1.54–13.52, $p = 0.0046$) and reserve for colistin (odds ratio 2.64, 95% CI 1.00–6.93, $p = 0.049$) (Supplementary Data, Table 1).[17] When presence of each gene type was compared for results from each of the locations, those from earlier in the patient care pathway were more likely to be associated with OXA-type carbapenemases ($p = 0.0098$). Isolates from early post-injury were more likely to be associated with multiple carbapenemases than those in later in the patient care pathway (odds ratio 3.10, 95% CI 1.31–7.32, $p < 0.01$) (Supplementary Data, Table 1). No other combinations demonstrated significant differences in their prevalence.

Discussion

Our data support prior observations of high levels of beta-lactam resistance among infection associated with conflict wound infections from Ukraine, while also recognising an increasing pattern of resistance against aminoglycosides and colistin later in the patient care pathway. Additionally, use of a novel molecular resistance assay has demonstrated prevalence of a broad range of resistance genes in addition to the more commonly reported NDM-1 and/or OXA-48-type

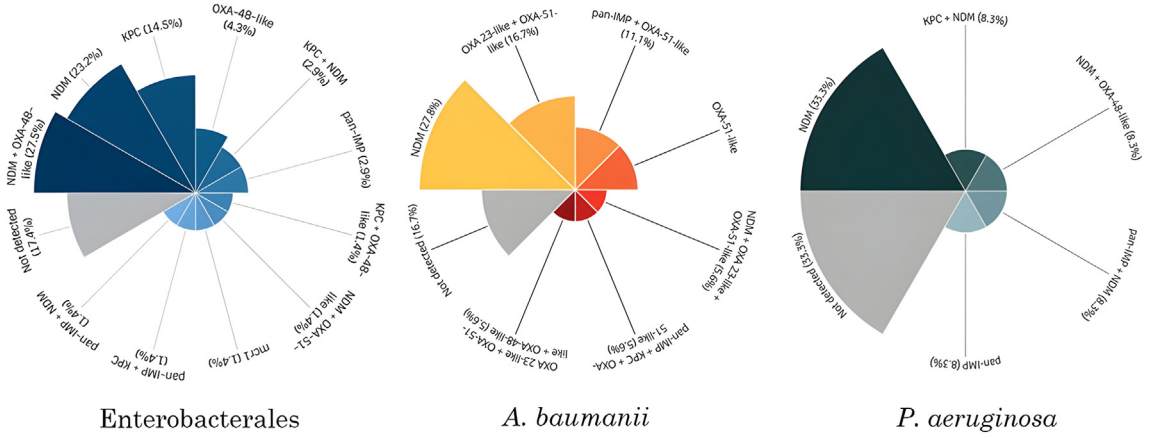

Fig. 2: **Identification of prevalent genes associated with among Gram-negative isolates from conflict-associated wound infections in Ukraine, 2024**. Each sector's radius is proportional to the prevalence of each identified genotype among tested XDR Gram-negative organisms associated with infected wounds from Ukraine. Percentages are provided in brackets for each detected gene for that organism/group. Genotype testing conducted by the 24 well CRE reference polymerase chain reaction assay (AusDiagnostics, Sydney, Australia). The pan-IMP target screens for carriage of imipenemase metallo-β-lactamases 1, 4–7, 10, 13, 26, 29, 34, 40, 42.

combinations. Of note, our data show a higher burden of carbapenemases (per patient) early following wounding from samples derived near the fighting in Kharkiv, which may reflect more limited capacity for IPC measures or early infection from contaminated wounds in contrast to those samples derived later in the patient care pathway, that may be more associated with healthcare transmission.

While previous data on XDR Gram-negative wound infections published since the onset of the wider Ukrainian conflict in 2022 have been limited, they have been consistent in reporting high levels of beta-lactam resistance.[4–8,10–12] Ceftazidime-avibactam, imipenem-relebactam and meropenem-vaborbactam were observed to have >80% resistance among 45 Enterobacterales isolates from 2022, while cefiderocol resistance was 78%.[7] Notably, colistin resistance from the same study was only 22% for Enterobacterales and 0% among 16 *P. aeruginosa* and 46 *A. baumanii* isolates,[7] considerably lower than our observations here. The reporting of aminoglycoside susceptibilities from infections within Ukraine has been less consistent. Prior to the wider conflict in 2022, aminoglycoside resistance among MDR Gram-negative clinical isolates from a multicentre study ranged from 9.2 to 25.4%,[18] while data from national blood-stream Enterobacterales infections (data considered of medium representativeness across Ukraine) reported higher rates of gentamicin resistance of 24.3–79.%.[9] Reports from the Netherlands in 2024 were more fitting with our data, observing aminoglycoside resistant of >72–94%,[19] although passage through multiple healthcare facilities and international travel had made relevance of comparison for this data for early management post-injury unclear. Our data suggests the reality of aminoglycoside resistance early following injury, when the surgical burden, use of prosthetic lines and potential for sepsis is likely to be greatest is more likely to reflect reports for Ukrainian injured patients overseas.[19] While newer beta-lactam agents, including combination agents such as aztreonam-avibactam, may offer alternatives for longer antibiotic courses, the reduced activity of aminoglycosides is highly concerning and highlights the vital importance of access to early and aggressive surgical debridement and effective IPC measures to limit the likelihood of Gram-negative infection in the early post-injury period. Likewise, the value of strict antimicrobial stewardship (AMS) programmes cannot be overstated. Where lacking, international support for AMS programme development is available through organisations such as the British Society for Antimicrobial Chemotherapy or European Society for Clinical Microbiology and Infectious Diseases and are an important consideration for reducing selective pressures on vital treatment options.[20]

