Colonization of Extended-spectrum β-lactamase producing Enterobacterales and meticillin-resistant *S. aureus* in the intensive care unit at a tertiary hospital in Tanzania: Implications for Infection control and prevention

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A R T I C L E   I N F O

S U M M A R Y

Background: Multi-drug resistant (MDR) bacteria pose a major global threat to public-health and are of particular concern to hospitalized intensive care unit (ICU) patients. This study aimed at addressing the burden of MDR and the associated factors at admission to ICU.

Methods: This was a cross-sectional study conducted at the ICU of a tertiary hospital in Tanzania. Rectal and anterior nares swabs were collected within 48 hours of ICU admission to screen for extended-spectrum beta-lactamase-producing Enterobacterales (ESBL-PE) and meticillin-resistant *Staphylococcus aureus* (MRSA), respectively.

Results: The proportion of fecal carriage for ESBL-PE at admission to ICU was 54.54% (95% CI, 47.52−61.39), and nasal carriage for MRSA was 9.32% (95%CI, 5.67−14.93). The nasal MRSA colonization (OR = 1.52) and fecal carriage for ESBL-PE (OR=1.38) were more likely in participants who had received antibiotics before ICU admission than not, but association was not statistically significant. Hospitalization for ≥2 days (OR=1.18) was associated with fecal carriage of ESBL-PE, though not statistically significant. Overall, 66% and 73.5% of patients received antibiotics before and upon admission to ICU, respectively. Ceftriaxone, metronidazole and meropenem were commonly prescribed antibiotics. More than 84% of Enterobacterales were resistant to ciprofloxacin and trimethoprim-sulfamethoxazole, and 2.90% were resistant to meropenem. MRSA isolates showed a high rate of resistance to gentamicin and erythromycin.

Conclusion: MDR bacteria are common in patients admitted to ICU. To reduce the risk associated with MDR, we recommend use of simple screening methods to screen for MDR at ICU admission as part of infection control and prevention.

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Background

The intensive care unit (ICU) is often considered the epicenter of infections due to its extremely vulnerable population and the high use of invasive devices. As a result, the ICU has one of the highest incidences of nosocomial infections ranging between 20% to 36% [1,2]. Invasive procedures and high consumption of broad-spectrum antimicrobial agents make the ICU environment a focal point for the emergence and spread of antimicrobial-resistant (AMR) pathogens. Antibiotic use exerts selective pressure leading to the overgrowth of resistant bacterial populations (endogenous colonization). Theoretically, colonization of patients with these pathogens is the prerequisite for subsequent invasive disease [3], and infections in ICU result in significant morbidity, mortality, and high healthcare costs [2,4].

Globally, MRSA and vancomycin-resistant enterococci (VRE) are the most common Gram-positive resistant microorganisms causing infection in ICU patients [3–6], whereas resistance in Gram-negative bacteria is primarily due to the rapid increase of ESBL-PE and MDR in *Pseudomonas aeruginosa*, *Acinetobacter* spp, and *Stenotrophomonas maltophilia* [6–8]. In addition, studies have revealed an increase in ESBL-PE and MDR bacteria in Africa, causing healthcare-acquired infections in ICU [9–12]. Irrational antimicrobial use and MDR bacteria colonization are recognized risk factors for MDR infections leading to increased mortality [12–14].

Recent studies in Tanzania observed an increase in the prevalence of MDR bacteria causing infections and colonization of healthy populations [15–18]. The prevalence of fecal carriage of ESBL-PE in Tanzania ranges between 30% and 50% in hospitals and communities [17–21]. Studies have reported the isolation of MRSA and ESBL-PE in bloodstream infections [15,16], surgical site infections [22,23], and urinary tract infections [24,25]. A more recent study at a referral hospital in Northern Tanzania reported that contaminated cots were associated with MDR-Gram negative bloodstream infections in the critical care unit [26].

Due to increased MDR bacteria reported in clinical settings, control of their spread in the ICU remains a major concern. Developed countries advocate for universal screening of MDR bacteria at ICU admission, but this is not the case in Tanzania. So far in Tanzania, data on MDR bacteria infections and colonization in ICU has been limited to a few studies that found ESBL-PE to be the most common cause of infections in ICUs [26,27]. In addition, MRSA nasal colonization for healthcare workers and patients in ICU was 2.1% and 11.38%, respectively [28]. However, none of these studies looked at MDR bacteria colonization at admission to the ICU. Therefore, we designed this study to address the burden of MDR colonization among patients on admission to the ICU and associated factors.

Materials and methods

Study setting and population

This cross-sectional study was performed for eight months, from July 2018 to February 2019, in the ICUs at Muhimbili National Hospital (MNH), in Dar es Salaam, Tanzania. The MNH is the largest tertiary health care facility in Tanzania with a 1500-bed capacity, which serves as a teaching and tertiary hospital for the population of Dar es Salaam and Tanzania at large. The hospital attends to 1000 to 1500 outpatients per day, admitting 1000 to 1200 inpatients per week. The facility has three ICUs for medical, surgical, obstetrics and gynecology. The medical ICU admits patients with medical-related conditions, the surgical ICU admits patients with different surgical conditions as well as post-surgical procedures, and obstetrics and gynaecology admits patients with obstetrical and gynaecological conditions. In rare cases, children are also admitted to medical and surgical ICUs. Our study enrolled patients admitted to medical and surgical ICUs, which have 31 beds in total.

