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Multidrug-resistant organism colonisation and infection in paediatric patients from Ukraine receiving specialised care in Germany: a multicentre study

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Multidrug-resistant organism colonisation and infection in paediatric patients from Ukraine receiving specialised care in Germany: a multicentre study

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Abstract

Purpose

Children with chronic medical conditions are at increased risk of colonisation and infection with multidrug-resistant organisms (MDROs) because of repeated healthcare exposure and antimicrobial use. We aimed to characterise MDRO-positive screening findings and documented MDRO infections among paediatric patients from Ukraine receiving specialised care in Germany.

Methods

We conducted a multicentre retrospective study at ten tertiary paediatric centres in Germany between 24 February 2022 and 31 March 2023. Eligible patients were 28 days to <18 years, had resided in Ukraine for ≥3 months, had previously received medical care in Ukraine for a chronic medical condition or war-related injury, and underwent MDRO screening. Resistance phenotypes were classified using the German Multidrug-Resistant Gram-Negative bacteria (MRGN) classification.

Results

Among 198 children, 85 (43%) had at least one MDRO-positive screening result. Multidrug-resistant Gram-negative organisms predominated; 44% of colonisation events were 3MRGN and 19% were 4MRGN, indicating carbapenem resistance. Twenty-three of 85 MDRO-positive children (27%) had a clinically documented MDRO infection, and in 21/ 23 episodes (91%) the same species with a compatible resistance phenotype had been identified in a preceding screening sample. No in-hospital deaths occurred; six infected patients (26%) had newly documented residual impairment at discharge. None of the participating centres performed

complete multisite screening as recommended by the German Society for Paediatric Infectious Diseases.

Conclusions

MDRO-positive screening findings and infections were common in this selected cohort. Risk-adapted admission screening may inform IPC and empirical treatment decisions. These findings may also apply to children with previous healthcare exposure in other high-prevalence settings.

Keywords: Antimicrobial resistance; Multidrug-resistant organisms; Paediatrics; Ukraine; Colonisation; Infection prevention and control

Statements and Declarations

Funding

No funding was received for conducting this study.

Competing interests

The authors have no relevant financial or non-financial interests to disclose.

Data availability

The datasets generated and analysed during the current study are not publicly available due to data protection requirements and the retrospective multicentre nature of the study. Data may be available from the corresponding author upon reasonable request and subject to applicable ethical, institutional, and data protection requirements.

Author contributions

Conceptualization: S.C.G., T. H., C.D.S., L.M.; Methodology: S.C.G., T. H., H.v.B., U. F.-M., C.D.S., L.M.; Investigation and data collection: S.C.G., T.H., L.F., M.A., J.D., G.B.F., O.B., T.D., P.K-L., R.K., S.S., U. S-S., B.S., M.S., C.H.; Data curation: S.C.G., T.H., A.F,; Formal analysis: S.C.G., T.H.; Writing – original draft: S.C.G., T. H., C.D.S., L.M.; Writing – review and editing: all authors; Supervision: C.D.S., L.M. All authors read and approved the final manuscript.

Ethics approval

The study was approved by the Ethics Committee of the Medical Faculty of the University of Duisburg–Essen (reference 22-10943-BO). The study was conducted in accordance with the Declaration of Helsinki and applicable German and European data protection regulations.

Consent to participate

The requirement for informed consent was waived by the Ethics Committee of the Medical Faculty of the University of Duisburg–Essen because only anonymised retrospective data were analysed.

Consent for publication

Not applicable.

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Introduction

Antimicrobial resistance (AMR) threatens to erode decades of medical progress, compromising the effectiveness of routine treatments and complicating infection prevention and control (IPC) worldwide [1,2]. Among multidrug-resistant organisms (MDROs), carbapenem-resistant *Acinetobacter baumannii* and Enterobacterales are major causes of healthcare-associated infection, characterised by limited therapeutic options and high mortality [2,3]. Together with methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococcus faecium* (VRE), these pathogens are included in the 2024 WHO Bacterial Priority Pathogens List [4].

Children with chronic or complex medical conditions - such as malignancy, transplantation, cystic fibrosis, or congenital disorders, are at risk of MDRO colonisation and infection due to repeated healthcare exposure, invasive procedures, and repeated antibiotic courses [5-9]. Once colonised, they may serve as reservoirs for onward transmission, and colonisation itself is an important risk factor for subsequent MDRO infection, underscoring the need for robust IPC measures in paediatric care [10].