Published data have suggested an association with organisms expressing NDM-1 or OXA-48-type carbapenemases but understanding the full spectra of resistance mechanisms for war wounds infected with MDRO/XDROs in Ukraine remains incomplete. Our data likewise show a high prevalence of NDM and/or OXA-48-type genes among XDR Gram-negative infections of war wounds but also suggests a considerably greater breadth of contributing mechanisms. Despite observing a rise in colistin resistance, only one sample was positive for the plasmid-mediated *mcr1* gene. It is also interesting to note that, despite using a broad 90 plus-target assay, a considerable portion of phenotypically XDR Gram-negative organisms had no detected resistance

genes. Given their XDR phenotypes, this is likely to represent alternative mechanisms of carbapenem resistance including combinations of porin expression modification,[21] extended-spectrum β-lactamase and AmpC expression,[22] efflux pumps overexpression,[23] or potentially uncommon genes of hydrolysing enzymes not included in the molecular resistance assay. The genotype findings for *P. aeruginosa* producing NDM and/or KPC are unusual, as reported by our group separately.[24] These findings highlight the evolving nature of Gram-negative carbapenemase resistance organisms in Ukraine and the vital importance of continued surveillance activity to help guide both mitigation and treatment policies. Further understanding of the full spectrum of prevalent resistance mechanisms is needed to fully inform antimicrobial decision making and stewardship strategies and is likely to require international support for surveillance and/or reporting of conflict-associated infections from Ukraine with whole genome sequencing of carbapenem-resistant isolates.

This study is limited by the small number of isolates. However, even among these a pattern of evolving resistance phenotypes and genotypes among XDR Gram-negative wound infections was evident. The study is also limited to assessment of *in vitro* phenotypes, while the addition of clinical data would allow greater understanding of the proportional impact of these infections on clinical outcomes. While such data can be difficult to obtain in this setting, future studies would benefit from more granular data on time of infection since injury, number of healthcare facilities visited, prior antibiotic exposure and clinical outcomes. This is particularly following prior recognition of an association between multiple healthcare facility transfers and resistant infections in prior conflicts.[25] While use of a broad molecular resistance assay revealed the involvement of a range of different resistance genes, observation of XDROs with no gene detected highlights the need for whole genome sequencing to support future surveillance work in this setting. Additionally, given high aminoglycoside resistance, further evaluation of 16 S rRNA methylase genes or other aminoglycoside inactivating enzymes would be of further use. Given the evolving resistance pattern observed here, further work to establish susceptibility patterns among new combination agents would have value in planning treatment approaches.

The ongoing conflict in Ukraine has been associated with MDR/XDR Gram-negative infections as a complication of conflict-associated wounds. Our data suggest evolving patterns of resistance, particularly among aminoglycosides and colistin, compared with previous studies. While NDM and OXA-48-type carbapenemases continue to predominate, a broad range of resistance genes were identified. A considerable proportion of phenotypically resistant organisms without a detectable genotype associated with resistance further suggests additional mechanisms of resistance are prevalent.

Support to infection control and surveillance in Ukraine is paramount if the evolving nature of antimicrobial resistance is to be addressed in real-time. Understanding of the full spectra of prevalent resistance mechanisms is likely to require whole genome sequencing while global efforts need to be coordinated to ensure this region has access to appropriate antimicrobial agents given the burden of infection observed.

Contributors

SJCP, SDW, SEB, MOS, LSPM and OM designed the study. VP, KR and MO conducted initial testing in Ukraine and prepared samples for transport. SJCP and NT supported transport of samples to the UK. SJCP, AM, ZL and VS conducted additional testing in the UK. SJCP, SDW accessed the data and conducted analyses. SJCP, SEB, MOS, OM and LSPM wrote the initial draft. All authors reviewed the manuscript and contributed significantly to revisions. All authors agreed on the final version for submission.

Data sharing statement

Further information is available from the corresponding author (SJCP; scott.pallett@nhs.net) on reasonable request, as long as this meets local ethical and research governance.

Declaration of interests

LSPM has consulted for or received speaker fees from bioMerieux (2013–2025), Eumedica (2016–2025), Pfizer (2018–2025), Sumitovant (2021–2023), Shionogi (2021–2025), Qiagen (2023), Gilead (2024), BioNTech (2024), Insmed (2024), & Advanz (2024–2025) and received research grants from the National Institute for Health and Care Research (2013–2025), CW + Charity (2018–2025), North West London Pathology (2022–2024), LifeArc (2020–2022), Shionogi (2024), Infectopharm (2022–2024), the Joint Programming Initiative on AntiMicrobial Resistance (2023–2025), & the Healthcare Infection Society (2024–2025). SEB has consulted for or received speaker fees for bioMerieux, Shionogi, UK Clinical Pharmacy Association, and received funding support for attending meetings from Advanz Pharma. SEB has participated on a Scientific Advisory Board for Sumitovant Biopharma and has an unpaid role as a Young Scientist Committee member for the British Society for Antimicrobial Chemotherapy Antimicrobial Susceptibility Testing Committee. SEB declares stock options as a dividend reinvestment with Scottish and Southern Energy. SJCP has received research grants from the John Muir Trust, the Drummond Foundation not in connection with this work and from the Healthcare Infection Society in connection with this work. SJCP has a role as a British Society for Antimicrobial Chemotherapy Parliamentary Intern to the Office of Dr Danny Chambers MP. All remaining authors have no potential conflicts of interest to declare.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.lanepe.2025.101274.

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