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The challenge of antibiotic resistance in post-war Mosul, Iraq: an analysis of 20 months of microbiological samples from a tertiary orthopaedic care centre

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ABSTRACT

Objectives: Iraq has suffered unrest and conflicts in the past decades, leaving behind a weakened health-care system. In 2018, Médecins Sans Frontières (MSF) opened a tertiary orthopaedic care centre in Mosul providing reconstructive surgery with access to microbiological analysis.
Methods: A retrospective cross-sectional analysis of microbiological and clinical data of patients admitted between April 2018 and December 2019.
Results: There were 174 patients who were included in this study; there were more males than females (135 to 38, respectively), and the mean age was 32.6 y. Of the 174 patients, the majority had more than one bacterial isolate detected (n = 122, 70.1%); 141 (81.0%) had at least one multidrug-resistant (MDR) isolate detected during their hospital stay. *Staphylococcus aureus* (n = 197, 48.2%) was the most common organism isolated. Overall, most isolates detected were MDR (n = 352, 86%), mostly methicillin-resistant *S. aureus* (n = 186, 52.8%) or extended-spectrum beta-lactamase–producing *Enterobacterales* (n = 117, 33.2%). Among patients admitted to the operating department (n = 111, 63.7%), 81.1% (n = 90) were admitted for violent trauma injuries. Patients who had more than one procedure performed per surgery had significantly increased odds of having at least one MDR organism isolated (OR 8.66, CI 1.10–68.20, $P = 0.03$).
Conclusion: This study describes a high prevalence of antibiotic resistance in patients with trauma-related wounds in Mosul, Iraq. It highlights the importance of microbiological analysis and ongoing surveillance to provide optimal treatment. Additionally, it underscores the importance of infection prevention and control measures as well as antibiotic stewardship.

1. Introduction

Multidrug resistance (MDR) to antibiotics has become a major problem for the treatment of bacterial infections and is one of the greatest challenges to public health worldwide. Bacterial MDR–associated deaths were estimated to be 4.95 million (3.62–6.57) in 2019, including 1.27 million (95% CI 0.91–1.71) attributable deaths;

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it is estimated they will cause 10 million deaths by 2050 if the trend is not reversed [1,2]. The challenges in combating MDR infections include scarcity of effective antibiotics with few new antibiotics in the development pipeline, suboptimal infection prevention and control (IPC) measures, and poor antimicrobial stewardship programmes [1].

Armed conflicts act as force multipliers of infections and antibiotic resistance (ABR), and conflict-affected countries face tremendous challenges with microbiology surveillance because of the lack of functioning microbiology laboratories, antibiotic stewardship and IPC programmes [3,4]. In Iraq, a country that has been in various conflicts for decades, many people have been left with traumatic wounds, prone to infections caused by MDR bacteria that often result in poor outcomes [5]. The city of Mosul has been particularly affected by conflicts because of the most recent Islamic State of Iraq and Syria (ISIS) offensive in 2016–2017, which destroyed 70% of Mosul's public hospitals and left thousands of people with complex trauma injuries [6,7].

Ongoing violence, with the added pressure of the COVID-19 pandemic, continue to hinder the implementation of the National Action Plan on Antimicrobial Resistance (NAP AMR) that the country released in 2018 [8,9]. Therefore, microbial surveillance data from Iraq, and more so from Mosul, is still insufficient [10]. Additionally, there is little literature related to ABR in trauma-affected wounds in Iraq; most of the available evidence is from the time of the United States invasion prior to 2010 [11–14]. For those reasons, an increased understanding of the current ABR status in Iraq in general and in Mosul in particular is needed in order to improve the clinical management of trauma-affected wounds where there are still challenges with recovering health infrastructures.

This study aimed to describe the prevalence of ABR in bacteria isolated from patients admitted between April 2018 and December 2019 to the Médecins Sans Frontières (MSF) Tertiary Orthopaedic Centre (TOC) hospital in East Mosul, Iraq.

2. Methods

2.1. Study design

A cross-sectional analysis of microbiological and clinical data of patients admitted to the MSF TOC facility between April 2018 and December 2019.

2.2. Study population

All patients who had at least one sample collected for microbiological culture during the study period were included. Patients with positive microbiological results and isolates with insufficient microbiological data to determine their MDR status were excluded.