Across Europe, MDRO prevalence follows a distinct south-east to north-west gradient, with the highest rates in southern and eastern regions. Even before 2022, Ukraine reported a high burdens of WHO-priority Gram-negative pathogens [11, 12], and the ongoing war has been associated with substantial disruption of healthcare infrastructure, antimicrobial supply chains, and IPC capacity [13, 14].

By mid-2023, more than one million refugees from Ukraine - including several hundred thousand children - had received medical care in Germany, many after interruptions to chronic therapy and routine preventive care [15-18]. Although several European centres have reported MDRO carriage among Ukrainian patients, paediatric data remain limited [19-21]. Recognising

these risks, the German Society for Paediatric Infectious Diseases (DGPI) issued guidance recommending enhanced MDRO screening for children arriving from high-prevalence settings such as Ukraine, including screening at multiple anatomical sites [10, 22]. An English translation of the recommendation is provided in Online Resource 1.

This study aimed to describe MDRO-positive screening findings and documented MDRO infections in a selected cohort of paediatric patients from Ukraine with chronic medical conditions or war-related injuries who underwent MDRO screening at ten German tertiary-care centres during the first 13 months following Russia´s full-scale invasion of Ukraine.

Materials and Methods

Study design and setting

We conducted a multicentre, retrospective observational cohort study based on routinely collected clinical and microbiological data. The study included children and adolescents from Ukraine who presented to participating tertiary paediatric hospitals in Germany, had chronic medical conditions or war-related injuries, had previously received medical care in Ukraine, and underwent MDRO screening between 24 February 2022 and 31 March 2023. Chronic medical disease was defined as the presence of a serious underlying medical condition requiring ongoing or recurrent medical care for at least 3 months. The study aimed to characterise the frequency and spectrum of MDRO colonisation and infection in this selected patient population.

Study centres and coordination

Participating hospitals were recruited via the DGPI network. Of 30 tertiary paediatric centres invited, 10 contributed anonymised routinely collected clinical and microbiological data: Berlin, Bonn, Bremen, Essen, Freiburg, Halle, Hamburg, Mainz, Munich, and Würzburg. Among the 20 non-participating centres, six reported that they had treated no eligible patients, six were unable to participate because of limited staff capacity, and eight did not respond.

Patients were identified retrospectively at the participating centres. Consequently, the total number of potentially eligible patients assessed for inclusion and the number excluded before data submission could not be reliably reconstructed across all centres.

Study coordination, data management, and statistical analysis were undertaken at University Hospital Essen in collaboration with Charité – University Medical Center Berlin.

Study population

Patients were eligible if they were over 28 days old and younger than 18 years, had lived in Ukraine for at least three months before presentation to a participating hospital in Germany, and had previously received medical care as inpatients in Ukraine for a chronic medical condition or a war-related injury. Inclusion further required at least one MDRO screening sample obtained at admission or during hospitalisation within the study period.

Data collection

Potentially eligible patients were identified retrospectively from hospital administrative records, which were cross-referenced with local microbiology databases. Each centre was assigned a unique study identifier and submitted anonymised data using a secure, standardised electronic questionnaire [23 LimeSurvey; Online Resource 2].

Submitted data were reviewed centrally by the studyteam in Berlin and Essen for completeness, plausibility, and internal consistency. Where possible, participating centres were contacted to resolve missing or inconsistent entries before the database was finalised. Following consolidation of the study dataset, the submitted records were deleted from the online survey platform. Missing data were retained as such and were not inferred from other variables. The following variables were collected:

- demographic and social data: age, sex, and accommodation type in Germany
- clinical characteristics: underlying medical condition, prior medical care in Ukraine, and presence of indwelling medical devices
- MDRO screening and colonisation: screening date and anatomical site, bacterial species identified, and antimicrobial resistance profile, including classification according to the German multidrug-resistant Gram-negative organism (MRGN) syste [24-26]
- MDRO infection episodes: infection type, date or timing of infection, microbiological findings, and temporal relationship to a preceding MDRO screening result
- antimicrobial treatment of documented infection episodes: antimicrobial agents administered, treatment duration, surgical or other source-control interventions, and documented clinical response; Antibiotic prescriptions were categorised according to the WHO AWaRe classification, which groups agents into *Access*, *Watch*, and *Reserve* categories to evaluate stewardship-relevant prescribing patterns [27, 28]
- antimicrobial treatment regimens were reconstructed from treatment information provided by the participating centres, including free-text information and, where necessary, clarification with the reporting centres. We distinguished between the initial antimicrobial regimen, all antimicrobial agents administered during an infection episode, and the last documented antimicrobial regimen.
- clinical outcomes: clinical status at hospital discharge

Contextual reference data

For descriptive contextual comparison, aggregated routine data on MDRO-positive paediatric admissions were obtained from the two coordinating tertiary-care hospitals, University Hospital Essen and Charité – University Medical Centre Berlin.

