



Research article

An alarming prevalence of multidrug-resistant (MDR) ESKAPE pathogens and other drug-resistant bacteria isolated from patients with bloodstream infections hospitalized at Muhimbili National Hospital in Dar es Salaam, Tanzania

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Abstract

This study was conducted between April and May 2023 at the Muhimbili National Hospital in Tanzania to determine the prevalence of multidrug-resistant (MDR) ESKAPE and other drug-resistant bacteria isolated from 856 patients with bloodstream infections (BSIs). The prevalence of BSIs was 37.3% (319/856), with 5% (17/319) of the patients having polymicrobial infections. The prevalence of BSIs was slightly greater among males (38.3%, 162/423) than females (36.3%, 157/433) ($p=0.585$). Most of the infections occurred in children aged <1 year (45.3%, 149/329) or adults aged ≥ 61 years (45.7%, 37/81) ($p=0.001$). Patients admitted to the intensive care unit (ICU) had significantly greater BSIs (44%; 113/258) than those admitted to other wards (34.4%; 206/599) ($p=0.006$). The ESKAPE pathogens accounted for 43.28% of all the isolates, predominantly *Staphylococcus aureus* (16.4%), followed by *Klebsiella pneumoniae* (9.25%), *Acinetobacter* spp. (6.86%), and *Pseudomonas aeruginosa* (4.77%). The overall proportion of MDR bacteria was 83.8%, and 63.64% were resistant to more than four classes of antibiotics. Among the remaining strains, 23.4% of the ESKAPE pathogens and 10% of the MDR *Enterobacterales* were resistant to eight different classes of the tested antibiotics and were regarded as extensively drug-resistant (XDR). Resistance to 3rd generation cephalosporins was observed in 91% of the *Klebsiella pneumoniae* isolates and all the *Enterobacter* spp. The proportion of methicillin-resistant *S. aureus* (MRSA) was 71.4%. Based on these results, we strongly discourage empiric treatment of BSIs and recommend that laboratory results guide all prescriptions. Immediate action is undoubtedly needed to introduce rapid drug resistance tests and review the existing management guidelines.

Keywords: Bloodstream infections, ESKAPE pathogens, Multidrug-resistant, Sepsis, Tanzania

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Introduction

Bloodstream infections (BSIs) are often associated with life-threatening clinical conditions worldwide (Bassetti et al., 2016; Martinez and Wolk, 2016). These infections occur annually in approximately 30 million people, causing approximately 6 million deaths (Fleischmann et al., 2016; Fleischmann-Struzek et al., 2018). BSIs caused by drug-resistant bacteria have been associated with significant morbidity and mortality, prolonged hospital stays, and an increased cost of hospital care (Folgori et al., 2014). Among the most predominant multi-drug-resistant bacteria (MDR) that cause BSIs, the ESKAPE group of bacteria consists of *E. faecium*, *S. aureus*, *K. pneumoniae*, *A. baumannii*, *P. aeruginosa*, and *Enterobacter* spp (Navidinia, 2016; Mulani et al., 2019). Together with other MDR *Enterobacterales*, such as *E. coli*, the ESKAPE bacteria account for 5–7% of the infections observed in intensive care units (Di Franco et al., 2021). Globally, the prevalence of ESKAPE pathogens causing BSI has been reported, with an isolation rate of >40% among ESKAPE

pathogens (Marturano and Lowery, 2019; Benkő et al., 2020; Peng et al., 2021).

Like many other bacterial pathogens, the pathogenesis of BSIs by ESKAPE pathogens is often initiated by colonizing mucosal surfaces, subsequently invading tissues and evading the host's immune defenses. Their ability to form biofilms and resist antibiotics, coupled with a propensity for healthcare-associated transmission, underscores the challenge in managing bloodstream infections caused by ESKAPE pathogens (Thomer et al., 2016; Lisowska-Lysiak et al., 2021).

In many low- and middle-income countries (LMICs), the management of BSIs is predominantly empirical due to the constraints of performing blood cultures (Ombelet et al., 2019). This ineffective approach has been associated with poor clinical outcomes and escalation of antimicrobial resistance (Sommer et al., 2017; Micek et al., 2018; De Oliveira et al., 2020). Laboratory-based management of BSI through conventional susceptibility methods is less favorable due to a slow turnaround time (Tjandra

et al., 2022). Unfortunately, the advanced automated rapid culture and drug susceptibility tests readily available in high-income countries (HICs) are not affordable in most LMICs (Ombelet et al., 2019). To address this challenge, continuous antimicrobial surveillance of BSIs is highly recommended for generating antibiograms to guide empirical treatment of BSI pathogens (Mun et al., 2022).