2.3. Setting

Mosul is the second largest city in Iraq, located approximately 400 km north of Baghdad. Years of insecurity and ethnic and religious conflict have reshaped Mosul's demographics and vastly affected the functionality of its local administration, public institutions and economic establishments. Between October 2016 and July 2017, the battle to retake Mosul from ISIS resulted with an estimated death toll varying from 2500 to more than 9000 deaths.

After responding to the emergency needs of the injured of the Mosul battle being on the front lines in 2017, MSF Operational Centre Brussels (OCB) opened a TOC in East Mosul in April 2018, providing free reconstructive surgery, postoperative care and rehabilitation, pain management and physiotherapy services for people injured mainly by violent trauma. The hospital structure consists of one operating theatre and a 33-bed in-patient ward including 11 isolation rooms for MDR-infected patients. A semi-restrictive antibiotic stewardship strategy is implemented, with two general medicine doctors trained in antibiotic stewardship and appointed as antibiotic stewardship focal points. These two focal points are responsible for the daily antibiotic prescription revision and the only clinicians in the hospital who are authorized to prescribe antibiotics from the Watch and Reserve WHO AWaRe classification [15] in accordance with MSF clinical guidelines. An active antimicrobial stewardship committee meets regularly to discuss case management and antibiotic surveillance (e.g., prescriptions audits, consumption data). Infection prevention and control (IPC) measures (e.g., hand hygiene, transmission-based precautions, surgical site infection prevention) are in place and monitored regularly through audits and surveillance.

2.4. Study definitions

A traumatic injury was defined as one caused by a violent trauma (mines, gunshots and/or bombs) or a nonviolent or accidental trauma such as car accidents or falls.

Bacteria were classified as not sensitive to an antibiotic when they showed intermediate (I) or resistant (R) result to the antibiotic in question. Antibiotic classes were defined as not sensitive if at least one antibiotic from that class was resistant.

MDR status was determined based on antibiograms' results. An isolate was classified as an MDR organism (MDRO) when it showed no sensitivity to three or more antibiotic classes [16]. Carbapenem-resistant Enterobacteriaceae (CRE), extended-spectrum beta-lactamase (ESBL) producers and methicillin-resistant *Staphylococcus aureus* (MRSA) were defined as per standard definitions [17].

Since multiple samples were collected for the same patients according to the hospital protocol, a patient was defined as having an MDR infection if at least one sample had one MDRO isolated at admission, during hospital stay and/or at readmission.

2.5. Antimicrobial susceptibility testing (AST)

All samples were sent to a private external microbiology laboratory accredited by the College of American Pathologists for microbiological analysis. Bacteria were identified using the analytical profile index (API) strip method (bioMérieux SA, Marcy-l'Étoile, France). Antibiotic sensitivity testing (AST) was performed using the Kirby-Bauer disc diffusion method and interpretation rules as per the 2016 Clinical and Laboratory Standards Institute (CLSI) guidelines [17]. Phenotypic confirmation of ESBL production was performed using the double-disc synergy test diffusion method with ceftazidime (30 μg) and ceftriaxone (30 μg). Because of supply chain issues, some isolates were not tested for all the required pattern of antibiotics.

2.6. Statistical analysis

All microbiological information was recorded in and extracted from a WHONET laboratory database (Boston, MA). Clinical information was retrieved from the TOC clinical databases.

For multiple samples from the same patient on the same date from the same site, only one sample was included in the data analysis. Where the same bacteria were isolated the same day from a different site of injury of the same patient, they were included in the analysis; however, if isolated the same day from the same site with the same antibiogram profile, only one isolate was included.

Descriptive statistics to profile the study population were performed. The different type of bacteria detected as well as the prevalence and type of resistance to various antibiotics was reported overall and by bacterial species. Descriptive statistics were

computed at patient level (over the total number of patients) to describe the profile of the patients included in the study and at isolate level (over the total number of isolates detected) to describe the prevalence of MDRO, the resistance patterns and antibiotic sensitivity results. Analysis done at isolate level excluded sterile samples. A description of the total samples collected, among which the isolates were detected, was also computed. Variables with more than 5% missing values were excluded from analysis.