Patients admitted to ICU during the study period and able to have specimens collected were recruited in this study. Laboratory procedures were conducted at the bacteriology research laboratory at Muhimbili University of Health and Allied Sciences (MUHAS).

Infection prevention and control practice at the study setting

Hand washing is the cornerstone of infection prevention practices, but it is not used consistently. Wearing gloves is commonly practiced, specifically during patient examinations. There is also dedicated staff, primarily for the ICU. However, surveillance, antimicrobial stewardship, and educational interventions are not practiced. In addition, a small number of patients' relatives are also allowed to visit their loved ones.

Data collection

We obtained clinical and demographic information like patients' age, sex, ward before ICU admission, previous hospital antimicrobial exposures, antibiotic usage in hospital (before and after ICU admission), length of hospitalization before ICU admission, history of hospitalization in the past 6 months, co-existing conditions, history of surgery, and invasive procedures from patients' clinical notes.

Specimen collection and laboratory methods

Rectal and nasal swabs were collected within 48 hours of ICU admission for MDR organisms screening. Rectal swabs were screened for ESBL-PE, and MRSA colonization was screened from nasal swabs. Rectal swab specimens were cultured on selective and non-selective media.

The rectal swabs were inoculated on MacConkey agar (Oxoid, UK) supplemented with 2µg/ml of ceftazidime and MacConkey agar (Oxoid, UK) non supplemented by ceftazidime. Both plates were incubated aerobically at 37 °C for 18–24 hours. The plain MacConkey agar plate aimed to check if the swabs contained viable bacteria. Nasal swabs were cultured on sheep blood agar (Oxoid, UK) and incubated aerobically at 33 °C for 18–24 hours for isolation *S. aureus*.

Identification and confirmation of ESBL-PE

Colonies growing on MacConkey agar (Oxoid, UK) supplemented with 2μg/ml of ceftazidime were Gram stained, followed by oxidase testing. All Gram-negative and oxidase-negative colonies were further identified by API 20E (bioMérieux, Marcy-I-Etoile, France). Results were read on APIWEB™ (https://apiweb.biomerieux.com/identIndex). We confirmed ESBL-PE by double disk combination methods, using both ceftazidime (30g) plus ceftazidime-clavulanate (30/10μg) and cefotaxime (30μg) plus cefotaxime-clavulanate (30/10 μg). Performance and interpretation followed clinical and laboratory standard institute guidelines [29].

Identification and confirmation of MRSA

Colonies growing on sheep blood agar were first identified by Gram stain, followed by catalase testing. All Gram-positive cocci and catalase-positive isolates were subjected to tube coagulase test and mannitol fermentation test; positive isolates were identified as *S. aureus*. Finally, all *S. aureus* isolates were subjected to a multiplex polymerase chain reaction (PCR) for confirmation of *S. aureus* and detection of MRSA. The multiplex PCR used two set of primers for the *nuc* and *mec*A genes, which were used to detect *S. aureus* and MRSA, respectively. The primers and conditions for the multiplex PCR have been previously described [30].

Antimicrobial susceptibility testing

Antimicrobial susceptibility testing for both ESBL-PE and MRSA was performed by the Kirby Bauer disk diffusion method. Performance and interpretation were made following the clinical and laboratory standard institute (CLSI) guidelines [29].

Statistical analysis

Data were analyzed using STATA/IC 16.1 (StataCorp LCC, 4905 Lakeway Drive College Station, Texas 77845 USA). Categorical variables were presented by frequency, proportions, and percentages. Numerical variables like age were presented by means and standard deviation. The Chi-square test or Fisher's exact test was used to compare the association between two categorical variables. Logistic regression was used to analyze associations between independent variables and dependent variables. A *p*-value <0.05 was considered statistically significant.

Ethical consideration

We obtained ethical clearance from MUHAS Senate Research and Publications Committee. Permission to conduct the study at MNH was obtained from the MNH Director of Research. Written informed consent was requested from the patients or guardians or legally authorized persons (for unconscious patients) to participate in the study.

Results

Clinical and demographic characteristics of the study participants

The study enrolled a total of 228 patients admitted to ICUs, but only 198 had complete data analysed in this study. The age distribution ranged from 1−95 years, with a mean age of 40.70 years, standard deviation (SD) 22.51. Participants in the age group 46−60 years and 16−30 years were more frequent than other groups, and 1−15 years was the least frequent age group. Males accounted for most of the enrolled participants, and most of participants had more than one underlying disease. The majority of patients were transferred from the emergency medicine department (EMD) and medical wards. More than half of participants were hospitalized for one day before being transferred to ICU. More than two-thirds of participants had no prior hospitalization in the six months preceding ICU admission. However, the previous hospitalization status of 28 participants was unknown. Antibiotic use prior to ICU admission was widespread, accounting for 66% of all participants (Table I).

