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Original article

Prevalence of Carbapenem-Resistant Enterobacteriaceae Isolated from Clinical Samples in Medical Tobruk Center

Sara Fathi[1], Heba Hassan[1], Laila Alfageih[1,2]*

[1]*Libyan Academy for Postgraduate Studies, Tobruk Branch, Libya*
[2]*Department of Medical Science, Faculty of Dentistry, Tobruk University, Tobruk, Libya*
Corresponding Email. *Laila.alfageih@tu.edu.ly*

Abstract
Globally, intensive care units (ICUs) are encountering the emergence and spread of antibiotic-resistant pathogens, and for some pathogens, there are few therapeutic options available. This study tries to assess the prevalence, susceptibility pattern, and risk factors of Carbapenem-Resistant Enterobacteriaceae (CRE) infections among ICU patients, healthcare workers, and surface swabs in the medical center of Tobruk, Libya. Also, to assess the incidence and prevalence rate of CRE in the medical center of Tobruk. A descriptive cross-sectional study was used to study 119 collected samples. Of which, 119 samples were collected from patients. The above samples were collected from four units of intensive care were (intensive care unit (ICU) and cardiac care unit (CCU), Pediatric intensive care unit (PICU) Neonatal intensive care unit (NICU). The identified Enterobacteriaceae were first confirmed by biochemical methods, while the confirmed isolates were tested for carbapenemase production using three discs (EME, IMP, and ETP). The resistance to (Ertapenem, Imipenem, and Meropenem) was considered as CRE. A total of 79 (66.4%) out of the 119 samples yielded clinical isolates of Enterobacteriaceae and gram negative bacteria from patients as follows: 23 (29.1%) Klebsiella pneumoniae, 15 (19%) Acinetobacter baumannii, 12 (15.2%) Escherichia coli, 7 (9%) Pantoea sp., 5 (6.3%) Pseudomonas aeruginosa, 5 (6.3%) Citrobacter freundii, 4 (5.1%) Enterobacter cloacae, 2 (2.6%) Citrobacter freundii, 3 (3.8%) Chryseomonas luteola, 2 (2.5%) Proteus vulgaris, 2 (2.5%) Flavimonas oriyzihabitans, and 1 (1.3%) Serratia marcecens. Screening the Enterobacteriaceae-positive samples for carbapenem resistance showed 48 samples of 79 (60.8%) as carbapenem resistant Enterobacteriaceae as follows: 18 (22.8%) Klebsiella pneumonia, 9 (11.4%) Acinetobacter baumannii, 6 (7.6%) Escherichia coli, 4 (5.1%) Citrobacter freundii, 3 (3.8%) Pseudomonas aeruginosa, 3 (3.8%) Pantoea sp., 2 (2.5%) Enterobacter cloacae, 2 (2.5%) Chryseomonas luteola, 1 (1.3%) Serratia marcecens. The study provided evidence of the presence of CRE infections among patients admitted to ICUs in the study centers. This underscores the need for effective infection prevention and control measures to avoid the spread of CRE in a hospital setting.
Keywords. *ICUs, Enterobacteriaceae, CRE, Gram-Negative Bacteria, Antibiotic Resistance.*

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Introduction

Enterobacteriaceae play a crucial role in the intestinal microbiome and are among the most identified pathogens in humans. They are implicated in a range of infections, including cystitis, pyelonephritis with fever, septicemia, pneumonia, peritonitis, meningitis, and infections associated with medical devices. These organisms are responsible for both community-acquired and hospital-acquired infections, demonstrating a significant ability for human-to-human transmission via hand carriage and the consumption of contaminated food and water [1].

Carbapenems are vital components of the antibiotic repertoire. Among the various β-lactam antibiotics, carbapenems possess the broadest spectrum of activity and the highest effectiveness against both Gram-positive and Gram-negative bacteria. As a result, they are often utilized as "last-line agents" or "antibiotics of last resort" in situations involving severely ill patients or when resistant bacterial infections are suspected [2]. The infections associated with CRE show resistance to most existing antimicrobial treatments, resulting in poor clinical outcomes. This issue is particularly pronounced in low- and middle-income countries, where there is a lack of resources dedicated to the surveillance and management of CRE infections [3].