Demographic, clinical and surgical characteristics of patients with MDRO were compared to those with non-MDRO using the Pearson χ^2 test or the Fisher's exact test for categorical variables and the Mann-Whitney *U* test for continuous variables. Patients with an undetermined MDR status were excluded from these analyses. Statistical significance was defined as a two-sided *P* value ≤.05. Statistical analysis was performed using IBM SPSS Statistics version 22 (IBM Corp., Armonk, NY).

3. Results

A total of 326 patients were admitted to the MSF TOC facility during the study period, of which 178 (54.6%) had their microbiology results recorded. Four patients were excluded from analysis as their respective isolate results had undetermined MDR status. Therefore, a total of 174 patients were eligible and included in the study, corresponding to a total of 421 clinical samples collected and 409 isolates analysed.

3.1. Clinical and demographic profile of patients

Of the total 174 patients included in the study, there were more males than females (13.6:3.8, respectively), and the mean age of the study population was 32.6 y. Of them, 141 (81.0%) had at least one MDRO detected at any time during their hospital stay. Most patients presenting with at least one MDRO were male (n = 112, 79.4%), aged between 20 and 49 y (n = 77, 54.6%), and reported not having taken antibiotic therapy prior to their admission (n = 138, 97.9%; Table 1).

Most patients had less than three specimens (n = 113, 64.9%; median 2.0, IQR 1.0) collected during their hospital stay. The odds of having an MDRO detected were 3.7 times higher in patients who had three or more specimens taken during their stay than patients with fewer than three specimens taken (OR 3.7; CI 1.34–10.13; P = 0.01). The majority of patients had more than one bacterial isolate detected over the time of their stay (n = 122, 70.1%). Patients with two and three or more isolates detected had higher odds of having at least one MDRO than patients who had one isolate detected (OR 4.40, CI 1.80–31.24; OR 20.90, CI 4.60–94.95, respectively, $P < 0.001$).

Most of the patients who were admitted to the operating department (OD) had violent trauma injuries (n = 90, 81.1%) and underwent minor, wound-related or specialised procedures (n = 96, 86.5%). Patients who had more than one procedure performed per surgery had significantly increased odds of having at least one MDRO isolated (OR 8.66, CI 1.10–68.20, $P = 0.03$) compared to those who had one procedure (Table 1).

3.2. Distribution of bacterial isolates in clinical samples

Over the total number of samples included (n = 421), the two most commonly collected from patients were tissue (n = 201, 47.7%) and bone (n = 148, 35.1%; Table 2). MDROs were more commonly isolated from blood, screws and urine samples collected from patients (Table 2). Overall, there was no statistical difference between the sample type and the likelihood of detecting a MDRO ($\chi^2 = 3.1$, $P = 0.68$).

Ninety-six of the 421 samples collected (22.8%) did not have any bacteria detected. Half of the samples collected (58.2% N = 245/421) had only one bacterium isolated. In total, 409 isolates were detected from the total number of samples included (n = 421), with *S. aureus* (n = 197/409, 48.2%) being the most common organism isolated from all sample types. In tissue and bone samples, *Proteus mirabilis, Escherichia coli, Enterobacter cloacae, Pseudomonas aeruginosa* and *Klebsiella pneumoniae* together represented 35.9% (n = 147/409) of the organisms detected (Fig. 1). Overall, Gram-positive organisms were the most prevalent (n = 217/409, 53.1%).

3.3. Antibiotic and multidrug resistance

The overall resistance data presented in this section were analysed at isolate level among the total number of isolates detected (n = 409) or specific isolate type where relevant.

The overall MDRO prevalence was 86.0% (n = 352/409), with the majority of MDROs being MRSA (n = 186/409, 52.8%) or ESBL (n = 117/409, 33.2%) (Fig. 2).

Almost all *S. aureus* isolates were MDR (n = 188/197, 95.4%), with the majority (n = 186/188, 98.9%) being methicillin resistant (MRSA); two *S. aureus* isolates that had an MDR profile but were not MRSA were resistant to three antibiotics from three different classes (penicillin, tigecycline and chloramphenicol) but were sensitive to cefoxitin. Half of the *S. aureus* tested were resistant to clindamycin (n = 99, 50.8%) and highly resistant to ciprofloxacin, rifampicin and co-trimoxazole (respectively, n = 51, 42.5%; n = 80, 41.9%; n = 56, 38.4%), while no isolates were resistant to vancomycin. Resistance rates for the same antibiotics among the subgroup of MRSA were slightly higher (Table 3).