The proportion of feacal ESBL-PE and nasal MRSA colonization at ICU admission

Overall, the proportion of patients with fecal carriage of ESBL-PE at admission to ICU was 54.54% (108/198), 95% CI 47.52−61.39. Meanwhile, the proportion of patients with nasal carriage for MRSA was 9.32 (15/161), 95%CI 5.67−14.93. Patients who received antibiotics before admission had a higher proportion of ESBL-PE fecal carriage than those who did not (Table II). The difference, however, was not statistically significant (*p*-value 0.285). The proportion of patients with fecal carriage for ESBL-PE at ICU admission did not differ by age group, gender, ward prior to ICU admission, or days hospitalized prior to ICU admission (*p*-value > 0.05). Those who had no prior history of hospitalization in the previous six months had higher fecal carriage of ESBL-PE than those who had history of hospitalization (*P*-value 0.037).

Factors associated with feacal carriage of ESBL-PE and nasal MRSA colonization at ICU admission

Hospitalization for two or more days before ICU admission (OR=1.18) and antibiotic use prior to ICU admission (OR=1.38) showed a trend of increased odds of feacal carriage of ESBL-PE. However, the association was not statistically significant (Table III). Previous hospitalization in the last six months was protective for the fecal carriage of ESBL-PE, OR 0.50 (95%CI 0.26−0.96, *p* 0.038). Nasal MRSA colonization was more likely in participants who had received antibiotics prior to ICU admission (OR = 1.52) than those who had not. However, the likelihood was not statistically significant (95%CI 0.46−5.018, *p* 0.491) (Table III).

Antibiotic prescription patterns among the study participants

Overall, 66% of patients received antibiotics prior to admission to ICU. Subsequently, 73.5% of participants were prescribed antibiotics upon ICU admission. Ceftriaxone and metronidazole were two antibiotics that were commonly administered both before and after ICU admission. In addition, meropenem was also a common antibiotic prescribed in the ICU (Figure 1). In both cases, before and after ICU admission, antibiotics were administered to 37% of the participants without any documentation of an indication for antibiotic prescription. Sepsis, pneumonia, and surgical antimicrobial

Table I
Demographic and clinical characteristics of patients admitted to ICU

Variables	Frequency	Percentage/ mean (SD)
Age (years)		
Mean		40.70 SD 22.51
Age group		
1—15	29	14.65
16—30	47	23.74
31—45	36	18.37
46—60	47	23.74
≥61	37	18.88
Sex		
Male	115	58.09
Female	83	41.91
Underlying diseases		
Septicemia	46	23.23
Kidney disease & Respiratory disease	26	13.13
Post-exploratory laparotomy	33	16.67
Malginant & HIV	34	17.17
Stroke & DM	36	18.18
Others	23	11.62
Ward before ICU admission		
EMD	71	35.86
Medical	68	34.34
Surgical	47	23.74
Pediatric	12	6.06
Days hospitalized before ICU admission		
1	119	60.10
2—3	25	12.63
4—7	29	14.65
≥8	25	12.63
Hospitalization in last six months		
Yes	53	31.18
No	117	68.82
Antibiotic use before ICU admission		
Yes	131	66.16
No	67	33.84

HIV-Human immunodeficiency virus, DM-Diabetes mellitus, EMD-Emergency department, ICU-Intensive care unit, SD-standard deviation.

Table II
Proportion of fecal ESBL-PE and nasal MRSA colonization at ICU admission

Variables	Frequency	ESBL	p-value
Age (years)			
1—15	29	16 (51.72)	0.873
16—30	47	25 (53.19)	
31—45	36	23 (62.16)	
46—60	47	24 (51.06)	
≥61	37	21 (55.26)	
Sex			
Male	115	62 (53.91)	0.893
Female	83	45 (54.88)	
Underlying diseases			
Septicemia	46	25 (54.35)	0.752
Kidney diseases & Respiratory diseases	26	15 (57.69)	
Post-exploratory laparotomy	33	19 (57.58)	
Malginant & HIV	34	19 (55.88)	
Stroke & DM	36	19 (58.33)	
Others	23	9 (39.13)	
Ward before ICU admission			
EMD	71	40 (56.34)	0.437
Medical	68	34 [41]	
Surgical	47	25 (53.19)	
Pediatric	12	9 (75.00)	
Days hospitalized before ICU admission			
1	119	63 (52.94)	0.296
2—3	25	14 (56)	
4—7	29	20 (68.97)	
≥8	25	11 (44)	
Hospitalization in last 6 months			
Yes	53	24 (45.28)	0.037
No	117	73 (62.39)	
Antibiotic use before ICU admission			
Yes	131	75 (57.25)	0.285
No	67	33 (49.25)	

HIV-Human immunodeficiency virus, DM-Diabetes mellitus, EMD-Emergency department, ICU-Intensive care unit.

prophylaxis were the most common indications for antibiotic prescription in both settings for those with documented indication for antibiotic use.