These comparison datasets comprised: (1) all paediatric inpatients (over 28 days to <18 years), including previously healthy children, representing the pre-war historical reference population for the general German paediatric population; and (2) all paediatric inpatients treated at the same centres during the study period, representing a contemporaneous reference population.

The reference populations included children with a broad range of medical conditions, including previously healthy children, and were not matched to the Ukrainian cohort with respect to age, underlying conditions, previous healthcare exposure, medical devices, or screening indication. Screening was performed according to the routine IPC policies applicable at each centre and time period. Laboratory screening data were analysed for MDRO positivity using the operational microbiological definitions applied in the respective centre.

These data were therefore used for descriptive contextual comparison rather than as formal control cohorts.

Microbiological analysis

Colonisation screening

MDRO colonisation was assessed through routine screening according to institutional IPC protocols. Screening specimens from predefined anatomical sites, including the nasopharynx, rectum, wounds, and indwelling device sites, were processed in accredited microbiology

laboratories using standard culture methods. Bacterial identification and antimicrobial susceptibility testing were performed according to EUCAST or CLSI criteria applicable at the respective centre and time period.

For descriptive analyses, the detection of one MDRO species at one anatomical site was counted as one colonisation event. Detection of different MDRO species or detection of the same MDRO species at different anatomical sites was counted as separate colonisation events. Multiple colonisation was defined as the detection of more than one MDRO species in the same patient, either at the same or at different anatomical sites.

MRGN Classification

The German MRGN classification, developed by the Commission for Hospital Hygiene and Infection Prevention (KRINKO) at the Robert Koch Institute, categorizes MRGN based on resistance to four antibiotic classes: acylureidopenicillins (piperacillin), third-generation cephalosporins (cefotaxime or ceftazidime), fluoroquinolones (ciprofloxacin), and carbapenems (imipenem or meropenem). The classification is primarily intended to guide IPC measures.

Resistance to three of these four antibiotic classes defines 3MRGN; resistance to all four defines 4MRGN. The paediatric 2MRGN NeoPaed category was applied where appropriate according to KRINKO criteria [24-26].

Where available, carbapenemase production was investigated by molecular detection of carbapenemase genes, including *bla*KPC, *bla*NDM, and *bla*OXA-48-like. Antimicrobial susceptibility testing panels and access to molecular characterisation varied among centres. Consequently, not all 4MRGN isolates were fully characterised, reflecting both the

retrospective study design and variation in the availability of comprehensive molecular resistance testing in routine clinical microbiology laboratories.

MRSA and VRE were included as additional gram-positive MDRO categories because of their clinical and IPC relevance.

MDRO infection isolates

MDRO infections were identified through retrospective review of medical records and microbiology reports. An MDRO infection was defined as a clinically documented infection with compatible signs and symptoms and microbiological detection of an MDRO from a normally sterile site, such as blood or cerebrospinal fluid, or from a specimen considered relevant to the suspected site of infection, such as respiratory secretions, urine, or a wound specimen. Classification as infection rather than colonisation was based on the clinical assessment documented by the treating team. For each infection episode, the infection type, causative organism, and temporal relationship to a preceding MDRO colonisation finding were recorded.

Outcome measurements

Patient outcomes at hospital discharge were categorised as full clinical recovery or residual impairment. Residual impairment was defined as any newly documented neurological deficit, physical deterioration, or new dependence on a medical device at discharge.

Statistical analysis

Analyses were primarily descriptive. Categorical variables were summarised as counts and percentages. Continuous variables were summarised as medians with interquartile ranges or as means with standard deviations, as appropriate.

MDRO-positive admissions in the historical and contemporaneous reference populations were presented descriptively and were not treated as formal control groups. Analyses were based on available cases. Variable-specific denominators were reported where data were incomplete. Analyses were based on available cases without imputation for missing data. Statistical analyses were performed using SPSS version 27 (IBM Corp., Armonk, NY, USA).

