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# Carbapenem-resistant *Acinetobacter baumannii* infections: Antimicrobial resistance patterns and risk factors for acquisition in a Kenyan intensive care unit



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# ABSTRACT

*Objectives:* Multidrug-resistant (MDR) *Acinetobacter baumannii* (AB), especially carbapenem-resistant (CR) strains, presents a significant challenge in intensive care units (ICUs) but surveillance data in many resource-constrained countries is inadequate. Here, we determined the prevalence of MDRAB and risk factors for infection and mortality in ICU-admitted patients.

*Methods:* A cross-sectional study among 132 consecutive patients between July 2019 and July 2020, with infected patients followed for 30 days from sample collection to ICU discharge/death. Blood, urine, and tracheal aspirate samples were processed following the standard bacteriological procedures. Isolate identity and antimicrobial susceptibility were elucidated by VITEK 2 Compact system.

*Results*: The prevalence of MDRAB was 22.7% (30/132), mostly from urine samples (12.1%, 16/132), and dominated by CRAB (83.3%) that were colistin-nonresistant and exhibited high multiple antibiotic resistance indices, ranging from 0.64-0.91. Risk factors for infection were occupation (adjusted odds ratio = 4.41, P = 0.016) and interhospital referral status (adjusted odds ratio = 0.14, P = 0.001). ICU mortality was 20% (6/30).

*Conclusion:* Our findings underpin the need for strict adherence to and evaluation of infection prevention and control, and continuous surveillance of CRAB in ICU, especially among the risk groups, in the current study setting and beyond.

# Introduction

Antimicrobial resistance (AMR) surveillance in intensive care units (ICUs) is of paramount importance in combating the emergence and spread of multidrug-resistant (MDR) infections. ICUs, where patients have frequent antimicrobial exposure, face significant challenges in managing MDR strains due to limited treatment options and increased morbidity, mortality, and healthcare costs [1]. Effective AMR surveillance in ICUs provides crucial data on the prevalence, distribution, and trends in MDR infections, guiding optimized antimicrobial prescribing practices, targeted interventions, and formulation of evidence-based policies to prevent and manage MDR infections.

Acinetobacter baumannii (AB) is a significant pathogen in ICUs and hospitals due to its remarkable ability to survive in diverse environments and develop resistance to multiple antimicrobial agents [2]. This opportunistic bacterium poses a critical threat to patients with compromised immune systems, particularly those in ICUs, where invasive procedures

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and prolonged hospital stays increase their vulnerability to infections. The bacterium is notorious for its capacity to form biofilms on medical devices and surfaces, allowing it to persist and thrive in healthcare settings. These biofilms provide a protective barrier against antimicrobial agents, making the bacterium eradication difficult [3]. Additionally, AB has a remarkable ability to acquire resistance genes, leading to MDR and extensively drug-resistant (XDR) strains [3].

The drug resistance in AB is commonly attributable to the production of carbapenemases, such as the prevalent OXA-oxacillinases-23, OXA-24, and OXA-58 enzymes, which confer resistance to carbapenem antibiotics. Additionally, efflux pumps and modifications in outer membrane proteins decrease antibiotic uptake, while acquired resistance genes, including those encoding extended-spectrum  $\beta$ -lactamases (ES-BLs) and aminoglycoside-modifying enzymes, further expand resistance capabilities [2]. This resistance extends to critical antimicrobial classes, including carbapenems. Carbapenems are highly potent broad-spectrum  $\beta$ -lactam antibiotics, considered by clinicians as "last-resort" antibiotics for the treatment of severely ill patients with antimicrobial-resistant gram-negative infections. Carbapenem-resistant AB (CRAB), widely recognized as one of the difficult-to-treat pathogens and the World Health Organization's critical-priority pathogen for the development of newer

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antimicrobial agents, has become a growing global concern over the past decade [2].

Epidemiological studies have reported an alarming rise in CRAB infections, leading to a significant mortality rate ranging from 27.8-35% in various regions globally [4–6]. The CRAB burden in many low and middle-income countries could be estimated, as there is limited surveillance data, weak enforcement of infection prevention and control measures, overuse and misuse of antibiotics, and poor healthcare infrastructure [7]. In Sub-Saharan Africa, there is limited epidemiological data on CRAB, especially in ICU-admitted patients, presenting a critical knowledge gap to inform effective interventions and implement evidencebased policies to mitigate the risks associated with this MDR organism. This study sought to assess the prevalence, antimicrobial susceptibility profiles, and factors attributable to CRAB infection and admission outcomes in patients admitted to ICU in a Kenyan Tertiary Teaching and Referral Hospital.