Bacterial isolates and antimicrobial susceptibility patterns

Overall, 138 Enterobacterales were isolated from 108 participants with fecal carriage of ESBL-PE. *Escherichia coli* was the most common, accounting for 88 (64%) isolates, followed by *Klebsiella pneumoniae,* 39 (28%) isolates. Overall, 84% and 90% of Enterobacterales were resistant to ciprofloxacin and trimethoprim-sulfamethoxazole, respectively. *Klebsiella pneumoniae* showed a higher percentage of resistance above 69% to ciprofloxacin, trimethoprim-sulfamethoxazole, and gentamicin (Table IV). Overall, Enterobacterales displayed low

resistance to imipenem; only 2.9% were resistant. MRSA isolates showed a high percentage of resistance to gentamicin (80%), erythromycin (93%), and ciprofloxacin (60%).

Discussion

Review of previous studies on MDR bacteria in Tanzania revealed paucity of information regarding MDR bacteria colonization at admission to the ICU. Therefore, this study was designed to shed light on the burden of MDR colonization among patients on admission to the ICU and associated factors. The present study conducted during admission to the ICU revealed that more than half of the patients had fecal carriage of ESBL-PE. The finding indicates that most patients were at risk of contracting ESBL-PE infections during their course of admission to the ICU. As previous studies have shown, colonization with resistant bacteria is the pre-request for

Table III
Factors associated for fecal carriage of ESBL-PE and nasal colonization of MRSA

Variables	Frequency	Proportion of ESBL carriage	OR	95%CI	P-value
Days hospitalized before ICU admission					
1	119	63 (52.94)	1		
≥2	79	45 (56.96)	1.18	0.66−2.09	0.578
Hospitalization in last 6 months					
No	117	73 (62.39)	1		
Yes	53	24 (45.28)	0.50	0.26−0.96	0.038
Antibiotic use before ICU admission					
No	67	33 (49.25)	1		
Yes	131	75 (57.25)	1.38	0.76−2.49	0.286
Proportion of MRSA colonization					
Days hospitalized before ICU admission					
1	91	9 (9.89)	1		
≥2	70	6 (8.6)	0.96	0.86−1.06	0.410
Hospitalization in last 6 months					
No	123	12 (9.76)	1		
Yes	36	3 [42]	0.84	0.22−3.16	0.797
Antibiotic use before ICU admission					
No	56	4 (7.14)	1		
Yes	105	11 (10.48)	1.52	0.46−5.02	0.491

subsequent infections [3,31]. On the other hand, the high carriage we have observed in these patients at admission indicates a high risk of spreading ESBL-PE to other patients admitted to the ICU. Our findings align with those of our earlier investigations conducted in Dar es Salaam among inpatients (35−64%) and outpatients (32.6%) [18−20,32], which revealed a significant proportion of fecal carriage for ESBL-PE and previous use of antibiotic was found to be a reason for the high carriage. Previous use of antibiotics and hospitalization have all been associated with fecal carriage of ESBL-PE [13,19,20]. Almost 66% of the patients in the present study had used antibiotics before admission, but only 31% had previously been

hospitalization in the last six months. Our findings of high fecal carriage of ESBL-PE advocate for implementing targeted or universal screening for ESBL-PE during ICU admission to reduce the risk associated with ESBL-PE infections, including increased mortality and healthcare costs. Screening for ESBL-PE, on the other hand, should be combined with additional infection prevention strategies such as decolonization, contact precautions for confirmed cases, and isolation of patients at risk of ESBL-PE colonization during ICU admission. All these measures are not taken at our study setting, putting patients at an increased risk for ESBL-PE infections. However, in this limited resource setting, a cost analysis of screening in comparison
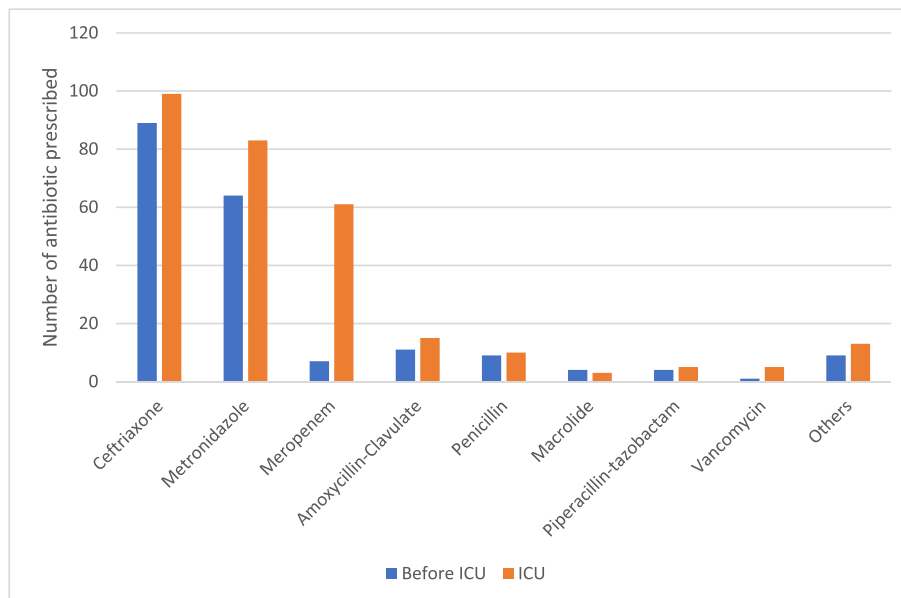

Figure 1. Antibiotic prescription patterns among the study participants.