A high percentage of ESBL and MDR profiles were noted among the Enterobacterales detected (Table 4); all *P. mirabilis* detected were ESBL-producing (n = 46, 100%), whilst 93.3% (n = 28) of *E. coli* were also ESBL-producing. Resistance to carbapenems was detected in many Gram-negative organisms. In *P. mirabilis*, 22.5% (n = 9) were resistant to meropenem, whilst 40.9% (n = 9) of *K. pneumoniae* were resistant to imipenem. Eighteen percent of all ESBL-producing Enterobacterales were resistant to a carbapenem (25/137). Five isolates of *P. aeruginosa* were resistant to meropenem (21.7%) (Table 5).

Three isolates of *Acinetobacter baumannii* were isolated from two patients, and three isolates of *Acinetobacter* spp. from two patients were identified. All isolates were resistant to the carbapenems they were tested against (meropenem and/or imipenem) and sensitive to colistin.

4. Discussion

This study brings to light the high prevalence of antibiotic resistance in bacteria in Mosul, Iraq. The majority of the isolates detected in the study were MDRO, mostly MRSAs followed by ESBL-producing *Enterobacterales*. With such a high prevalence of ABR, clinicians are obliged to commonly prescribe classes of antibiotics, such as carbapenems and glycopeptides, with higher selection pressure on more complex antibiotic resistance patterns.

We found a higher proportion of MDR isolates among patients (81%) than that reported by other studies in similar conflict contexts: 42% among patients admitted for wound infection during the 2011 Libyan conflict [18], 73% among acutely injured Syrian civilians with wound infections in Jordan in 2011–2013 [19] and 2014–2016 [5], and 55.7% in patients treated by ICRC in Lebanon [20], as well as among the U.S. military [12–14]. In Iraqis specifically, Murphy et al. reported that 55% of Iraqi civilians with osteomyelitis who had been operated on in Jordan had an MDR infection [21],

Table 1
Comparison of characteristics among MDRO vs. non-MDRO for patients enrolled in the study, Mosul TOC, April 2018 to December 2019

Characteristics	MDRO (n, %)N = 141	Non-MDRO (n, %)N = 33	Crude OR 95% (CI)	*P* value
Demographic characteristics (N = 174)				
Age (y)				
<20	42 (19.8)	7 (21.2)	Reference	0.39
20–49	77 (54.6)	18 (54.5)	1.40 (0.54–3.70)	
≥50	22 (15.6)	8 (24.2)	2.18 (0.70–6.70)	
Sex				
Female	29 (20.6)	9 (27.3)	Reference	0.54
Male	112 (79.4)	24 (72.7)	1.45 (0.61–1.45)	
Clinical characteristics (N = 174)				
Antibiotic therapy prior to admission				
No	138 (97.9)	32 (97.0)	Reference	0.57
Yes	3 (2.1)	1 (3.0%)	0.70 (0.07–6.91)	
Number of specimens taken per patient (throughout hospitalization)				
<3	85 (60.3)	28 (84.8)	Reference	0.01[a]
≥3	56 (39.7)	5 (15.2)	3.70 (1.34–10.13)	
Number of isolates detected per patient				
1	30 (21.3)	22 (66.7)	Reference	0.00[a]
2	54 (38.3)	9 (27.3)	4.40 (1.80–31.24)	
≥3	57 (40.4)	2 (6.1)	20.90 (4.60–94.95)	
Admission to operating department				
No	47 (33.3)	16 (48.5)	Reference	0.15
Yes	94 (66.7)	17 (51.5)	1.88 (0.86–4.08)	
Surgical characteristics (N = 111)				
American Society of Anesthesiologists Classification(ASA) class				
1	46 (48.9)	8 (47.1)	Reference	1.00
≥2	48 (51.1)	9 (52.9)	0.93 (0.33–2.61)	
Number of surgeons per operation				
1	35 (37.2)	10 (58.8)	Reference	0.16
≥2	59 (62.8)	(41.2)	2.41	
Reason for admission				
Accidental trauma	19 (20.2)	2 (11.8)	Reference	0.52[b]
Violent trauma	75 (79.8)	15 (88.2)	0.53 (0.11–2.50)	
More than one procedure per operation				
No	61 (64.9)	16 (94.1)	Reference	0.03[a]
Yes	33 (35.1)	1 (5.9%)	8.66 (1.10–68.20)	
Type of procedure				
Minor/wound or specialized	80 (85.1)	16 (94.1)	Reference	0.46[b]
Orthopaedic	14 (14.9)	1 (5.9)	2.80 (0.34–22.83)	
Operation theatre time				
30–80	22 (23.4%)	5 (29.4)	Reference	0.62
90–130	45 (47.9%)	9 (52.9)	1.14 (0.34–3.81)	
140–300	27 (28.7)	3 (17.6)	2.05 (0.44–9.54)	