We carried out this study to determine the antimicrobial profiles of ESKAPE pathogens and drug-resistant bacteria that cause BSI at the largest hospital in Tanzania. We intended to provide data that will be useful in managing BSI in a hospital setting similar to many other facilities in LMICs. Like in many other facilities in LMICs, the management of BSIs is largely empirical, and treatment is often administered before microbiological identification (ID) and antimicrobial susceptibility testing (AST) are performed.

Materials and methods

Study design, duration, and setting

This cross-sectional hospital-based study was conducted between April and May 2023 at Muhimbili National Hospital (MNH), the largest tertiary hospital in Tanzania. The hospital also serves as a teaching hospital for the Muhimbili University of Health and Allied Sciences (MUHAS).

Study population, sample size, and sampling procedure

We enrolled patients with clinical features suggestive of BSI who were hospitalized at MNH during the study period. The sample size was calculated using Cochran’s formula (Cochran, 1977).

$$N = Z^2 P(1 - P) / \varepsilon^2$$

Where N : is the sample size, ε : is the desired level of precision, the margin of error, P : is the fraction of the population (as a percentage) that displays the attribute, and Z : is the z-value, extracted from a z-table. Based on the results of a previous study performed at the same facility, we estimated the prevalence of BSIs to be 11.4% (Manyahi et al., 2020), which led to a minimum sample size of 155.

Data collection, blood specimen collection, culture, and identification of bacteria

Patient demographic characteristics, clinical information, and blood culture and antimicrobial susceptibility test (AST) results were recorded via a structured tool. 10 mL of blood was aseptically drawn from adult patients and 3 mL of blood from pediatric patients and collected into blood culture bottles (BD BACTEC Plus Aerobic/F Culture Vials, Becton Dickinson and Company, New Jersey, United States) for adults and (BD BACTEC Peds PlusTM/F Culture Vials, Becton Dickinson Co., New Jersey, USA) for children. The samples were incubated at 35°C in a BD BACTEC FX40 analyzer for a maximum of five days (120 hours) for negative cultures, as indicated by the BD BACTEC analyzer. 1mL of positive blood culture, as indicated by the BD BACTEC analyzer, was inoculated on blood agar (BA) and MacConkey agar (MCA) (Oxoid Ltd., Hampshire, UK) and incubated at 37°C for 18–24 hours. Gram-positive bacteria were identified using catalase, coagulase, DNase, Staphaurex (Remel Europe Ltd., Dartford, UK), and *Streptococcus* grouping tests (Remel Europe Ltd., Dartford, UK), while gram-negative rods were identified using API20 E and API20 NE kits (Biomérieux, France).

Antimicrobial susceptibility testing (AST) and quality control procedures

Kirby Bauer’s disc diffusion method was used for antimicrobial susceptibility testing following the Clinical and Laboratory Institute Guidelines (CLSI, 2022). The antibiotic disks (Oxoid Ltd., Hampshire, UK) used for Gram-positive bacteria were penicillin (10 µg), trimethoprim-sulfamethoxazole (1.25/23.75 µg), gentamicin (10 µg), erythromycin (15 µg), clindamycin (2 µg), ciprofloxacin (5 µg), cefoxitin (30 µg),

and chloramphenicol (30 µg). For Gram-negative bacteria, we used ampicillin (10 µg), ceftriaxone (30 µg), ceftazidime (30 µg), meropenem (10 µg), ciprofloxacin (5 µg), trimethoprim-sulfamethoxazole (1.25/23.75 µg), gentamicin (10 µg), amikacin (30 µg), piperacillin-tazobactam (100 µg/10 µg), amoxicillin-clavulanic acid (20 µg/10 µg), and chloramphenicol (30 µg). We screened for methicillin resistance using a cefoxitin (30 µg) disk (Oxoid Ltd., Hampshire, UK).

Isolates that exhibited resistance to three or more different antibiotics were considered multidrug-resistant (Magiorakos et al., 2012). For antimicrobial susceptibility tests, we used *E. coli* ATCC 25922, *P. aeruginosa* ATCC 27853, MSSA ATCC 25923, MRSA ATCC 43300, *K. pneumoniae* ATCC 1705, and *K. pneumoniae* ATCC 1706 as controls.

Data analysis

The data were analyzed using the Statistical Package for the Social Sciences (SPSS) Version 26.0 (Armonk, NY: IBM Corp.). Categorical variables are summarized as frequencies and percentages, while proportional differences were compared using the chi-square and Fisher’s exact tests. A p -value < 0.05 was considered to indicate statistical significance.

Results

Description of the study participants

A total of 856 patients were enrolled; the majority were aged < 1 year (38.4%, 329/856), and approximately half of them were females (50.6%, 433/856). Most patients were from neonatal, general medicine, pediatric, or intensive care units (ICUs) (Table 1).