Table IV
Antimicrobial susceptibility pattern ESBL PE and MRSA

Bacteria	Percentage resistance					
	Imipenem	SXT	Gentamicin	Ciprofloxacin	Erythromycin	Clindamycin
E. coli (88)	2.27	88.64	46.59	84.09	-	-
K. pneumoniae (39)	5.13	89.74	69.23	82.05	-	-
Other Enterobacterales (11)	0	100	81.81	90.91	-	-
Overall Enterobacterales (138)	2.90	89.86	55.47	84.06	-	-
MRSA [41]	-	-	80	60	93.33	46.67

SXT: Trimethoprim-sulfamethoxazole.

with the implication of not screening should be performed. But, in other settings, the benefit of screening for MDR colonization outweighs that of not screening in the prevention of infections.

We found a relatively low proportion (9%) of MRSA nasal carriage at admission to the ICU less than previously reported from the same hospital [28]. However, the previous study investigated patients already admitted to the ICU, accounting for a much higher proportion. The ICU itself has been regarded as an epicenter for the emergence and spread of MDR bacteria [33]. This explains the high proportion of MRSA observed in previous studies [13,28]. The low proportion of MRSA observed in our study could be accounted for by screening for colonization from only one anatomical site (the anterior nares). Combinations of swabs from anterior nares, perineal, and groins have been shown to increase the proportion of MRSA colonization [34,35]. In addition, we used general purpose medium instead of selective medium for MRSA, which could have led to missing some MRSA strains, as in colonization carriage of both phenotypic strains of MRSA and meticillin-susceptible *S. aureus* is a common phenomena. The proportion of nasal carriage of MRSA observed in our study still puts these patients at risk for subsequent MRSA infections, which are frequently serious and have a poor treatment outcome. Furthermore, these patients may also act as reservoirs for MRSA spread in the ICU if control and preventive measures are not implemented.

Identifying risk factors for carriage of MDR bacteria upon ICU admission is critical for selecting effective control and prevention strategies and planning for resource allocation. The present study demonstrated that antibiotic use before ICU admission was associated with both fecal carriage of ESBL-PE and nasal carriage of MRSA. On the other hand, hospitalization for ≥2 days before ICU admission was associated with fecal carriage of ESBL-PE. Antibiotic overuse exerts selective pressure, favoring the overgrowth of antibiotic-resistant bacteria populations. Meanwhile, hospitalization increases the chances of exogenous acquisition of antibiotic-resistant bacteria by direct or indirect transmission. Previous studies have also documented that antibiotic use before hospitalization and days of hospitalization are risk factors for the carriage of multidrug resistant bacteria [17,18,36].

Although our findings did not show a factor that had a strong association with fecal carriage of ESBL-PE or nasal carriage of MRSA, the likelihood of these factors being associated with carriage of MDR was present, as observed in univariate analysis. The lack of independent association between factors and carriage of MDR observed in the current study indicates that risks for carriage are evenly distributed. The lack of an independent

association with antibiotic use could be explained by recall bias, as we only collected data from clinical case notes. On the other hand, referral notes, in most instances, did not document a history of antibiotics. A small sample size could also explain the lack of an independent association between hospital stay and ESBL-PE and MRSA carriage. Our findings support the introduction of universal screening for carriage of MDR upon ICU admission in our settings, followed by either contact isolation or decolonization as previously advocated in settings with a high prevalence of MDR bacteria [37,38]. This would help reduce the risk of infection caused by MDR in already immunocompromised ICU patients.

The finding of previous hospitalization being protective against carriage of ESBL-PE in this population is contrary to observations from previous studies [13,39]. The single centre and small sample size may have underpowered our study to detect a plausible association. In addition, depending on information from clinical case notes to collect information could have led to recall biases. Most of the participants were seriously ill and some were not conscious; for other patients, we could not find relatives to gather information from or relatives could not recall.

We observed that most patients in this study were prescribed antibiotics before and upon admission to the ICU. More than a quarter of prescriptions had no indications. For those with indications, investigation of suspected infections was rarely done as bacterial culture results could not be traced in the patients' case notes. Ceftriaxone and meropenem were commonly prescribed antibiotics: these antibiotics have high resistance potential [40]. The association between the irrational use of a WHO "watch" group antibiotics and antibiotic-resistant bacteria is well known [18,19]. The use of ceftriaxone could explain the high proportion of fecal carriage of ESBL-PE observed in this study. On the other hand, if suspected infections in this study were due to ESBL-PE, treatment with ceftriaxone could have been ineffective. Our findings of ESBL-PE carriage, increased use of ceftriaxone and meropenem, and failure to perform bacteria culture and sensitivity tests in the study setting call for the establishment and strengthening of infection control and prevention, as well as antimicrobial stewardship programs.