CI, confidence interval; MDRO, multidrug-resistant organism; OR, odds ratio.
[a] $P \leq 0.05$.
[b] *P* value based on Fisher's exact test.

Table 2
Number and proportion of isolates detected per sample type and per multidrug-resistance status

Sample type	No growth (n, %[a])	Isolates detected (n)	MDRO (n, %[b])	Non-MDRO (n, %[b])
Tissue (n = 201)	36 (17.9)	212	148 (69.8)	64 (30.2)
Bone (n = 148)	37 (25.0)	135	98 (72.6)	37 (27.4)
Screw (n = 30)	6 (20.0)	30	24 (80.0)	6 (20.0)
Urine (n = 19)	4 (21.0)	19	14 (78.9)	5 (21.1)
Blood (n = 14)	11 (78.6)	4	3 (75.0)	1 (25.0)
Other (n = 9)	2 (22.2)	9	5 (55.6)	4 (44.4)
Total (n = 421)	96 (22.8)	409	292 (71.4)	117 (28.6)

MDRO, multidrug-resistant organism; Other = biofilm, bone marrow, fluid and pus.
[a] Calculated from the number of samples collected (n = 421).
[b] Calculated from the number of isolates detected (n = 409).

and Yaacoub et al. reported that isolates from Iraqi patients had the highest proportion of MDR in their cohort [20].

The difference between our results and previous studies in similar conflict contexts could have several reasons. First, it could be explained by the potential complexity of the cases. Specifically, in our cohort, patients with more than one procedure per surgical intervention were associated with MDR infections, which could reflect a link between wound complexity and MDR infection. This link has been shown elsewhere [21]. Other differences may be because of the types of wounds, the chronicity of infections and delays in accessing optimal treatment before their admission to the MSF TOC. There might also be differences in local epidemiology of

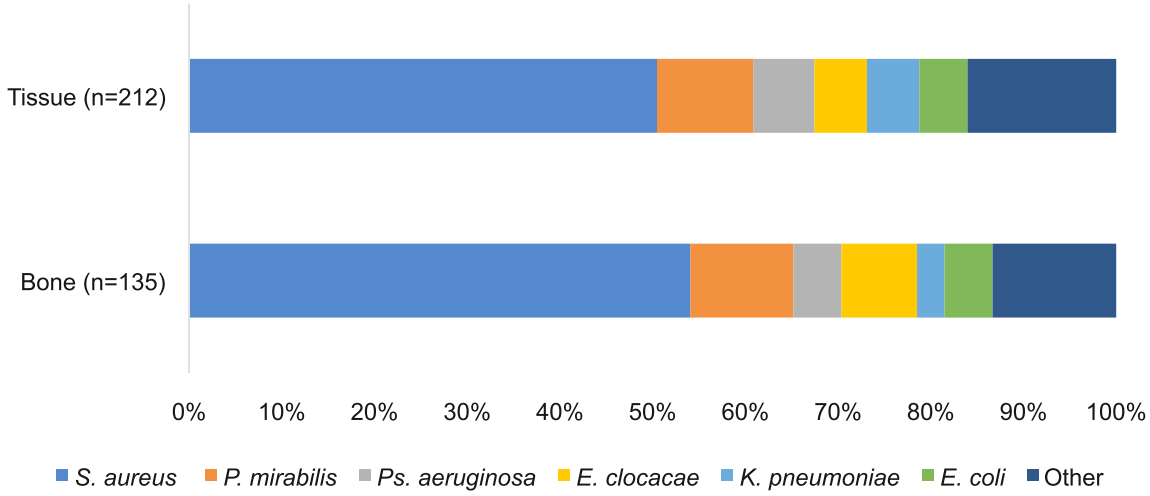
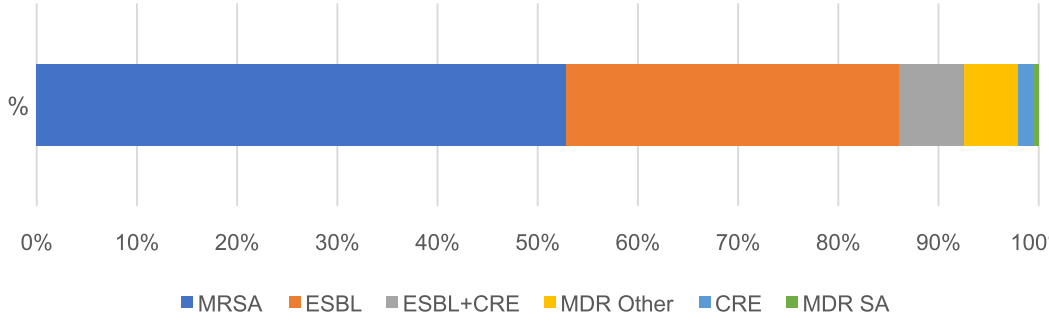