Ethics

The study was approved by the Ethics Committee of the Medical Faculty of the University of Duisburg–Essen (reference 22-10943-BO). Because only anonymised, retrospective data were analysed, the requirement for informed consent was waived. The study complies with the Declaration of Helsinki (2013 revision) and applicable German and EU data-protection regulations.

Results

Contextual comparison

At the two coordinating centres, the frequency of MDRO-positive admissions among the selected Ukrainian study cohort was compared with both pre-war and contemporaneous reference populations (Table 1).

At Charité Berlin, MDRO colonisation occurred in 26.67 per 100 Ukrainian admissions during the study period, compared with 3.48 per 100 among all paediatric inpatients in 2019 (pre-war historical group) and 3.08 per 100 among all paediatric inpatients admitted during 2022–2023 (contemporaneous reference population).

At University Hospital Essen, the corresponding rates were 23.81 per 100 for Ukrainian children during the study period, 2.02 per 100 among all paediatric inpatients in 2019, and 2.17 per 100 among general paediatric admissions admitted during 2022–2023.

These populations differed in case mix, previous healthcare exposure, screening indication and screening intensity and were therefore not formally compared.

Table 1. MDRO colonisation among paediatric inpatients at two coordinating tertiary centres in Germany: descriptive contextual comparison

MDRO = multidrug-resistant organism

Centre	Analysed period	Patient group	Total admissions (n)	Admissions with MDRO-positive screening (n)	MDRO-positive admissions per 100 admissions
Charité – University Medical Center Berlin	Feb–Dec 2019	All paediatric inpatients	8,473	295	3.48
	Feb 2022–Feb 2023	All paediatric inpatients	10,694	329	3.08
	Feb 2022–Feb 2023	Chronically ill Ukrainian paediatric inpatients* (study cohort; subset of all admissions)	90	24	26.67

University Hospital Essen	Feb–Dec 2019	All paediatric inpatients	5,201	105	2.02
	Feb 2022–Feb 2023	All paediatric inpatients	5,447	118	2.17
	Feb 2022–Feb 2023	Chronically ill Ukrainian paediatric inpatients* (study cohort; subset of all admissions)	63	15	23.81

MDRO = multidrug-resistant organism; Comparable data for chronically ill non-Ukrainian children were unavailable.

*The Ukrainian study cohort comprised children and adolescents with chronic medical conditions or war-related injuries and was included within the corresponding total number of paediatric admissions. Comparable data for non-Ukrainian paediatric patients with similar underlying conditions or previous healthcare exposure were unavailable. The reference populations were not matched to the Ukrainian study cohort with respect to case mix, previous healthcare exposure, screening indication or screening intensity. These data are therefore presented solely for descriptive contextual comparison and should not be interpreted as estimates of relative risk.

Patient cohort and demographics

The median age of the 198 included patients was 8 years (IQR, 3–13), and 82 (41%) were female (Table 2). The most common underlying conditions were oncological disorders (24%), neurological or neuromuscular disorders (22%), and gastrointestinal or hepatological disorders (9%). Nine children (5%) were treated for war-related injuries.

Indwelling medical devices, including feeding tubes, central venous catheters, and tracheostomies, were present in 64 patients (32%).

Accommodation status was available for 57 patients (29%). Among these, 13 (23%) lived in refugee shelters, 12 (21%) with host families, 12 (21%) in private accommodation, and 20 (35%) in institutional care.

Table 2: Demographic and clinical characteristics of Ukrainian paediatric patients (Percentages were calculated based on the total number of patients n = 198)

Characteristics	**n (%)[‡] or median (IQR)**
Sex	
Female	82 (41)
Male	116 (59)
Age (years)	8 (3-13)
Indwelling medical device[*]	64 (32)
Primary diagnosis[**]	
Oncologic	47 (24)
Neurologic/neuromuscular	43 (22)
Gastrointestinal/hepatologic	18 (9)
Respiratory	16 (8)
Endocrinologic	8 (4)
Renal	6 (3)
Haematologic	4 (2)
Cardiovascular	4 (2)
Psychiatric	2 (1)
Rheumatologic	1 (1)
Immunologic / HIV	1 (1)
War related injuries[**]	9 (5)
Other[***]	39 (20)
Accommodation status[****]	
Refugee shelter	13 (23)
Host family	12 (21)

Private flat	12 (21)
Institutional care	20 (35)
Unknown	141 (71)

* Includes central lines, feeding tubes, or tracheostomies

** Nine patients (5%) were treated for war-related injuries at least for 28 days within a Ukrainian hospital; the remainder had chronic non-traumatic conditions.