The majority of antibiotics tested in this study were ineffective in treating ESBL-PE infections. Even though these antibiotics were not regularly prescribed in our study population, they are widely available and marketed over-the-counter in the country. Our findings align with prior research reports from around the country [15,24,27], demonstrating that ESBL-PE and MRSA are highly resistant to most antibiotics. However, only 3% of Enterobacterales were resistant to meropenem, indicating that it is

still useful in treating ESBL-PE infections. This antibiotic has a high potential of developing resistance, being grouped in WHO watch classification has a relatively high risk of selecting bacterial resistance [40]. The use of meropenem in this setting needs to be controlled and closely monitored and should be a key target in the local antimicrobial stewardship program. Without robust control measures, this antibiotic will soon become ineffective, as our observation is that it is commonly prescribed in the ICU without confirmatory objective evidence of causative agents by culture.

One of the limitations of our study is that we were not able to account for antibiotic use in the community, leading to this high rate of fecal carriage for ESBL-PE, and this is a single-center study that is not necessarily generalizable. Furthermore, this study failed to take into account whether the ESBL-PE was acquired from community or hospital.

In conclusion: MDR bacteria are common in patients admitted to our ICU. To reduce the risk of ESBL-PE and other MDR bacteria, we recommend that facilities across the country use the simple screening method for ESBL-PE at ICU admission. Furthermore, we recommend that further infection-prevention strategies for MDR bacteria be used in the study setting, such as preemptive isolation of patients at risk of MDR bacteria carriage, decolonization, and contact precautions.

Credit author statement

JM conceived the study, collected data and funding acquisition. JM and UK performed the microbiological investigations. JM performed formal analysis and drafted the manuscript. MM, DK and EFL revised the manuscript. All authors approved the final version.

Conflict of interest statement

The authors declare that they have no conflicts of interests.

References

[1] Araç E, Kaya Ş, Parlak E, Büyüktuna SA, Baran A, Akgül F, et al. [Evaluation of Infections in Intensive Care Units: A Multicentre Point-Prevalence Study]. Mikrobiyoloji Bulteni 2019;53(4):364—73. https://doi.org/10.5578/mb.68665.

[2] Ntusi NB, Badri M, Khalfey H, Whitelaw A, Oliver S, Piercy J, et al. ICU-associated *Acinetobacter baumannii* colonisation/infection in a high HIV-prevalence resource-poor setting. PLoS One 2012;7(12):e52452. https://doi.org/10.1371/journal.pone.0052452.

[3] Nurjadi D, Eichel VM, Tabatabai P, Klein S, Last K, Mutters NT, et al. Surveillance for Colonization, Transmission, and Infection With Methicillin-Susceptible *Staphylococcus aureus* in a Neonatal Intensive Care Unit. JAMA Netw Open 2021;4(9):e2124938. https://doi.org/10.1001/jamanetworkopen.2021.24938.

[4] Alhunaif SA, Almansour S, Almutairi R, Alshammari S, Alkhonain L, Alalwan B, et al. Methicillin-Resistant *Staphylococcus Aureus* Bacteremia: Epidemiology, Clinical Characteristics, Risk Factors, and Outcomes in a Tertiary Care Center in Riyadh, Saudi Arabia. Cureus 2021;13(5):e14934. https://doi.org/10.7759/cureus.14934.

[5] Sivaradjy M, Gunalan A, Priyadarshi K, Madigubba H, Rajshekar D, Sastry AS. Increasing Trend of Vancomycin-resistant Enterococci Bacteremia in a Tertiary Care Hospital of South India: A Three-year Prospective Study. Indian J Crit Care Med 2021;25(8):881—5. https://doi.org/10.5005/jp-journals-10071-23916.

[6] Chang Y, Jeon K, Lee SM, Cho YJ, Kim YS, Chong YP, et al. The Distribution of Multidrug-resistant Microorganisms and Treatment Status of Hospital-acquired Pneumonia/Ventilator-associated Pneumonia in Adult Intensive Care Units: a Prospective Cohort Observational Study. J Kor Med Sci 2021;36(41):e251. https://doi.org/10.3346/jkms.2021.36.e251.

[7] Mao P, Deng X, Yan L, Wang Y, Jiang Y, Zhang R, et al. Whole-Genome Sequencing Elucidates the Epidemiology of Multidrug-Resistant *Acinetobacter baumannii* in an Intensive Care Unit. Front Microbiol 2021;12:715568. https://doi.org/10.3389/fmicb.2021.715568.

[8] Fursova NK, Astashkin EI, Ershova ON, Aleksandrova IA, Savin IA, Novikova TS, et al. Multidrug-Resistant *Klebsiella pneumoniae* Causing Severe Infections in the Neuro-ICU. Antibiotics 2021;10(8). https://doi.org/10.3390/antibiotics10080979.

[9] Morkel G, Bekker A, Marais BJ, Kirsten G, van Wyk J, Dramowski A. Bloodstream infections and antimicrobial resistance patterns in a South African neonatal intensive care unit. Paediatr Int Child Health 2014;34(2):108—14. https://doi.org/10.1179/2046905513y.0000000082.

[10] El Kettani A, Zerouali K, Diawara I, Ouhadous M, Harrar N, Belabbes H, et al. [Healthcare-associated bacteraemia in intensive care units of Ibn Rochd University Hospital, Casablanca]. Sante Publique 2017;29(2):209—13.