Fig. 1. Proportion of bacteria by type isolated from tissue and bone samples collected April 2018–December 2018, MSF TOC, Mosul, Iraq.



	MRSA	ESBL	ESBL+CRE	MDR Other	CRE	MDR SA
n	186	117	23	19	5	2
%	52.8%	33.2%	6.5%	5.4%	1.4%	0.6%

MRSA: methicillin-resistant *S. aureus*; ESBL: Extended-spectrum β-lactamase producing; CRE: Carbapenem-resistant Enterobacterales

Fig. 2. Proportion of different multidrug-resistant (MDR) profiles isolated from samples collected in this study, April 2018–December 2018, MSF TOC, Mosul, Iraq.

Table 3
Percentage of resistance to key antibiotics of Staphylococcus aureus isolated from samples of patients admitted to the Mosul TOC, April 2018–December 2019

Antibiotic	Number tested (%)[a]	No. *S. aureus* resistant (%)[b]	Number MRSA resistant (%)[c]
Clindamycin	195 (99.0)	99 (50.8)	98 (53.3)
Ciprofloxacin	120 (60.9)	51 (42.5)	51 (44.7)
Rifampicin	191 (95.9)	80 (41.9)	78 (43.3)
Co-trimoxazole	146 (74.1)	56 (38.4)	74 (41.1)
Vancomycin	196 (99.5)	0 (0)	0 (0)

R, resistance.
[a] Out of total number of *S. aureus* isolated (n = 197).
[b] Out of number tested.
[c] Out of number of MRSA isolates tested.

bacteria or changes in resistance patterns over time. In fact, antibiotic resistance is not a static phenomenon, and where no mitigation efforts are made, the resistance trend is ever increasing. Finally, the results could as well be explained by methodological differences.

We found in this study that Gram-positive bacteria, mostly *S. aureus*, were more prevalent than Gram-negative bacteria, which is consistent with recent findings from the context in similar patient groups [20] but differs from what has been reported in past studies in similar contexts [21,22]. This study reported that 95.4% of all *S. aureus* isolates were MRSA, which is alarming and much higher than in previous MSF studies in the region [19,21–23]. This finding could be related to either a high circulation of MRSA in Iraqi healthcare structures and among healthcare workers or a possible high prevalence of MRSA carriers in the Mosul community, which has been reported elsewhere in Iraq [24–26]. In light of this, MRSA

Table 4
Proportion of ESBL and MDR profiles of Enterobacterales isolated from samples of patients admitted to the Mosul TOC, April 2018–December 2019