# Methods

# Study area, study design, and study population

We conducted this study at Moi Teaching and Referral Hospital (MTRH), the second largest national teaching and referral hospital located 310 Kilometers Northwest of Nairobi City, along Nandi Road in Eldoret Town, Uasin Gishu County, Kenya. The facility has a bed capacity of 991 patients and serves approximately 1800 outpatients daily, drawn from the Western Kenya Region, parts of Eastern Uganda, and Southern Sudan, with a population catchment of over 24 million. MTRH provides specialized services such as ICUs with an annual capacity of 1500 patients, oncology, renal transplants, and advanced surgical procedures, establishing itself as a crucial healthcare facility in Western Kenya and a regional referral center.

The project adopted a hospital-based prospective cross-sectional study design. We enrolled consecutive adult patients ( $\geq$ 18 years) presenting with clinical symptoms of lower respiratory tract infections, bloodstream infections, or urinary tract infections after 48 hours of ICU admission between July 2019 and July 2020. The study followed the participants with AB infection from sample collection time until death or discharge to determine ICU admission outcome. The authors sought patients' consent to participate in this study through close relatives or legal representatives.

# Data and clinical sample collection

Demographic and clinical data, including age, gender, ICU admission dates, and comorbidities, were collected using a pretested structured questionnaire, whereas clinical samples, including tracheal aspirates, blood, and urine, were collected by qualified and registered nurses following standard bacteriological procedures [8]. Tracheal aspirates were collected into sterile containers using a sterile suction catheter and transported to the microbiology laboratory. Blood samples were collected aseptically using venipuncture techniques directly into BD BACTEC<sup>TM</sup> Blood Culture Media (Becton, Dickinson and Company, United States). Urine samples were collected from indwelling catheters into sterile containers using clean-catch techniques. Except for blood samples (transported at room temperature), samples were transported to the microbiology laboratory in cold boxes at 2-8°C, and analyzed within 2 hours of collection, to ensure sample integrity and accurate results.

### Isolation, identification, and antimicrobial susceptibility testing

*AB* isolation and identification followed the standard and automated bacteriological procedures [8]. Blood samples were incubated in the BACT/ALERT® VIRTUO 3D Microbial Detection Systems (bioMérieux, Marcy l'Etoile, France), following manufacturer's instructions, and samples fagging positive sub-cultured onto sheep blood agar (Oxoid, United Kingdom). Tracheal aspirates were streaked onto sheep blood agar (Oxoid, United Kingdom), while urine samples were on cysteine lactose electrolyte deficient (CLED) agar. All cultures were incubated in ambient air at 37°C overnight. We identified the resultant colonies using VITEK 2 Compact system with the updated Advanced Expert System (bioMerieux, Marcy l'Etoile, France), with *Escherichia coli* ATCC 8739 as a Quality Control (QC) organism.

Antimicrobial susceptibility testing (AST) was done using AST GN 83 cards in the VITEK 2 COMPACT system (bioMérieux, Marcy l'Etoile, France) in accordance with the CLSI-Clinical and Laboratory Standards Institute guidelines 2019 [9]. Escherichia coli (ATCC 25922) and Pseudomonas aeruginosa (ATCC 27853) were used as QC organisms. The antibiotic (in  $\mu$ g/ml) panels tested were piperacillin (4-64), amoxicillinclavulanic acid (4/2-16/8), minocycline (1-16), tetracycline (0.256-2), levofloxacin (1-4), tigecycline (1-4), ceftriaxone (1-32), cefepime (1-16), amikacin (8-32), meropenem (0.5-4), and colistin (1-4). We defined carbapenem resistance as resistance to meropenem ( $\geq 4 \ \mu g/ml$ ), whereas resistance to either ceftriaxone ( $\geq 4 \mu g/ml$ ) as third-generation cephalosporin resistance. AB isolates exhibiting resistance to three or more antibiotic classes were considered MDR [10]. Multiple antibiotic resistance indices (MARI) were calculated as a/b, where a = number of antibiotics the isolate was resistant to, b = the total number of antibiotics tested [11].

# Statistical analysis

We described the continuous data in means and medians, while categorical data in frequencies and percentages. The data were analyzed using IBM SPSS Statistics (Version 25). This study used bivariate logistic regression (crude odds ratios) to assess the associations between patients' demographic and clinical characteristics and 30-day ICU admission outcome (death or discharge) with AB infection. Variables with  $P \leq 0.2$  were analyzed further by multivariate logistic regression analysis to calculate the adjusted odds ratio (aOR). Statistical significance level evaluated at P < 0.05, at a 95% confidence interval (CI). The statistically significant associations are bolded, Table 4.