[11] Talaat M, Hafez S, Saied T, Elfeky R, El-Shoubary W, Pimentel G. Surveillance of catheter-associated urinary tract infection in 4 intensive care units at Alexandria university hospitals in Egypt. Am J Infect Control 2010;38(3):222—8. https://doi.org/10.1016/j.ajic.2009.06.011.

[12] El Mekes A, Zahlane K, Ait Said L, Tadlaoui Ouafi A, Barakate M. The clinical and epidemiological risk factors of infections due to multi-drug resistant bacteria in an adult intensive care unit of University Hospital Center in Marrakesh-Morocco. J Infect Public Health 2020;13(4):637—43. https://doi.org/10.1016/j.jiph.2019.08.012.

[13] Fouda R, Soliman MS, ElAnany MG, Abadeer M, Soliman G. Prevalence and risk factors of MRSA, ESBL and MDR bacterial colonization upon admission to an Egyptian medical ICU. J Infect Dev Ctries 2016;10(4):329—36. https://doi.org/10.3855/jidc.6798.

[14] Gallaher JR, Banda W, Lachiewicz AM, Krysiak R, Cairns BA, Charles AG. Colonization with Multidrug-Resistant Enterobacteriaceae is Associated with Increased Mortality Following Burn Injury in Sub-Saharan Africa. World J Surg 2018;42(10):3089—96. https://doi.org/10.1007/s00268-018-4633-7.

[15] Manyahi J, Kibwana U, Mgimba E, Majigo M. Multi-drug resistant bacteria predict mortality in bloodstream infection in a tertiary setting in Tanzania. PLoS One 2020;15(3):e0220424. https://doi.org/10.1371/journal.pone.0220424.

[16] Moyo SJ, Manyahi J, Blomberg B, Tellevik MG, Masoud NS, Aboud S, et al. Bacteraemia, Malaria, and Case Fatality Among Children Hospitalized With Fever in Dar es Salaam, Tanzania. Front Microbiol 2020;11:2118. https://doi.org/10.3389/fmicb.2020.02118.

[17] Moremi N, Claus H, Rutta L, Frosch M, Vogel U, Mshana SE. High carriage rate of extended-spectrum beta-lactamase-producing Enterobacteriaceae among patients admitted for surgery in Tanzanian hospitals with a low rate of endogenous surgical site infections. J Hosp Infect 2018;100(1):47–53. https://doi.org/10.1016/j.jhin.2018.05.017.

[18] Tellevik MG, Blomberg B, Kommedal Ø, Maselle SY, Langeland N, Moyo SJ. High Prevalence of Faecal Carriage of ESBL-Producing Enterobacteriaceae among Children in Dar es Salaam, Tanzania. PLoS One 2016;11(12):e0168024. https://doi.org/10.1371/journal.pone.0168024.

[19] Manyahi J, Moyo SJ, Tellevik MG, Langeland N, Blomberg B. High Prevalence of Fecal Carriage of Extended Spectrum β-Lactamase-Producing Enterobacteriaceae Among Newly HIV-Diagnosed Adults in a Community Setting in Tanzania. Microb Drug Resist 2020;26(12):1540–5. https://doi.org/10.1089/mdr.2020.0066.

[20] Kibwana UO, Majigo M, Kamori D, Manyahi J. High fecal carriage of extended Beta Lactamase producing Enterobacteriaceae among adult patients admitted in referral hospitals in Dar es Salaam, Tanzania. BMC Infect Dis 2020;20(1):557. https://doi.org/10.1186/s12879-020-05272-4.

[21] Seni J, Akaro IL, Mkinze B, Kashinje Z, Benard M, Mboowa G, et al. Gastrointestinal Tract Colonization Rate of Extended-Spectrum Beta-Lactamase-Producing Gram-Negative Bacteria and Associated Factors Among Orthopaedic Patients in a Tertiary Hospital in Tanzania: Implications for Infection Prevention. Infect Drug Resist 2021;14:1733–45. https://doi.org/10.2147/idr.S303860.

[22] Manyahi J, Matee MI, Majigo M, Moyo S, Mshana SE, Lyamuya EF. Predominance of multi-drug resistant bacterial pathogens causing surgical site infections in Muhimbili National Hospital, Tanzania. BMC Res Notes 2014;7:500. https://doi.org/10.1186/1756-0500-7-500.

[23] Moremi N, Claus H, Vogel U, Mshana SE. The role of patients and healthcare workers *Staphylococcus aureus* nasal colonization in occurrence of surgical site infection among patients admitted in two centers in Tanzania. Antimicrob Resist Infect Control 2019;8:102. https://doi.org/10.1186/s13756-019-0554-y.

[24] Manyahi J, Moyo SJ, Tellevik MG, Ndugulile F, Urassa W, Blomberg B, et al. Detection of CTX-M-15 beta-lactamases in Enterobacteriaceae causing hospital- and community-acquired urinary tract infections as early as 2004, in Dar es Salaam, Tanzania. BMC Infect Dis 2017;17(1):282. https://doi.org/10.1186/s12879-017-2395-8.