Laboratory-confirmed bloodstream infection

The overall incidence of BSIs was 37.3% (319/856), with 5% (17/319) of the patients having polymicrobial infections. The BSIs were slightly greater among males (38.3%, 162/423) than females (36.3%, 157/433) ($p = 0.585$). The rate of BSIs was high among children < 1 year old (45.3%; 149/329) and among patients aged ≥ 61 years (45.7%; 37/81), $p = 0.001$. Patients admitted to the ICU had significantly greater BSIs (44%; 113/258) than those admitted to other wards (34.4%; 206/599) ($p = 0.006$) (Table 2).

Bacterial isolates

We isolated a total of 335 pathogens. Among them, Gram-positive bacteria were the most common, accounting for 63.28% (212/335) of all the isolates. Coagulase-negative *Staphylococcus* (CoNS) isolates were the most common at 41.79% (140/335), followed by *S. aureus* at 16.4% (55/335). The most predominant Gram-negative bacteria were *K. pneumoniae* (9.25%; 31/335), followed by *E. coli* (7.16%; 24/335), *Acinetobacter* spp. (6.86%; 23/335), and *P. aeruginosa* (4.77%; 16/335) (Figure 1).

Distribution of ESKAPE pathogens

The proportion of ESKAPE pathogens isolated from BSIs was 43.28% (145/335). *S. aureus* (16.4%) was the most predominant, followed by *K. pneumoniae* (9.25%), *Acinetobacter* spp. (6.86%), and *P. aeruginosa* (4.77%). *Acinetobacter* spp., *K. pneumoniae*, and *P. aeruginosa* were isolated mainly from children aged < 1 year and patients aged ≥ 61 (Figure 2). *Acinetobacter* spp. and *S. aureus* were the most prevalent isolates in the neonatal unit, while *P. aeruginosa* were the most prevalent isolates in the pediatric units, respectively (Figure 3).

Table 1: Demographic and clinical characteristics of the study participants.

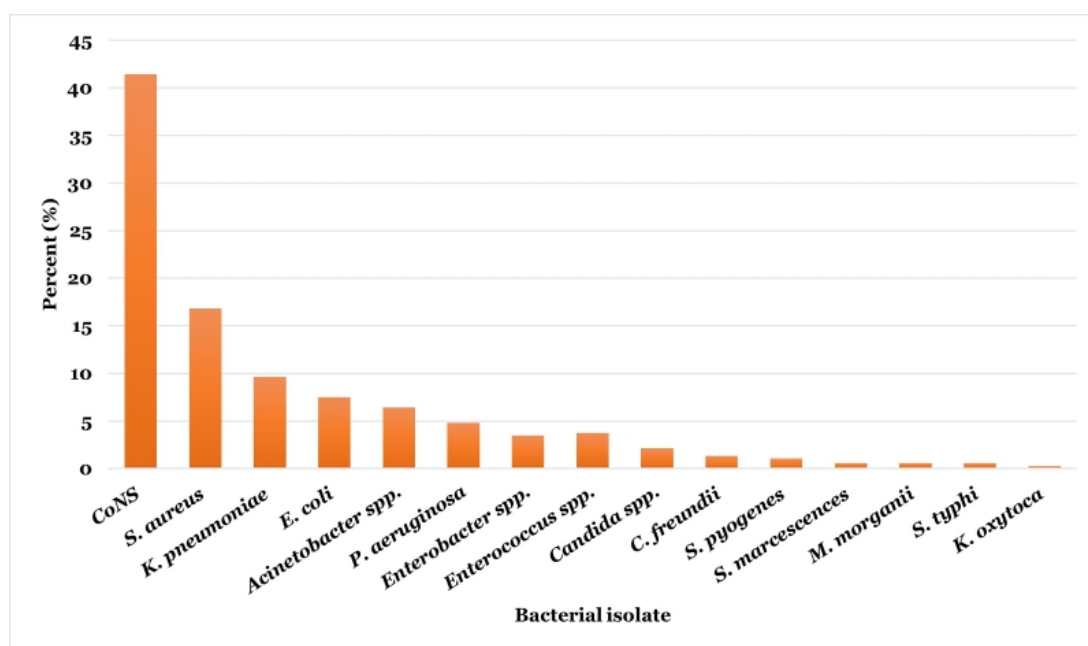
Variable	Frequency	Percent (%)	
Age	<1-year	329	38.4
	1-10	170	19.9
	11-20	72	8.4
	21-30	70	8.2
	31-40	53	6.2
	41-50	41	4.8
	51-60	40	4.7
	≥61-years	81	9.5
Sex	Male	423	49.4
	Female	433	50.6
Unit	Oncology	13	1.5
	Intensive care units	143	16.7
	General medicine	202	23.6
	Neonatal	278	32.5
	Gynecology	36	4.3
	Pediatrics	178	20.8
	Surgery	6	0.7
Reason	Diagnosis	669	78.2
	Follow-up*	187	21.8

* Patients with more than 3 different blood samples collected within a month.

Table 2: The proportion of bloodstream infections among study participants at Muhimbili National Hospital.