*** Other diagnoses include metabolic, surgical, or genetic conditions not listed above

**** Accommodation status was available for 57 of 198 patients (29%); percentages for accommodation categories were calculated among patients with available data (n=57)

‡ Percentages were calculated using the total cohort of 198 patients, except for accommodation categories, which were calculated among the 57 patients with available accommodation data. Percentages may not total 100% due to rounding.

MDR Colonisation and Pathogen Distribution

Of 198 included patients, 85 (43%) had at least one MDRO-positive screening result. These 85 patients accounted for 128 individual colonisation events some patients had different MDRO species and/or positive findings at more than one anatomical site. Thirteen of the 85 patients (15%) carried more than one MDRO species.

The anorectal region was the most frequent site of MDRO detection, accounting for 73 of 128 colonisation events (57%), followed by the nose (21/128, 16%), urine (11/128, 9%), and the throat, groin, and wounds (4/128 each, 3%) (Table 3). No patient underwent complete multisite screening according to the DGPI recommendations, and most patients were screened at only one anatomical site.

Among the 128 colonisation events, 32 (25%) involved 2MRGN NeoPaed, 57 (44%) 3MRGN, 24 (19%) 4MRGN, 7 (5%) MRSA and 8 (6%) VRE.

Carbapenemase genes, including *bla*NDM, *bla*KPC, and *bla*OXA-48-like, as well as extended-spectrum β-lactamase or AmpC mechanisms, were reported when corresponding testing had been performed. Carbapenem-resistant non-fermenters included *Pseudomonas aeruginosa* (n = 3) and *Acinetobacter baumannii* (n = 2). The extent of phenotypic and molecular resistance testing varied among and within centres; consequently, not all 4MRGN isolates were fully characterised.

Seven patients carried methicillin-resistant *Staphylococcus aureus* (MRSA). PVL testing was performed for three MRSA isolates, of which two were negative. Eight patients carried vancomycin-resistant *Enterococcus* spp., comprising six *E. faecium* and two *E. faecalis* isolates.

Table 3: Anatomical Distribution and MDRO Categories of Positive Screening Events in 85 Patients

(Percentages within this table were calculated based on the total number of colonisation events n=128; multiple sites possible per one of the 85 MDRO positive patients)

Parameter	**n (%)**
Anatomical site of MDRO detection, based on 128 colonisation events	
Anorectal	73 (57)
Nasal	21 (16)
Urine	11 (9)
Wound	4 (3)
Throat	4 (3)
Groin	4 (3)
Tracheal aspirate/sputum	4 (3)
Indwelling device site	7 (5)
MDRO classification, based on 128 colonisation events	
2MRGN NeoPaed (resistant to two major antibiotic classes)	32 (25)

3MRGN (resistant to three major antibiotic classes)	57 (44)
4MRGN (carbapenem-resistant; resistant to four major classes)	24 (19)
MRSA	7 (5)
VRE	8 (6)
Number of MDRO species per patient, based on 85 MDRO-positive patients	
One MDRO species	72 (85)
More than one MDRO species	13 (15)

A colonisation event was defined as the detection of one MDRO species at one anatomical site. Detection of different MDRO species or of the same species at different anatomical sites was counted as separate events. Multiple colonisation was defined as the detection of more than one MDRO species in the same patient.

MDRO, multidrug-resistant organism; MRGN, multidrug-resistant Gram-negative organism; MRSA, methicillin-resistant Staphylococcus aureus; VRE, vancomycin-resistant Enterococcus

MDRO-associated infections

Among the 85 patients with MDRO-positive screening results, 23 (27%) had a documented clinically significant MDRO infection. Infection sites included the respiratory tract (6/23, 26%), skin, bone or soft tissue (6/23, 26%), urinary tract (5/23, 22%), bloodstream/sepsis (4/23, 17%), gastrointestinal tract (1/23, 4%), and central nervous system (1/23, 4%). In 21 of the 23 infection episodes (91%), the infecting organism was concordant with an MDRO identified in a screening sample, based on species and, where available, a compatible resistance phenotype (Table 4).