### Results

# Socio-demographic and clinical characteristics of the study population

A total of 132 participants were enrolled, with the majority being male (51.5%). The median age of the participants was 52 years. Most participants were married (74.2%) and had at least one comorbidity, with renal-related conditions being the most prevalent (50.8%). Majorly of the patients were referrals (87.9%) from other hospitals. The participants' median length of stay was 32.5 days, with most participants staying for more than 10 days. The median body mass index was 24.0, Table 1.

### Prevalence of AB infections

We recovered non-replicate AB isolates from 30 patients in this study (30/132, 22.7%), mostly from urine samples (12.1%, 16/132), Figure 1.

# Antimicrobial susceptibility profiles of AB isolates

We isolated AB displaying 100% resistance to beta-lactam/inhibitor (amoxicillin-clavulanic acid), levofloxacin, third-generation cephalosporin (3GC) (ceftriaxone), and aminoglycosides (amikacin). The isolates were 83.3% carbapenem (meropenem)-resistant but remained 100% colistin-susceptible and 73.3% minocycline-susceptible, Table 2.



Figure 1. Prevalence of Acinetobacter baumannii infections. BD, blood; TA, tracheal aspirate.

# Table 1

Demographic and clinical characteristics of the study population.

Characteristics	Frequency, n	Percent (%)
Gender		
Male	68	51.5
Female	64	48.5
Age (median, IQR)	52.0(36-58.0)	
<24	10	7.6
25-44	42	31.8
45-59	51	38.6
≥60	29	22.0
Marital status		
Single	34	25.8
Married	98	74.2
Education level		
No formal education	17	12.9
Primary level	52	39.4
Secondary level	52	39.4
Tertiary level	11	8.3
Occupation		
Unemployed	50	37.9
Self employed	59	44.7
Employed	23	17.4
Body mass index (median, IQR)	24.0(21-26)	
<18.5	12	9.1
18.5-24.9	64	48.5
25-29.9	56	42.4
Referral status		
Referral	116	87.9
Non-referral	16	12.1
Comorbidities		
Respiratory related conditions	56	42.4
Renal-related conditions	67	50.8
Central nervous system-related conditions	10	7.6
Autoimmune related conditions	14	10.6
Metabolic disorder	11	8.3
Asthmatic	10	7.6
Burns	6	4.5
Injuries	8	6.1
Bloodstream conditions	8	6.1
Other conditions	20	15.2
Length of stay (median, IQR)	32.5(22-52.8)	
≤5 days	2	1.5
6-10 days	6	4.5
>10 days	124	93.9

IQR, interquartile range

### Multidrug-resistant phenotypes among AB isolates

All isolates were MDRAB, dominated by CRAB (83.3%), Table 3. Of the CRAB MDR phenotypes, 50% were minocycline-resistant and 100% resistant to 3GCs. MDRAB isolates in our study were 100% sensitive to colistin and displayed a high MARI, ranging from 0.64-0.91, Table 3. Factors associated with AB infections and mortality

Patient's occupation and referral status were the independent risk factors for AB infections, whereby employed patients were four times more likely to harbor AB when compared to unemployed (aOR = 4.41, 95% CI: 1.32-14.79, P = 0.016), while those referred from other health-care facilities were 14% more likely to have an infection compared to non-referred patients (aOR = 0.14, 95% CI: 0.05-0.45, P = 0.001), Table 4.

The 30-day ICU mortality rate among patients with MDRAB was 20% (6/30), and we found no significant association between mortality and the participants' socio-demographic and clinical characteristics (data not shown).

# Discussion

This study revealed a high prevalence of AB infections among ICUadmitted patients, with 22.7% of the participants carrying non-replicate isolates. Banerjee et al. reported a higher prevalence (42.9%) in an ICU of a tertiary care hospital in Varanasi, India [12]. These authors, however, did not differentiate AB from other species, which may explain the high prevalence of infections compared to the current study. In our study, AB infection prevalence is higher than documented in Africa (4.7%), Asia (9.4%), Europe (3.3%), Latin America (3.5%), Middle East (9.7%), and North America (0.6%) [13]. This current study targeted AB infections only and defined infection based on clinical judgment by treating physicians. However, AB can be isolated from patients with infections caused by other bacteria, mostly Pseudomonas spp. and Enterobacteriaceae, as reported by Uwingabiye et al. in an ICU in a Moroccan teaching hospital [14], suggesting that AB was not solely responsible for all patients' clinical presentation in our study and that some of the infections could have been caused by other pathogens, with AB as an asymptomatic colonizer.