Variable	Culture results		N	p-value
	Positive	Negative		
Patients sex	Male	162(38.3%)	261(61.7%)	p= 0.5
	Female	157(36.3%)	276(63.7%)	
Age in years	<1	149(45.3%)	180(54.7%)	p= 0.001
	1-10	52(30.6%)	118(69.4%)	
	11-20	22(30.6%)	50(69.4%)	
	21-30	25(35.7%)	45(64.3%)	
	31-40	15(28.3%)	38(71.7%)	
	41-50	8 (19.5%)	33(80.5%)	
	51-60	11(27.5%)	29(72.5%)	
	≥61	37(45.7%)	44(54.3%)	
Ward	IN	206(34.4%)	393(65.6%)	p= 0.006
	ICU	113(44.0%)	144(56.0%)	

* ICU- patients admitted to the intensive care unit, IN- patients admitted to other wards excluding the ICU.

**Figure 1:** The distribution of pathogens causing bloodstream infections.

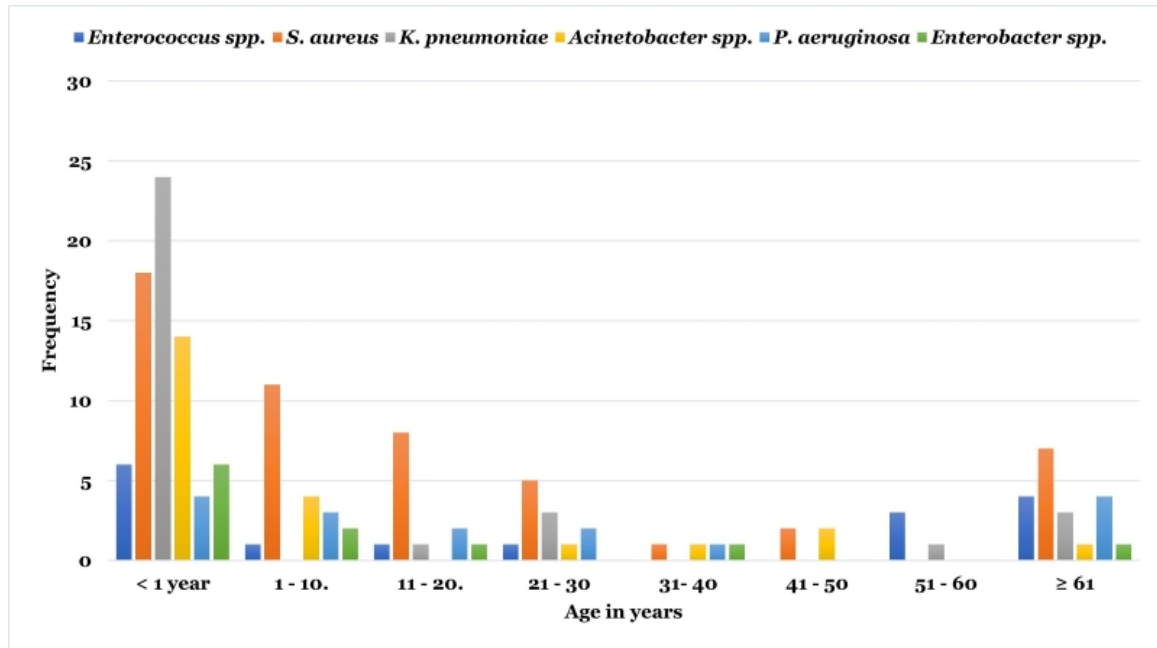


Figure 2: Distribution of common isolates across different age groups.

Table 3: Antimicrobial resistance pattern of ESKAPE and non-ESKAPE pathogens causing bloodstream infections.

Isolates	Number	Antimicrobial resistance (%) [*]														
		AK	AMP	FE	CZ	CR	AG	CN	PZ	ME	CIP	CH	SXT	DA	ER	P
CoNS	140	-	-	-	-	-	-	62	-	-	65	15	81	40	92	94
<i>S. aureus</i>	55	-	-	-	-	-	-	53	-	-	67	27	77	35	86	98
<i>K. pneumoniae</i>	31	43	97	94	91	89	80	57	77	27	89	37	74	-	-	-
<i>E. coli</i>	24	18	71	79	68	7	75	61	71	14	78	14	68	-	-	-
<i>Acinetobacter spp.</i>	23	63	-	83	83	-	-	83	79	67	79	-	75	-	-	-
<i>P. aeruginosa</i>	16	-	-	67	61	-	-	61	71	67	61	-	-	-	-	-
<i>Enterobacter spp.</i>	11	27	100	91	100	100	82	82	70	27	82	18	82	-	-	-
<i>E. faecalis</i>	9	-	56	100	-	-	-	-	-	-	100	11	0	-	100	100
<i>Enterococcus spp.</i>	4	-	100	-	-	-	-	-	-	-	100	20	0	-	100	100
<i>C. freundii</i>	4	40	80	60	60	60	60	40	40	0	60	40	40	-	-	-
<i>S. pyogenes</i>	4	-	-	-	-	-	-	0	-	0	0	0	0	0	100	25
<i>S. marcescens</i>	2	0	100	100	100	100	100	0	100	50	0	100	0	-	-	-
<i>S. typhi</i>	2	0	0	0	0	50	0	0	0	0	0	0	50	-	-	-
<i>M. morgani</i>	2	0	100	100	100	100	100	50	100	0	50	0	100	-	-	-
<i>K. oxytoca</i>	1	100	100	100	100	100	100	100	100	100	100	0	100	-	-	-