Treatment and Outcomes

All 23 patients with MDRO infections received systemic antimicrobial therapy, with a median of 14 days (IQR 9.5–24.5).

The initial antimicrobial regimen consisted of monotherapy in 5 infection episodes (22%), dual therapy in 12 (52%), triple therapy in 5 (22%), and ≥4 agents in 1 (4%). Ten patients (44%) additionally required surgical intervention for source control (Table 4).

Across the 23 infection episodes, a total of 60 antimicrobial agents were administered. Meropenem was most frequently used (n = 20). Other agents included linezolid (n = 4), colistin (n = 5), amikacin (n = 1), tigecycline (n = 1), ceftazidime–avibactam (n = 1), clindamycin (n = 2) and cefiderocol (n = 2) (Table 4).

Known MDRO colonisation was reported to have been taken into account when selecting empirical antimicrobial therapy in 2 of 23 infection episodes (9%).

No in-hospital deaths occurred. Seventeen patients (74%) achieved full clinical recovery by hospital discharge, while six (26%) had newly documented residual impairment, including new

device dependence or neurological sequelae. Details of the individual infection episodes and antimicrobial regimens are provided in Online Resource 3 Supplementary Table 1.

Table 4: MDRO infection episodes, treatment characteristics, and outcomes among paediatric patients with MDRO-positive screening results

(Unless otherwise indicated, percentages are based on 23 clinically documented MDRO infection episodes among 85 patients with an MDRO-positive screening result.)

Parameter	**N (%)* or value**
Overall infection burden	
Colonised patients who developed MDRO infection	23/85 (27%)
Infection episodes concordant with a preceding MDRO screening result	21/23 (91%)
Patients with an infection concordant with a preceding MDRO screening result**	21/85 (25%)
Type of infection	
Respiratory tract	6 (26%)
Skin, bone or soft tissue	6 (26%)
Urinary tract	5 (22 %)
Sepsis	4 (17 %)
Gastrointestinal	1 (4 %)
Central nervous system	1 (4 %)
Treatment characteristics	
Surgical intervention for source control	10 (44%)
Received antibiotic therapy	23 (100%)

Known MDRO colonisation reported to have been taken into account when selecting empirical antimicrobial therapy	2 (9%)	
Initial antimicrobial regimen		
Single-agent therapy	5 (22%)	
Dual therapy	12 (52%)	
Triple therapy	5 (22%)	
≥4 antibiotics	1 (4%)	
Duration of antibiotic therapy, days, median (IQR)	14 (9.5–24.5)	
Antimicrobial agents	**All administered during the infection episodes, n = 60**	**Included in the last documented regimen, n = 34**
WHO AWaRe Access group		
Cotrimoxazole	5	2
Ampicillin-sulbactam	3	0
Clindamycin	2	1
Metronidazole	1	0
Amikacin	1	1
WHO AWaRe Watch group		
Meropenem	20	13
Piperacillin-Tazobactam	4	0
Vancomycin	6	4
Moxifloxacin	1	0

Ciprofloxacin	3	0
Aztreonam	1	1
WHO AWaRe Reserve group		
Linezolid	4	3
Colistin	5	5
Tigecycline	1	1
Ceftazidime-avibactam	1	1
Cefiderocol	2	2
Outcomes at hospital discharge		
Full clinical recovery without newly documented residual impairment	17 (74%)	
Newly documented residual impairment	6 (26%)	
In-hospital mortality	0 (0%)	

MDRO, multidrug-resistant organism; IQR, interquartile range; AWaRe, Access, Watch and Reserve

* Percentages may not total 100 % due to rounding.

** Concordance was defined as detection of the same MDRO species and, where available, a compatible resistance phenotype in a screening sample obtained before the infection episode. Molecular identity of the isolates was not established.

Discussion

This multicentre study provides a comprehensive analysis of MDRO colonisation and infection among paediatric patients from Ukraine with chronic medical conditions or war-related injuries who received specialised care in German tertiary hospitals during the first year following the

full-scale invasion. Among screened children, MDRO-positive findings were common (43%), and more than one quarter of MDRO-positive patients had a clinically documented MDRO infection. In most infection episodes, the infecting organism was concordant with an organism identified in screening. Together, these findings support the clinical relevance of MDRO carriage for IPC and clinical decision-making in suspected infection.