In our study, most of the AB isolates were obtained from urine samples, corroborating previous studies [15,16]. In a mouse model of urinary tract infection (UTI), Hazen et al. found that mice infected with AB displayed high bacterial burdens in urine for several weeks and that inserting a catheter into the bladder of mice with a 2-months-resolved infection led to the resurgence of a UTI caused by the same strain in ~53% of the mice within 24 hours [17]. These authors also found AB intracellularly in bladder epithelial cells of mice with resolved UTI, which they proposed could act as host reservoirs activated upon catheterization, allowing a resurgent of secondary UTI [17]. Du Toit [18] speculated that AB asymptomatic carriage occurs intracellularly in the bladder (or other organs) before hospitalization and that subsequent medical interventions, such as catheter insertion, could trigger a resurgence of AB infection from such reservoirs. The current study collected all urine samples from patients with urinary catheters, suggesting that catheters are crucial players in the epidemiology of AB-associated UTI in ICU-

### Table 2

Antimicrobial susceptibility profile of Acinetobacter baumannii isolates.

Antimicrobial class	ABS- antibiotics	Antimicrobial susceptibility status	Blood, n (%)	Tracheal aspirate, n (%)	Urine, n (%)	Overall, n (%)
Penicillin	Piperacillin	R	3 (100)	11 (100)	16 (100)	30 (100)
		S	0 (0)	0 (0)	0 (0)	0 (0)
	Amoxicillin-clavulanic	R	3 (100)	11 (100)	16 (100)	30 (100)
	acid	S	0 (0)	0 (0)	0 (0)	0 (0)
3GC	Ceftriaxone	R	3 (100)	11 (100)	16 (100)	30 (100)
		S	0 (0)	0 (0)	0 (0)	0 (0)
4GC	Cefepime	R	3 (100)	11 (100)	16 (100)	30 (100)
		S	0 (0)	0 (0)	0 (0)	0 (0)
Tetracyclines	Tetracycline	R	3 (100)	11 (100)	16 (100)	30 (100)
		S	0 (0)	0 (0)	0 (0)	0 (0)
	Tigecycline	R	2 (66.7)	6 (54.5)	12 (75)	20 (66.7)
		S	1 (33.3)	5 (45.5)	4 (25)	10 (33.3)
	Minocycline	R	1 (33.3)	3 (27.3)	3 (18.8)	7 (23.3)
		S	2 (66.7)	8 (54.5)	13 (81.3)	23 (76.7)
Fluoroquinolone	Levofloxacin	R	3 (100)	11 (72.7)	16 (100)	30 (100)
		S	0 (0)	0 (0)	0 (0)	0 (0)
Carbapenem	Meropenem	R	2 (66.7)	9 (81.8)	14 (87.5)	25 (83.3)
		S	1 (33.3)	2 (18.2)	2 (12.5)	5 (16.7)
Polymyxins	COL- colistin	R	0 (0)	0 (0)	0 (0)	0 (0)
		S	3 (100)	11 (100)	16 (100)	30 (100)

R, resistant; S, susceptible.

# Table 3

Multidrug resistance phenotypes.

Drug resistance profile	No. ABs R	Multiple antibiotic resistance indices	No. of ABs class R	Frequency, n (%)
CSAB				5 (16.7)
PIP, AMC/TET/LVX/CRO, FEP/AMK	7	0.64	5	2 (6.7)
PIP, AMC/TET/LVX/CRO, FEP/AMK	7	0.64	5	2 (6.7)
PIP, AMC/MIN, TET/LVX/CRO, FEP/AMK	8	0.73	5	1 (3.3)
CRAB				25 (83.3)
PIP, AMC/TET/LVX/CRO, FEP/AMK/MEM	8	0.73	6	3 (10.0)
PIP, AMC/MIN, TET/LVX/CRO, FEP/AMK/MEM	9	0.82	6	2 (6.7)
PIP, AMC/TET/LVX/TGC/CRO, FEP/AMK/MEM	9	0.82	7	15 (50.0)
PIP, AMC/MIN, TET/LVX/TGC/CRO, FEP/AMK/MEM	10	0.91	7	5 (16.7)

AB, Acinetobacter baumannii; AMC, amoxicillin-clavulanic acid; AMK, amikacin; CRAB carbapenem-resistant AB; CRO, ceftriaxone; CSAB carbapenem-sensitive AB; FEP, cefepime; LVX, levofloxacin; MEM, meropenem; MIN, minocycline; PIP, piperacillin; TET, tetracycline; TGC, tigecycline.

admitted patients, and this calls for interventions to limit indwelling urinary catheter use and prompt removal when no longer needed, and for systematic surveillance of MDRAB in catheterized ICU-admitted patients.