^{*} AMP: Ampicillin, CZ: Ceftazidime, CR: Ceftriaxone, ME: Meropenem, P: Penicillin, AG: Amoxicillin-clavulanic acid, SXT: Trimethoprim-sulfamethoxazole, FE: Cefepime, AK: Amikacin, CH: Chloramphenicol, CN: Gentamicin, CIP: Ciprofloxacin, DA: Clindamycin, ER: Erythromycin, PZ: Piperacillin-Tazobactam, CoNS: Coagulase-negative Staphylococci.

Table 4: Resistance pattern of the isolated MDR bacterial pathogens causing bloodstream infections among patients at Muhimbili National Hospital.

Bacteria	No. of resistance genes	Resistant antibiotic classes*	%	
Enterobacterales	3	AMN-QNL-CAR	19.5	
		PEN-AMN-QNL	58.4	
		PEN-AMN-SUL	54.5	
		PEN-CEP-QNL	77.9	
		PEN-PHE-QNL	27.3	
		PEN-QNL-CAR	22.1	
		PEN-QNL-SUL	64.9	
		PHE-QNL-SUL	24.7	
		PEN-CEP-PHE	28.6	
	4	CEP-AMN-QNL-CAR	19.5	
		CEP-QNL-CAR-SUL	18.2	
		PEN-AMN-QNL-CAR	19.5	
		PEN-AMN-QNL-SUL	52	
		PEN-CEP-AMN-QNL	57.1	
		PEN-CEP-AMN-SUL	52	
		PEN-CEP-PHE-QNL	26	
		PEN-CEP-QNL-CAR	22.1	
		PEN-CEP-QNL-SUL	63.6	
		PEN-QNL-CAR-SUL	18.2	
		PEN-PHE-CEP-AMN	24.7	
		5	CEP-AMN-QNL-CAR-SUL	37.7
			PEN-AMN-QNL-CAR-SUL	16.9
			PEN-CEP-AMN-QNL-CAR	20.8
			PEN-CEP-QNL-CAR-SUL	18.2
	PEN-PHE-QNL-CAR-SUL		11.7	
	6	PEN-CEP-AMN-QNL-CAR-SUL	16.9	
		PEN-CEP-AMN-BLC-QNL-CAR	19.5	
		PEN-CEP-PHE-BLC-QNL-SUL	22.1	
		PEN-CEP-BLC-CAR-QNL-SUL	18.2	
	7	PEN-PHE-AMN-BLC-QNL-SUL	23.4	
		PEN-CEP-AMN-BLC-QNL-CAR-SUL	16.9	
		PEN-CEP-PHE-AMN-BLC-QNL-CAR	13	
	8	PEN-CEP-PHE-BLC-QNL-CAR-SUL	10.4	
PEN-PHE-AMN-BLC-QNL-CAR-SUL		10.4		
<i>Acinetobacter spp</i>	3	PEN-CEP-PHE-AMN-BLC-QNL-CAR-SUL	10.4	
		CEP-AMN-QNL	89.5	
		CEP-CAR-QNL	84.2	
	4	CEP-CAR-SUL	84.2	
		CEP-BLC-QNL	100	
	5	CEP-AMN-QNL-CAR	84.2	
		CEP-AMN-QNL-SUL	84.2	
	6	CEP-AMN-QNL-CAR-SUL	84.2	
		CEP-AMN-BLC-CAR-SUL	84.2	
	<i>Pseudomonas aeruginosa</i>	3	CEP-QNL-CAR-BLC-AMN	84.2
			CEP-QNL-AMN-CAR-BLC-SUL	84.2
CEP-AMN-QNL			91.7	
CEP-CAR-QNL			83.3	
4		CEP-BLC-QNL	91.7	
		CEP-BLC-AMN	91.7	
5		CEP-AMN-QNL-BLC	91.7	
		CEP-AMN-CAR-QNL	83.3	
<i>Staphylococcus aureus</i>		3	CEP-QNL-AMN-CAR-BLC	83.3
			CEP-PHEN-QNL	29.7
	PEN-CEP-AMN		55.6	
	4	PEN-MAC-CEP	72.2	
		LINC-PHEN-AMN	18.5	
	5	PEN-CEP-MAC-AMN	519	
		PEN-LINC-MAC-QNL	27.8	
	6	CEP-PHEN-LINC-AMN	18.5	
		PEN-CEP-MAC-AMN-PHEN	25.9	
		PEN-CEP-QNL-MAC-AMN	44.4	
7	CEP-PHEN-LINC-QNL-AMN	18.5		
	PEN-CEP-QNL-MAC-AMN-PHEN	25.9		
<i>Enterococcus spp.</i>	3	PEN-CEP-QNL-MAC-AMN-LINC	25.9	
		PEN-CEP-PHEN-QNL-LINC-MAC-AMN	18.5	
		PEN-PHEN-QNL	14.3	
	4	PEN-MAC-PHEN	14.3	
		MAC-QNL-PEN	100	
		MAC-QNL-PHEN	14.3	
		PEN-PHEN-QNL-MAC	14.3	