The high proportion of MDRO-positive screening results observed in our cohort is likely multifactorial, reflecting underlying medical complexity, indwelling medical devices and repeated healthcare exposure, including care in a high-prevalence setting. Previous antimicrobial exposure, which may also have contributed, was not systematically captured in this study [13, 14, 29]. Ukraine already had a high burden of resistant Gram-negative organisms before 2022, while the war subsequently disrupted healthcare infrastructure, antimicrobial supply chains and IPC capacity [14, 30]. Our study was not designed to quantify the effect of the war itself on AMR; the findings should therefore be interpreted primarily in relation to healthcare exposure in a high-prevalence setting.

In the two coordinating centres, MDRO-positive admissions were substantially more frequent among children from the Ukrainian study cohort than among general paediatric inpatients before the war and during the study period (Table 1). Although these comparator cohorts included all paediatric admissions rather than exclusively children with chronic diseases, previous German data indicate that chronic medical conditions and repeated healthcare exposure are themselves associated with increased MDRO carriage. In a prospective study of 3,964 children admitted to a paediatric hospital in Hamburg, the overall prevalence of MDRO carriage was 4.31%, while a chronic condition requiring permanent care was independently associated with higher odds of MDRO carriage (OR 2.67, 95% CI 1.07–6.13) [31]. Nevertheless, the observed differences in our study considerably exceeded these background rates, suggesting that MDRO prevalence in German paediatric hospitals and chronic medical

complexity alone are unlikely to explain the high proportion of MDRO-positive patients in the Ukrainian cohort. Instead, the findings likely reflect the combined effects of chronic medical complexity, repeated healthcare and antimicrobial exposure, and previous healthcare exposure in a high-prevalence setting.

One of the clinically relevant findings of this study was the high concordance between preceding MDRO screening findings and clinically documented infections [14, 29]. More than one quarter of patients with an MDRO positive screening result had a clinically documented MDRO infection, and in 21 of 23 infection episodes, the same species with a compatible resistance phenotype had been identified in a preceding screening sample. These observations support previous evidence identifying MDRO colonisation as a major predictor of subsequent MDRO infection and highlight the practical value of systematic admission screening [32]. Early knowledge of colonisation status has the potential to improve risk stratification, guide IPC measures and inform empirical antimicrobial therapy in critically ill children [33-36].

Despite the high concordance between preceding screening findings and subsequent infections finfings, known MDRO colonisation was reported to have been taken into account when selecting empirical antimicrobial therapy in only 2 of 23 infection episodes. Management frequently required prolonged combination therapy and the use of reserve antibiotics, including colistin, linezolid and cefiderocol. These observations illustrate the considerable therapeutic challenges associated with paediatric MDRO infections and emphasise the need for closer integration of microbiological screening results into antimicrobial stewardship programmes. Timely recognition of high-risk patients may facilitate more appropriate empirical therapy while simultaneously limiting unnecessary exposure to prolonged broad-spectrum antibiotics in lower-risk patients [35, 36].

Our findings also have important implications for IPC. Although recommendations for enhanced MDRO screening of children arriving from high-prevalence regions were issued by the DGPI in 2022, implementation varied substantially between participating centres. None of the centres fully adhered to the recommended screening strategy as provided in Online Resources 1 primarily because complete multisite screening was not performed and most children were screened at only one anatomical site. The main reasons reported were deviations from established routines and unintentional omission in the context of a high workload. In practical terms, implementation of the adapted recommendations should prioritise three elements: identification of children with relevant previous healthcare exposure in high-prevalence settings; complete, standardised multisite screening according to national recommendations; and rapid communication of screening results to IPC and clinical teams so that isolation measures and empirical therapy can be adapted when clinically indicated. These principles are not specific to Ukrainian children and may apply more broadly to vulnerable paediatric patients transferred from healthcare systems with a high MDRO prevalence [10].

The microbiological findings further highlight the need for harmonised diagnostic approaches. Although the German MRGN classification provides a practical framework for infection prevention within Germany, it is not widely used internationally, limiting direct comparison with studies from other countries [25]. In addition, molecular characterisation of carbapenem resistance mechanisms was inconsistently available across participating centres. More consistent diagnostic approaches to characterise carbapenem resistance, including carbapenemase detection and molecular characterisation where available, would improve pathogen characterisation, support antimicrobial stewardship and facilitate surveillance of emerging resistance mechanisms.