Enterobacterales	ESBL-producing n (%)	MDR n (%)
Escherichia coli (n = 30)	28 (93.3)	29 (96.7)
Enterobacter cloacae (n = 26)	24 (92.3)	26 (100)
Klebsiella pneumoniae (n = 22)	20 (90.9)	20 (90.9)
Proteus mirabilis (n = 46)	46 (100)	46 (100)
Other Enterobacterales (n = 27)	22 (81.5)	23 (85.2)
Total (n = 151)	140 (92.7)	142 (94.0)

NOTE: Other Enterobacterales: *Serratia marcescens, Morganella, Providencia stuartii, Proteus rettgerii, Proteus* spp., *Kluyvera intermedia.*

screening for carriers and decolonization should be considered for patients with trauma-affected wounds in Mosul along with specific research on MRSA prevalence in the community. Whilst there was no resistance to vancomycin detected, MRSA isolates were highly resistant to other possible treatment options, thus making vancomycin almost always the obligate choice option; vancomycin is an antibiotic that should be prioritised as a key target of stewardship programme, and it should be carefully monitored because of its potential to form complex resistance according to the WHO AWaRe classifications [15].

The general prevalence of ESBL-producing Gram-negative bacteria was also very high (80.6%) in our study. All *P. mirabilis* isolated were ESBL-producing, as well as 93.3% of *E. coli* and 90.9% of *K. pneumoniae.* When compared to similar studies from trauma centres in the region, many did not perform specific ESBL testing or had small sample sizes. Ronat et al. reported ESBL expression observed in 8 of 13 (61.5%) *Enterobacteriaceae* isolates [23]. The resistance to cefepime by Gram-negative organisms reported in Murphy (67%–93%), Teicher (62% *E. coli*) and Fily (88.0%) indicates that there may be a significant proportion of Enterobacterales in the region that are ESBL [19,21,22]. These findings may indicate that the prevalence of ESBL-producing *Enterobacterales* identified in their studies may be similar to our results.

Resistance to carbapenems was detected in many Gram-negative organisms. Whilst the rate of resistance to meropenem in *P. aeruginosa* is lower than what was reported for other places in the region such as Tehran, Iran [27], it is higher than what was reported in other MSF reports from the context for *P. aeruginosa* and other types of isolates. For instance, Murphy et al. reported carbapenem resistance only in *A. baumannii* [21], Fily et al. reported that overall carbapenem resistance was 'quite rare' (<10% of isolates) [22], Teicher et al. reported 14% imipenem resistance in *E. coli* and 80% resistance in *A. baumannii* [19], and Ronat et al. reported 23% imipenem resistance in *P. aeruginosa* and 33% resistance in *A. baumannii* [23]. Whilst carbapenem-resistant *A. baumannii* has been long reported in the region, in our study *A. baumannii* was rarely isolated among samples. The latter is close to what we have seen in a recent analysis from the region showing that 2% of the isolates included in the study were *A. baumannii* [20]. The low proportion of *Acinetobacter* species seen in recent data, including our results, could be related to a change of the epidemiological landscape of this organism in Iraq, specifically in Mosul.

Carbapenem-resistant infections are difficult to manage. They require antibiotics that are often difficult to obtain in Iraq, and they require strict transmission-based precautions that affect length of stay, patients' and families' psychological wellbeing and healthcare organisation as well as adding a significant economic burden. However, precise figures on the extent of the societal economic burden on ABR in this setting is not known, and further studies are needed [28].

This study showed that among patients with an MDR infection, a very low proportion reported having taken prior antibiotic therapy (2.1%), although this was not statistically significant compared to patients who were non-MDR. This is in contradiction with the known link between previous antibiotic exposure and antibiotic resistance [29]. The low proportion of prior use of antibiotics could be because of underreporting or to a lack of standardised data collection among the healthcare team. It could also reflect a true low self-prescription of antibiotics in this population compared to other populations as trauma wound infections might be considered more complex to treat compared to other types of infections.

Whilst this study brings new information related to ABR patterns in trauma-affected wounds, it has some limitations. Although its strength is in the lengthy study period resulting in a larger sample size than previous MSF studies in the region, the sample is small for measuring statistical significance to detect significant associations between patients' characteristics and MDR infections. However, most of our results were plausible in comparison to others in the literature. Also, some of the characteristics of war-wounded patients were excluded from the study because of their incompleteness. Data encoding is often challenging in a humanitarian setting [30]. Although we do not know how this could have affected our results, we were able to include the main variables of interest.