*CEP: cephalosporins, PHE: phenolics, AMN: aminoglycosides, QNL: quinolones, CAR: carbapenems, SUL: sulfonamides, MAC: macrolides, BLC: B-lactam combination agents, LINC: lincosamides.

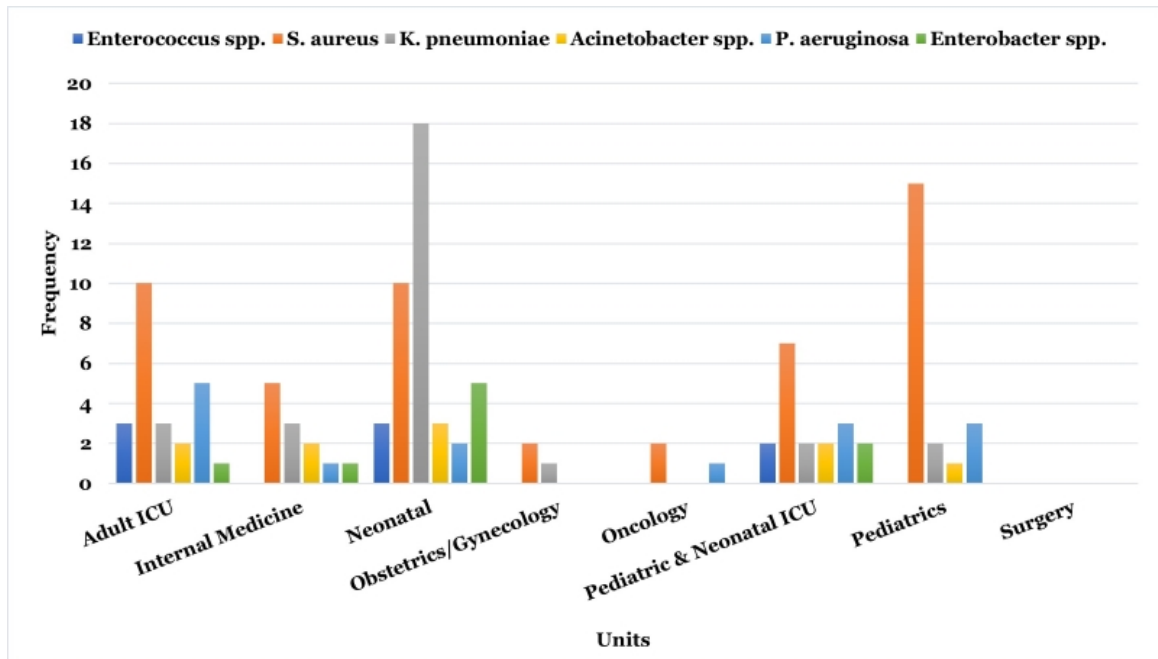


Figure 3: Distribution of ESKAPE pathogens across different units.