This study has several limitations. First, participation was voluntary, and only ten of the 30 invited tertiary paediatric centres contributed data, introducing potential centre-level selection

bias. In addition, eligibility required that an MDRO screening sample had been obtained. The total number of potentially eligible patients, including those who were not screened, could not be reconstructed across participating centres. The reported proportion of MDRO-positive patients therefore applies to this selected cohort of screened children and should not be interpreted as a population-based prevalence estimate. Second, screening indications, anatomical sampling sites, microbiological methods and the extend of molecular resistance and molecular characterisation differed between and within centres. Follow-up duration was not standardised, limiting interpretation of the proportion of colonised patients with a documented infection. The distinction between infection and colonisation was based on the clinical assessment recorded by the treating team. Infections diagnosed from non-sterile specimens, particularly respiratory, urinary and wound samples, may therefore have been subject to misclassification. Moreover, concordance between screening and infection findings was based on species identification and, where available, compatible resistance phenotypes; molecular typing was not performed and strain of the isolates could not be confirmed. The reference populations from the two coordinating centres differed from the study cohort in case mix, healthcare exposure, screening indication and screening intensity and were therefore suitable only for descriptive contextual comparison. Finally, long-term follow-up was unavailable, precluding assessment of persistent colonisation, recurrent infection and outcomes after hospital discharge.

In conclusion, chronically ill paediatric refugees from Ukraine, a region with a high prevalence of MDROs, had a high burden of MDRO colonisation and clinically documented infection, predominantly involving MRGN organisms, including carbapenem-resistant isolates. Our findings suggest that admission screening is not only important for IPC but also a valuable clinical tool to identify high-risk patients, guide empirical antimicrobial therapy, and support antimicrobial stewardship.

Although this study was conducted in children from Ukraine displaced during the full-scale war, its clinical implications are not Ukraine-specific. The same principles may apply to children with previous healthcare exposure in other high-prevalence regions. Risk assessment should therefore integrate individual healthcare exposure with regional MDRO epidemiology rather than nationality or country of origin alone.

In the context of increasing global mobility and cross-border healthcare, these findings have implications beyond the Ukrainian refugee population and may be relevant to children with previous healthcare exposure in other high-prevalence regions. This underscores the importance of risk-adapted screening strategies that integrate individual healthcare exposure with regional MDRO epidemiology.

At the healthcare-system level, harmonised screening strategies, consistent diagnostic approaches to characterise carbapenem resistance, including carbapenemase detection and molecular characterisation, rapid communication of microbiological results, and access to paediatric infectious diseases and antimicrobial stewardship expertise are needed to support appropriate treatment and IPC in children transferred across healthcare systems.

Abbreviations

- AMR – Antimicrobial Resistance
- WHO – World Health Organization
- MDRO – Multidrug-Resistant Organism
- MRSA – Methicillin-Resistant *Staphylococcus aureus*
- VRE – Vancomycin-Resistant Enterococci
- LRE – Linezolid-Resistant Enterococci
- IPC – Infection Prevention and Control
- AMS – Antimicrobial Stewardship
- KRINKO – Kommission für Krankenhaushygiene und Infektionsprävention (Commission for Hospital Hygiene and Infection Prevention)
- MRGN – Multiresistente Gramnegative Stäbchen (Multidrug-Resistant Gram-Negative Rods)
- DGPI – Deutsche Gesellschaft für Pädiatrische Infektiologie (German Society for Paediatrics

  Infectious Diseases)
- ESBL – Extended-Spectrum Beta-Lactamase
- AmpC – AmpC Beta-Lactamase
- NDM – New Delhi Metallo-Beta-Lactamase
- KPC – Klebsiella pneumoniae Carbapenemase
- OXA-48 – Oxacillinase-48
- CRPA – Carbapenem-Resistant Pseudomonas aeruginosa
- CRAB – Carbapenem-Resistant Acinetobacter baumannii
- AWaRe – Access, Watch, and Reserve (WHO antibiotic classification)

- EUCAST – European Committee on Antimicrobial Susceptibility Testing
- CLSI – Clinical and Laboratory Standards Institute
- CNS – Central Nervous System
- PVL – Panton-Valentine Leukocidin
- UTI – Urinary Tract Infection
- BSI – Bloodstream Infection
- CLABSI – Central Line-Associated Bloodstream Infection
- NIV – Non-Invasive Ventilation
- PEG/PEJ – Percutaneous Endoscopic Gastrostomy / Jejunostomy
- CVC – Central Venous Catheter

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