We isolated AB displaying 100% resistance to beta-lactam/inhibitor (amoxicillin-clavulanic acid [AMC]), similar to that reported in Tanzania [19]. Inhibitors destroy the  $\beta$ -lactamase activity, thus preventing beta-lactam drugs inactivation by TEM-type. Resistance to  $\beta$ -lactamase inhibitors such as clavulanic acid, sulbactam, and tazobactam is attributable to bacterial strains producing inhibitor-resistant TEM (IRT) enzymes that differ from the parental enzymes TEM-1 or TEM-2 by one, two, or three amino acid substitutions at different locations [20]. In the meantime, AB isolates in our study were 3GC (ceftriaxone [CRO]), as previously reported [19]. In AB, resistance to 3GCs occurs following overexpression of intrinsic genes, *ampC*, and *bla*OXA-51-like betalactamase when the Tn6168 or ISAba1 sequences, acquired by horizontal gene transfer, insert themselves in 5' ends upstream of these genes [21]. Our finding suggests the possible resistance mechanism of AMC and CRO in our setting.

Further, AB isolates in our study were 83.3% carbapenem (meropenem, MEM)-resistant but remained 100% colistin-susceptible. The MEM-resistance was higher than 3% reported by Agyepong et al. in Ghana [22], 40% by Manyahi et al. in Tanzania, and 63.6% by Odewale et al. in Nigeria [23]. Our finding contradicts that of Suphansatit and Uitrakul in a Thailand pilot study [24] that supported monotherapy antibiotic regimens, including ceftazidime and meropenem, for AB in-

fections in secondary hospitals. The current study finding on AB colistinsusceptibility corroborates that of Revathi et al. in Kenya [25] and Odewale et al. in Nigeria [23] but lower than 16.2% reported by Agyepong et al. in Ghana [19].

In our study, all isolates were MDRAB, dominated by CRAB (83.3%). The MDRAB rates were higher than 76.8% reported in Jordan [26], 80% in Kenya [10], and 98.1% in Saudi Arabia [27]. Similar to the finding by Bshabshe et al., MDRAB isolates in our study were 100% sensitive to colistin [27]. In this study, AB isolates displayed a high MARI, ranging from 0.64-0.91. It helps to determine whether the isolates are from a region of high or low antibiotic use, with a MAR index greater than 0.2 indicating a 'high-risk' source of contamination [10]. A recent pointprevalence survey by Omulo et al. on antibiotic use at three public referral hospitals in Kenya, Kenyatta National Hospital, Coast Provincial General Hospital (CPGH), and the current study site, reported suboptimal antibiotic use practices, including missed antibiotic doses, low use of specimen cultures to guide therapy, high rates of antibiotic use, particularly in the pediatric and surgical population, and preference for broad-spectrum antibiotics. The authors showed that 46% (489/1071) of participants received at least one antibiotic, with those in critical care units being the highest users. Further, Omulo et al. [28] reported that 43% (326/756) of all antibiotic prescriptions had at least one missed dose, 42% (204/489) of patients on antibiotics had specific infectious disease diagnoses, and 27% (56/204) had bacterial culture ordered, with only 68% (38/56) of tests culture results available. Generally, our finding suggests antibiotic abuse or misuse due to suboptimal antibiotic

# Table 4

Factors associated with AB infections.

	AB present n (%)	AB absent n (%)	Crude OR (95% CI)	<i>P</i> -value	Adjusted OR (95% CI)	P-value
Gender						
Male	16(53.3)	52(51.0)	1.10(0.47-2.48)	0.839		
Female	14(46.7)	50(49.0)	Ref			
Age						
<24	2(6.7)	8(7.8)	1.27(0.22-7.45)	0.789		
25-44	12(40.0)	30(29.4)	0.80(0.27-2.35)	0.679		
45-59	9(30.0)	42(41.2)	1.49(0.49-4.52)	0.487		
≥60	7(23.3)	22(21.6)	Ref			
Marital status						
Single	10(33.3)	24(23.5)	1.63(0.67-3.94)	0.343		
Married	20(66.7)	78(76.5)	Ref			
Education level						
No formal	5(16.7)	12(11.8)	0.53(0.08-3.40)	0.506		
Primary level	10(33.3)	42(41.2)	0.93(0.17-5.01)	0.936		
Secondary level	13(43.3)	39(38.2)	0.67(0.13-3.49)	0.631		
Tertiary level	2(6.7)	9(8.8)	Ref			
Occupation						
Unemployed	8(26.7)	42(41.2)	Ref		Ref	
Self-employed	13(43.3)	46(45.1)	2.28(0.81-6.43)	0.121	2.66(0.89-7.93)	0.080
Employed	9(30.0)	14(13.7)	3.38(1.09-10.43)	0.035	4.41(1.32-14.79)	0.016
Body mass index						
<18.5	4(13.3)	8(7.8)	0.44(0.11-1.73)	0.237		
18.5-24.9	16(53.3)	48(47.1)	Ref			
25-29.9	10(33.3)	46(45.1)	0.65(0.27-1.58)	0.345		
Referral status						
Referral	21(70.0)	95(93.1)	0.17(0.06-0.51)	0.002	0.14 (0.05-0.45)	0.001
Non-referral	9(30.0)	7(6.9)	Ref		Ref	
Sample type						
Urine	16(53.3)	44(43.1)	1.51(0.67-3.41)	0.405		
Tracheal aspirate	11(36.7)	38(37.3)	0.98(0.42-2.27)	0.566		
Blood	3(10.0)	20(19.6)	0.46(0.13-1.65)	0.282		
Outcome						
Discharged	24(80.0)	69(67.6)	1.91(0.71-5.13)	0.256		
Died	6(20.0)	33(32.4)	Ref			
Length of hospital stay	$41.8 \pm 21.3$	$38.1 \pm 23.0$	0.99(0.98-1.01)	0.421		