There was inconsistency in the microbiology analysis for several species, and the susceptibility patterns were performed with the disc diffusion method, which was not confirmed by a more accurate method such as Etest or microbroth dilution method because temporary supply issues. Moreover, the CLSI reference document used was from 2016 and was not updated over time during the study period. Additionally, this analysis utilised the combining of resistant and intermediate results, which at the time of analysis was accepted practice but is now under reconsideration [31]. However, if we were to redo the analysis with the intermediate removed from the resistant category, it would not make a significant effect on our findings.

The study points to further investigation on several fronts. Further investigation of the prevalence of resistance at the community level in Iraq is needed, as well as an understanding of risk factors associated with MDR infections in patients affected by trauma

Table 5
Percentage of resistance to key antibiotics by Enterobacterales isolated from samples of patients admitted to the Mosul TOC, April 2018–December 2019

	E. coli (n = 30)		*E. cloacae* (n = 26)		*K. pneumonia* (n = 22)		*P. mirabilis* (n = 46)		Other Enterobacterales (n = 27)		Total (n = 151)
Antibiotic	n[a]	R (n, %)	n[a]	R (n, %)	n[a]	R (n, %)	n[a]	R (n, %)	n[a]	R (n, %)	R (n, %)
Amikacin	30	3 (10.0)	26	6 (23.1)	21	8 (38.1)	46	8 (17.4)	23	6 (26.1)	31 (20.5)
Ceftriaxone	30	28 (93.3)	26	24 (92.3)	22	20 (90.9)	46	42 (91.3)	23	19 (82.6)	133 (88.1)
Ciprofloxacin	22	15 (68.2)	24	17 (70.8)	12	7 (58.3)	30	10 (33.3)	13	10 (43.5)	49 (32.4)
Gentamycin	30	18 (60.0)	26	24 (92.3)	22	14 (63.6)	46	27 (58.7)	23	17 (73.9)	100 (66.2)
Levofloxacin	9	6 (66.7)	8	5 (62.5)	13	5 (38.5)	25	14 (56.0)	8	3 (13.0)	33 (21.8)
Meropenem	28	4 (14.3)	18	0	14	6 (42.9)	40	9 (22.5)	22	6 (26.1)	25 (16.1)
Imipenem	30	0	26	1 (3.8)	22	9 (40.9)	46	0	23	1 (4.3)	11 (7.3)

R, resistance.
[a] Number tested against antibiotic; other Enterobacterales: *Serratia marcescens, Morganella, Providencia stuartii, Proteus rettgerii, Proteus* spp., *Kluyvera intermedia.*

wounds. More studies are needed to understand the economic and psychological effect of MDR infections and to explore contextual and adapted ways of mitigating the effect of ABR in Iraq and similar post-conflict contexts.

5. Conclusion

This study showed that the prevalence of antibiotic resistance in patients with trauma-affected wounds in Mosul, Iraq, is alarmingly high. It highlights the necessity of having access to microbiological diagnostics and conducting regular microbiology surveillance in order to provide optimal treatment in this kind of context, not only at the facility level, but the establishment of national surveillance systems. Additionally, this study brings to light the need for screening of patients for MRSA in this context to prevent possible healthcare-associated infections and transmission within the facility. The study underscores the importance of antibiotic stewardship in this context as the commonest ABR patterns oblige clinicians to use costly, difficult-to-obtain antibiotics with high resistance selection pressure.

Data sharing

Deidentified microbiological and clinical data and any research documents can be made available on request to the corresponding author. Please note that any request will be assessed by the research committee of MSF Operational Centre Brussels and must be with support from the LuxOR Unit, a signed research agreement and ethics approval from the MSF Ethics Review Board.

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Competing interests

None declared.

Ethical approval

This research fulfilled the exemption criteria set by the Médecins Sans Frontières Ethics Review Board for a posteriori analyses of routinely collected clinical data and thus did not require MSF ERB review. It was conducted with permission from Medical Director, Operational Centre Brussels, Médecins Sans Frontières. ERB approval was obtained from the Ministry of Health and Environment of the Nineveh Health Directorate protocol number 20911 (06/12/2020).

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