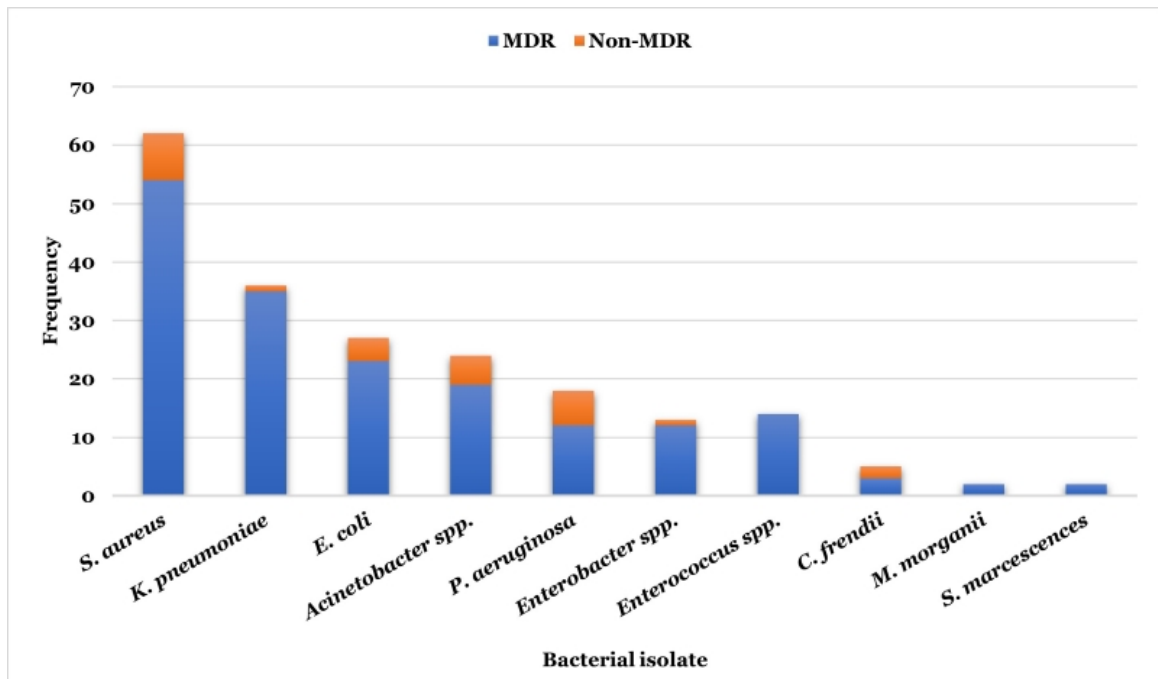


Figure 4: Overall multidrug-resistant pathogens among common pathogens isolated.

Antimicrobial resistance pattern

Isolates belonging to the ESKAPE group exhibited a very high level of resistance against ampicillin (80–100%) and ceftriaxone (50–100%), while *Enterococcus* spp. and *S. aureus* were highly resistant to β -lactam antibiotics, including penicillin (94–100%). *K. pneumoniae* strains exhibited a very high level of resistance (>91%) to 3rd-generation cephalosporins, including ceftazidime and ceftriaxone. *Acinetobacter* spp. exhibited very high resistance to gentamicin (83%), ceftazidime (83%), ciprofloxacin (79%), and trimethoprim-sulfamethoxazole (75%). *P. aeruginosa* was highly resistant to ceftazidime (61%), gentamycin (61%), and piperacillin-tazobactam (71%). Both *Acinetobacter* spp. and *P. aeruginosa* had high resistance rates to meropenem (67%), while all the *Enterobacter* spp. were resistant to cephalosporins (100%) (Table 3).

The overall proportions of MDR pathogens are shown in Figure 4 and Table 4. A total of 83.8% of the isolated bacteria were MDR. Most (63.6%) were resistant to at least four different classes of antibiotics. Most ESKAPE pathogens (85.5%) were MDR, with 23.4% being resistant to all the tested antibiotics. Approximately 10% of the MDR *Enterobacterales* were resistant to eight different classes of antibiotics (Table 4). The proportion of methicillin-resistant *S. aureus* isolates was 71.4%.

Discussion

Globally, BSIs cause significant morbidity and mortality, especially in LMICs (Verway et al., 2022). In these countries, the rates of morbidity and mortality are very high, while treatment options are very limited (Ombelet et al., 2019). In this study, we found the prevalence of BSIs to be 37.3%, which is much greater than that previously reported (13%) among children and adults at the same hospital (Blomberg et al., 2007; Moyo et al., 2010). Among the different bacteria, the ESKAPE pathogens comprised approximately half of the isolates, supporting the findings of other studies that have shown this group to be the leading cause of nosocomial infections (Santajit and Indrawattana, 2016). The most common species were *S. aureus*, *K. pneumoniae*, *Acinetobacter* spp., and *P. aeruginosa*, similar to the findings of other studies (Qiao et al., 2017; Santoro et al., 2020; Alcántar-Curiel et al., 2023).

In the current study, most of these isolates were highly resistant to antibiotics widely used for the empiric treatment of BSIs in the country (Sangeda et al., 2021). For example, the ESKAPE group exhibited a very high level of resistance to ampicillin (80–100%) and ceftriaxone (50–100%), while *Enterococcus* spp. and *S. aureus* were highly resistant to β -lactam antibiotics, including penicillin (94–100%). We also observed a very high percentage of *K. pneumoniae* isolates (>91%) resistant to 3rd-generation cephalosporins, including ceftazidime and ceftriaxone. These findings contrast with findings from a study in Nigeria, in which the resistance rate to 3rd-generation cephalosporins was lower (46.5%) and from Latin American countries (Karlowsky et al., 2017; Akinyemi et al., 2021).