AB, Acinetobacter baumannii; CI, confidence interval; OR, odd ratio; Ref, reference.

use policies and guidelines, and reserved colistin clinical value in the current study setting. Colistin is one of the last therapeutic options for CR Gram-negative bacteria infections considering the high cost, availability, and limited comprehensive clinical data for the newer agents, including ceftazidime-avibactam, ceftolozane-tazobactam, meropenemvaborbactam, imipenem-cilastatin-sulbactam, plazomicin, eravacycline, and cefiderocol.

Participants' occupation and referral status were the independent risk factors for AB infections, whereby employed patients were four times more likely to harbor AB when compared to unemployed. A community carriage of AB on human hands (10.4%) and skin (17%, forehead or feet), vegetables collected in supermarkets, greengrocers, and private gardens, and inanimate surfaces that are often in contact with humans, like tables in parks and a game console, is documented [29]. Our finding suggests cases of asymptomatic AB colonization from the patient's working environment before ICU admission, with medical interventions predisposing to infections. We found patients referred from other healthcare facilities were 14% more likely to have an infection compared to non-referred patients, corroborating other studies [30]. Intrahospital transfers increase a patient's exposure to both hospital surfaces and other patients [30]. We observed a 20% 30-day ICU mortality rate among patients with MDRAB, lower than reported (27.8-35%) in various regions globally [4-6]. Infections caused by drug-resistant bacteria, especially CR strains, have limited treatment options and are frequently associated with increased mortality. We found no significant association between mortality and the participants' socio-demographic and clinical characteristics, contradicting Brotfain et al. who reported age >65 years and the presence of comorbid disease (chronic obstructive pulmonary disease and chronic renal failure) as independent risk factors for in-hospital mortality in this population [5]. The current study finding could be due to the small size of the population subsection, whereby only six out of 30 patients with AB died during hospitalization. A multicenter study with a large study population is required to decipher the risk factors for mortality in patients with AB infections in our setting.

This study data has several limitations. First, the generalization of the findings may be limited, considering this was a monocenter study and the prevalence of MDRAB and risk factors may vary across different healthcare settings. Second, this study targeted only AB making it impossible to ascertain cases of coinfection with other bacterial pathogens that can present with clinical symptoms we used to interpret infection. There could have been cases whereby the clinical symptoms were caused by other bacteria, with AB as an asymptomatic colonizer; however, all the AB isolates were MDR, and the majority were CRAB, underscoring the public health significance of our study. To inform infection prevention and control programs, continuous surveillance of MDRAB, particularly CRAB, among the risk groups is urgently warranted in our study setting. Further studies utilizing large and diverse samples and a deeper exploration of mortality factors are warranted to provide a more comprehensive understanding of this critical issue.

# Conclusion

In the study, we report a prevalence of MDRAB (20.7%), dominated by CRAB isolates among ICU-admitted patients, with the patient's occupation and interhospital transfer as the risk factor for infection. All the AB isolates were colistin-nonresistant, suggesting a reserve clinical value in our study setting. The isolates exhibited high MARI values, indicating the cumulative impact of antibiotic exposure. Our findings underpin the need for strict adherence to and evaluation of infection prevention and control, and continuous surveillance of CRAB in ICU, especially among the risk groups, in the current study setting and beyond.

# **Declarations of competing interests**

The authors have no competing interests to declare.