[25] Ahmed M, Moremi N, Mirambo MM, Hokororo A, Mushi MF, Seni J, et al. Multi-resistant gram negative enteric bacteria causing urinary tract infection among malnourished underfives admitted at a tertiary hospital, northwestern, Tanzania. Ital J Pediatr 2015;41:44. https://doi.org/10.1186/s13052-015-0151-5.

[26] Silago V, Kovacs D, Msanga DR, Seni J, Matthews L, Oravcová K, et al. Bacteremia in critical care units at Bugando Medical Centre, Mwanza, Tanzania: the role of colonization and contaminated cots and mothers' hands in cross-transmission of multidrug resistant Gram-negative bacteria. Antimicrob Resist Infect Control 2020;9(1):58. https://doi.org/10.1186/s13756-020-00721-w.

[27] Ndugulile F, Jureen R, Harthug S, Urassa W, Langeland N. Extended spectrum beta-lactamases among Gram-negative bacteria of nosocomial origin from an intensive care unit of a tertiary health facility in Tanzania. BMC Infect Dis 2005;5:86. https://doi.org/10.1186/1471-2334-5-86.

[28] Geofrey A, Abade A, Aboud S. Methicillin-resistant *Staphylococcus aureus* (MRSA) colonization among Intensive Care Unit (ICU) patients and health care workers at Muhimbili national hospital, Dar Es Salaam, Tanzania, 2012. Pan Afr Med J 2015;21:211. https://doi.org/10.11604/pamj.2015.21.211.4207.

[29] Clinical and Laboratory Standards Institute. Performance Standards for Antimicrobial Susceptibility Testing; Twentieth Informational Supplement CLSI Document M100–S20. Wayne, PA: Clinical and Laboratory Standards Institute; 2019.

[30] Moyo SJ, Aboud S, Blomberg B, Mkopi N, Kasubi M, Manji K, et al. High nasal carriage of methicillin-resistant *Staphylococcus aureus* among healthy Tanzanian under-5 children. Microb Drug Resist 2014;20(1):82–8. https://doi.org/10.1089/mdr.2013.0016.

[31] Ruppé E, Lixandru B, Cojocaru R, Büke C, Paramythiotou E, Angebault C, et al. Relative fecal abundance of extended-spectrum-β-lactamase-producing *Escherichia coli* strains and their occurrence in urinary tract infections in women. Antimicrob Agents Chemother 2013;57(9):4512–7. https://doi.org/10.1128/aac.00238-13.

[32] Mwandigha AM, Kamori D, Kibwana UO, Masoud S, Manyahi J, Majigo M. Fecal carriage and factors associated with extended-spectrum β-lactamase-producing Enterobacteriaceae among pregnant women at the tertiary referral hospital, Tanzania. Trop Med Health 2020;48:84. https://doi.org/10.1186/s41182-020-00271-2.

[33] Fridkin SK. Increasing prevalence of antimicrobial resistance in intensive care units. Crit Care Med 2001;29(4 Suppl):N64–8. https://doi.org/10.1097/00003246-200104001-00002.

[34] Chipolombwe J, Török ME, Mbelle N, Nyasulu P. Methicillin-resistant *Staphylococcus aureus* multiple sites surveillance: a systemic review of the literature. Infect Drug Resist 2016;9:35–42. https://doi.org/10.2147/idr.S95372.

[35] Kyaw WM, Lee LK, Siong WC, Ping AC, Ang B, Leo YS. Prevalence of and risk factors for MRSA colonization in HIV-positive outpatients in Singapore. AIDS Res Ther 2012;9(1):33. https://doi.org/10.1186/1742-6405-9-33.

[36] Moschou A, Ioannou P, Moraitaki E, Stafylaki D, Maraki S, Samonis G, et al. Rectal Colonization by Drug Resistant Bacteria in Nursing Home Residents in Crete, Greece. Trav Med Infect Dis 2021;6(3). https://doi.org/10.3390/tropicalmed6030123.

[37] Huskins WC. Interventions to prevent transmission of antimicrobial-resistant bacteria in the intensive care unit. Curr Opin Crit Care 2007;13(5):572–7. https://doi.org/10.1097/MCC.0b013e3282efc30e.

[38] Chaberny IF, Schwab F, Ziesing S, Suerbaum S, Gastmeier P. Impact of routine surgical ward and intensive care unit admission surveillance cultures on hospital-wide nosocomial methicillin-resistant *Staphylococcus aureus* infections in a university hospital: an interrupted time-series analysis. J Antimicrob Chemother 2008;62(6):1422–9. https://doi.org/10.1093/jac/dkn373.

[39] Jolivet S, Vaillant L, Poncin T, Lolom I, Gaudonnet Y, Rondinaud E, et al. Prevalence of carriage of extended-spectrum β-lactamase-producing enterobacteria and associated factors in a French hospital. Clin Microbiol Infect 2018;24(12):1311–4. https://doi.org/10.1016/j.cmi.2018.03.008.

[40] Hsia Y, Lee BR, Versporten A, Yang Y, Bielicki J, Jackson C, et al. Use of the WHO Access, Watch, and Reserve classification to define patterns of hospital antibiotic use (AWaRe): an analysis of paediatric survey data from 56 countries. Lancet Global Health 2019;7(7):e861–71. https://doi.org/10.1016/s2214-109x(19)30071-3.