The proportion of MRSA among *S. aureus* was 71.4%, more than twice that reported in other studies at the same hospital (Moyo et al., 2010). On the other hand, *Acinetobacter* spp. exhibited high levels of resistance to gentamicin (83%), ceftazidime (83%), ciprofloxacin (79%), and trimethoprim-sulfamethoxazole (75%). Our results showed that *P. aeruginosa* strains had high levels of resistance to ceftazidime (61%), gentamicin (61%), and piperacillin-tazobactam (71%), while *Acinetobacter* spp. and *P. aeruginosa* exhibited high levels of resistance to meropenem (67%). All the *Enterobacter* spp. were resistant to cephalosporins (100%). Our results indicate that empiric treatment of BSIs is most likely to fail, leading to further escalation of antimicrobial resistance and poor clinical outcomes (Onken et al., 2015; Williams et al., 2018; Silago et al., 2020; Chumbita et al., 2023). Of particular concern is the resistance to carbapenems, which are reserved antibiotics in our setting as a last resort option for the treatment of critically ill patients, patients with sepsis and septic shock, and infections due to multidrug-resistant

organisms when all alternatives have failed or are not suitable (Martinez and Wolk, 2016).

The ESKAPE group of pathogens strongly resisted this group of antibiotics, especially *Acinetobacter* spp. and *P. aeruginosa*. This observation is alarming, given that infections caused by these pathogens have limited treatment options (Liu et al., 2016; Buehrle et al., 2017). According to a wide survey conducted in Asia, carbapenem resistance among *A. baumannii* isolates were reported to be more than 90% (Liu et al., 2018). Moreover, a high proportion of the isolates were multidrug resistant. Overall, 83.8% of the strains were resistant to at least four different classes of antibiotics, 85.5% of the ESKAPE pathogens were MDR, and 23.4% of the ESKAPE pathogens were resistant to all the tested antibiotics. Among the *Enterobacterales*, 10% of the MDR isolates were resistant to more than eight different classes of antibiotics. This observation, which is referred to as extensive drug resistance (XDR), is extremely alarming given the limited advances in the development of new drugs that have been reported in the last few years (Gigante et al., 2022). Our findings indicate a predominance of high MDR pathogens causing BSIs at the Muhimbili National Hospital. This finding is comparable to a previous study conducted at the same hospital, which showed that 70.5% of bacteria isolated from patients with BSIs were MDR, and, tragically, the study showed that MDR pathogens were associated with increased mortality (Manyahi et al., 2020).

Based on our findings, we recommend the following interventions: i) a major policy change in the current management of BSIs at the hospital, which at the moment is largely empirical; ii) the introduction of rapid diagnostic methods for AST to address the challenges that are encountered in routine clinical microbiology laboratories, where results may take up to 96 hours (Tabak et al., 2018; Banerjee and Humphries, 2021); iii) improvement in infection control and prevention measures to reduce the incidence of nosocomial infections; and iv) strict antimicrobial stewardship to reduce the burden of AMR and ensure appropriate and targeted antimicrobial therapy (Banerjee and Humphries, 2021; Ryu et al., 2023).

Finally, we acknowledge that this study has several limitations. Due to the limited patient information, we could not establish the source of the BSIs, whether these infections were hospital-acquired or community-acquired, information that is critical in formulating preventive strategies (Lenz et al., 2012). Furthermore, we could not test for vancomycin resistance, which is the antibiotic of choice for treating BSIs caused by MRSA (Moise et al., 2016; Schweizer et al., 2021).

Conclusion

This study revealed a wide range of MDR and XDR bacteria that cause BSIs at a national hospital in Tanzania. More than eighty percent (83.84%) of the isolated bacteria were MDR, and more than sixty percent (63.64%) of the MDR isolates were resistant to at least four different classes of antibiotics. Approximately 23.4% of the ESKAPE pathogens and 10% of the MDR *Enterobacterales* were resistant to eight different classes of tested antibiotics and could be considered XDR. This alarming situation calls for i) exclusive laboratory result-based prescriptions, ii) extensive review of the current management guidelines, iii) strengthening of antimicrobial stewardship and IPC practices, iv) continuous surveillance to monitor antimicrobial resistance and v) cohort studies for early prediction of bloodstream infection, including identification of biomarkers that are indicative of BSIs, sepsis, and antimicrobial resistance.

Article Information

Ethical Approval. This study received ethical clearance from the Senate Research and Publication Committee and the Institutional Review Board of the Muhimbili University of Health and Allied Science (MUHAS) (Ref. NO.: MNH-CRTC/Perm/2023/312). The Directorate of Research, Training, and Consultancy of the MNH granted permission to conduct the study. We enrolled participants who consented to participate in the study.

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Conflict of Interest. The authors have no conflicts of interest to declare relevant to the article's content.

Authors contributions. Conceptualization and study design (FF and MIM); data collection, curation, and laboratory investigations (FF and FM); preparation of the manuscript (FF, EMN, SAY, and MIM). All the authors read and approved the final version.

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