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# Ethics approval and consent to participate

The study was conducted with approval from the School of Medicine, Moi University, and the superintendent at Moi Teaching and Referral Hospital (ELD/MTRH/R&P/10/2/V.2/2010), while ethical clearance was granted by the Institutional Research and Ethics Committee (IREC) at Moi University under reference number (IREC/2019/126 -0003392). The National Commission of Science Technology and Innovation (NACOSTI) also issued a permit for data collection under licensure number (NACOSTI/P/19/75649/29865). Before sample collection, informed consent was obtained from all participants or their representatives, and they were given the opportunity to opt-out or withdraw from the study at any time. To ensure confidentiality, data relating to patient characteristics were anonymized with codes. Samples were disposed of safely through the established hospital system after analysis, and all data collected will be deleted and shredded 3 years after the completion of the study.

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# Author contributions

The authors made significant contributions to this study. FK was responsible for data collection, cleaning, and analysis, and writing the manuscript. AM conducted data analysis, and wrote the manuscript. JM and NM contributed by reviewing the manuscript, ensuring its quality and accuracy.

### Consent for publication: Not applicable.

### References

- Brusselaers N, Vogelaers D, Blot S. The rising problem of antimicrobial resistance in the intensive care unit. Ann Intensive Care 2011;1:47. doi:10.1186/2110-5820-1-47.
- [2] Asif M, Alvi IA, Rehman SU. Insight into Acinetobacter baumannii: pathogenesis, global resistance, mechanisms of resistance, treatment options, and alternative modalities. *Infect Drug Resist* 2018;11:1249–60. doi:10.2147/IDR.S166750.
- [3] Gedefie A, Demsis W, Ashagrie M, Kassa Y, Tesfaye M, Tilahun M, et al. Acinetobacter baumannii biofilm formation and its role in disease pathogenesis: a review. *Infect Drug Resist* 2021;14:3711–19. doi:10.2147/IDR.S332051.
- [4] Antunes LCS, Visca P, Towner KJ. Acinetobacter baumannii: evolution of a global pathogen. Pathog Dis 2014;71:292–301. doi:10.1111/2049-632X.12125.
- [5] Brotfain E, Borer A, Koyfman L, Saidel-Odes L, Frenkel A, Gruenbaum SE, et al. Multidrug resistance Acinetobacter bacteremia secondary to ventilator-associated pneumonia: risk factors and outcome. J Intensive Care Med 2017;32:528–34. doi:10.1177/0885066616632193.
- [6] Garnacho-Montero J, Gutiérrez-Pizarraya A, Díaz-Martín A, Cisneros-Herreros JM, Cano ME, Gato E, et al. Acinetobacter baumannii in critically ill patients: molecular

epidemiology, clinical features and predictors of mortality. Enferm Infecc Microbiol Clin 2016;34:551–8. doi:10.1016/j.eimc.2015.11.018.

- [7] Rizk SS, Elwakil WH, Attia AS. Antibiotic-resistant Acinetobacter baumannii in lowincome countries (2000–2020): twenty-one years and still below the radar, is it not there or can they not afford to look for it? *Antibiotics (Basel)* 2021;10:764. doi:10.3390/antibiotics10070764.
- [8] Indian Council for Medical Research. Standard Operating Procedures Bacteriology, https://main.icmr.nic.in/sites/default/files/guidelines/Standard\_Operating\_Procedures\_Bacteriology\_1stEdition.pdf; 2015 [accessed 14 August 2023].
- [9] eBay. M100 Performance Standards for Antimicrobial Susceptibility Testing CLSI 29th Ed 9781684400324, https://www.ebay.com/itm/143234256540; 2023 [accessed 17 August 2023].
- [10] Mutua JM, Njeru JM, Musyoki AM. Multidrug resistant bacterial infections in severely ill COVID-19 patients admitted in a national referral and teaching hospital, Kenya. BMC Infect Dis 2022;22:877. doi:10.1186/s12879-022-07885-3.
- [11] Oli AN, Ogbuagu VI, Ejikeugwu CP, Iroha IR, Ugwu MC, Ofomata CM, et al. Multi-antibiotic resistance and factors affecting carriage of extended spectrum βlactamase-producing enterobacteriaceae in pediatric population of Enugu Metropolis, Nigeria. Med Sci (Basel) 2019;7:104. doi:10.3390/medsci7110104.
- [12] Banerjee T, Mishra A, Das A, Sharma S, Barman H, Yadav G. High prevalence and endemicity of multidrug resistant Acinetobacter spp. in Intensive Care Unit of a tertiary Care Hospital, Varanasi, India. J Pathog 2018;2018:9129083. doi:10.1155/2018/9129083.
- [13] Lob SH, Hoban DJ, Sahm DF, Badal RE. Regional differences and trends in antimicrobial susceptibility of Acinetobacter baumannii. Int J Antimicrob Agents 2016;47:317– 23. doi:10.1016/j.ijantimicag.2016.01.015.
- [14] Uwingabiye J, Lemnouer A, Baidoo S, Frikh M, Kasouati J, Maleb A, et al. Intensive care unit-acquired Acinetobacter baumannii infections in a Moroccan teaching hospital: epidemiology, risk factors and outcome. *GERMS* 2017;7:193–205. doi:10.18683/germs.2017.1126.
- [15] Ding R, Li X, Zhang X, Zhang Z, Ma X. The epidemiology of symptomatic catheterassociated urinary tract infections in the intensive care unit: a 4-year single center retrospective study. Urol J 2019;16:3 Art. no.. doi:10.22037/uj.v0i0.4256.
- [16] Bizuayehu H, Bitew A, Abdeta A, Ebrahim S. Catheter-associated urinary tract infections in adult intensive care units at a selected tertiary hospital, Addis Ababa, Ethiopia. *PLoS One* 2022;17:e0265102. doi:10.1371/journal.pone.0265102.
- [17] Hazen JE, Di Venanzio G, Hultgren SJ, Feldman MF. Catheterization of mice triggers resurgent urinary tract infection seeded by a bladder reservoir of Acinetobacter baumannii. Sci Transl Med 2023;15:eabn8134. doi:10.1126/scitranslmed.abn8134.
- [18] Du Toit A. A bacterial reservoir. Nat Rev Microbiol 2023;21:3 Art. no.. doi:10.1038/s41579-023-00858-6.
- [19] 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. doi:10.1186/1756-0500-7-500.
- [20] Chaïbi EB, Sirot D, Paul G, Labia R. Inhibitor-resistant TEM β-lactamases: phenotypic, genetic and biochemical characteristics. J Antimicrob Chemother 1999;43:447– 58. doi:10.1093/jac/43.4.447.
- [21] Domingues S, Rosário N, Ben Cheikh H, Da Silva GJ. ISAba1 and Tn6168 acquisition by natural transformation leads to third-generation cephalosporins resistance in Acinetobacter baumannii. *Infect Genet Evol* 2018;63:13–16. doi:10.1016/j.meegid.2018.05.007.
- [22] Agyepong N, Govinden U, Owusu-Ofori A, Essack SY. Multidrug-resistant gramnegative bacterial infections in a teaching hospital in Ghana. Antimicrob Resist Infect Control 2018;7:37. doi:10.1186/s13756-018-0324-2.
- [23] Odewale G, Adefioye OJ, Ojo J, Adewumi FA, Olowe OA. Multidrug resistance of Acinetobacter baumannii in Ladoke Akintola University Teaching Hospital, Osogbo, Nigeria. Eur J Microbiol Immunol (Bp) 2016;6:238–43. doi:10.1556/1886.2015.00018.
- [24] Suphansatit R, Uitrakul S. A pilot study of antibiotic regimens for infections caused by Acinetobacter baumannii in a Secondary Hospital in Thailand. *Infect Drug Resist* 2020;13:4495–500. doi:10.2147/IDR.S285261.
- [25] Revathi G, Siu LK, Lu PL, Huang LY. First report of NDM-1-producing Acinetobacter baumannii in East Africa. Int J Infect Dis 2013;17:e1255–8. doi:10.1016/j.ijid.2013.07.016.
- [26] Al-Tamimi M, Albalawi H, Alkhawaldeh M, Alazzam A, Ramadan H, Altalalwah M, et al. Multidrug-resistant Acinetobacter baumannii in Jordan. *Microorganisms* 2022;10:5 Art. no.. doi:10.3390/microorganisms10050849.
- [27] Al Bshabshe A, Joseph MRP, Al Hussein A, Haimour W, Hamid ME. Multidrug resistance Acinetobacter species at the intensive care unit, Aseer Central Hospital, Saudi Arabia: a one year analysis. Asian Pac J Trop Med 2016;9:903–8. doi:10.1016/j.apitm.2016.07.016.
- [28] Omulo S, Oluka M, Achieng L, Osoro E, Kinuthia R, Guantai A, et al. Pointprevalence survey of antibiotic use at three public referral hospitals in Kenya. PLoS One 2022;17:e0270048. doi:10.1371/journal.pone.0270048.
- [29] Eveillard M, Kempf M, Belmonte O, Pailhoriès H, Joly-Guillou ML. Reservoirs of Acinetobacter baumannii outside the hospital and potential involvement in emerging human community-acquired infections. Int J Infect Dis 2013;17:e802–5. doi:10.1016/j.ijid.2013.03.021.
- [30] Boncea EE, Expert P, Honeyford K, Kinderlerer A, Mitchell C, Cooke GS, et al. Association between intrahospital transfer and hospital-acquired infection in the elderly: a retrospective case–control study in a UK hospital network. *BMJ Qual Saf* 2021;30:457–66. doi:10.1136/bmjqs-2020-012124.