Extended-spectrum beta-lactamases (ESBLs) or AmpC enzymes, in conjunction with decreased permeability from drug loss due to porin loss, are the primary cause of CRE infections. As a result, isolates generating carbapenemases from Ambler Classes A, B, and D emerged in response to pressure on carbapenems, which are the last resort for treating infections caused by bacteria that produce ESBL [4]. A class of β-lactam antibiotics with a remarkably wide range of

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action is carbapenems [5]. These agents are employed as a final measure in the treatment of various multidrug-resistant, gram-negative bacteria, particularly in instances of infections caused by Enterobacteriaceae that produce Extended-Spectrum Beta-Lactamase (ESBL) and AmpC enzymes [6]. The public's health is seriously threatened by the recent rise and spread of bacteria resistant to carbapenem. Members of the Pseudomonas and Acinetobacter genera, as well as several Enterobacteriaceae, have been found to exhibit resistance [6,7]. This study tries to assess the prevalence, susceptibility pattern, and risk factors of Carbapenem-Resistant Enterobacteriaceae (CRE) infections among ICU patients, healthcare workers, and surface smears in the medical center of Tobruk, Libya

Methods

Site of study

This study was carried out in Eastern Libya, the city of Tobruk.

Study population

Specimens were taken from patients immediately upon admission to the hospital and again before discharge from the hospital in order to find out whether they were carriers of carbapenem-resistant Enterobacteriaceae before admission or if they acquired the infection during their hospital stay. And medical staff, specimens were taken from all surfaces, including medical devices within the departments concerned with the study, the intensive care unit (ICU), and cardiac care unit (CCU), and Pediatric intensive care unit (PICU), Neonatal intensive care unit (NICU).

Sample collection

In this study, clinical isolates from pus swabs, urine, stool, blood, sputum, nasal swabs, ear swabs, and amniotic fluid were collected. Isolations were taken over a period 8 months cross section study.

Inclusion criteria

This study on carbapenem-resistant Enterobacteriaceae at the Tobruk medical center was follow ethical standards to protect participants, ethical considerations include informed consent, voluntary participation, and confidentiality, the research protocol was reviewed before data collection, risks and purpose of the study was explained to participants, adhering to ethical considerations is important for the study's integrity and trust between researchers and participants.

Cultivation of samples

Swabs were taken from the environment of the care units: the Intensive Care Unit, the Cardiac Care Unit, the Pediatric Intensive Care Unit, and the Neonatal Intensive Care Unit, where the swabs included the environment surrounding the patients. The study was carried out in the period from July 2023 to August 2024.

The samples were cultured on the blood agar (blood agar in order to grow types of bacteria of medical importance), such as streptococcus and staphylococci, and several types of gram-negative bacteria, and cultured on MacConkey agar, this medium is specifically designed for the growth of gram-negative bacteria. And incubate it at a temperature of 37°C for a period of 8-24 hours for the purpose of isolating it without color and which was tested by the API -E20 (Analytical Profile Index) system and the biochemical tests.

Ethical considerations

This study on carbapenem-resistant Enterobacteriaceae at the Tobruk medical center was follow ethical standards to protect participants, ethical considerations include informed consent, voluntary participation, and confidentiality, the research protocol was reviewed before data collection, risks and purpose of the study was explained to participants, adhering to ethical considerations is important for the study's integrity and trust between researchers and participants.

Microbiological investigation

All samples collected from patients in intensive care units were processed. The identified Enterobacteriaceae were first confirmed by biochemical methods, while the confirmed isolates were tested for carbapenemase production using three discs (EME, IMP, and ETP). The resistance to (EME, IMP, and ETP) was considered as CRE (Figure 1).

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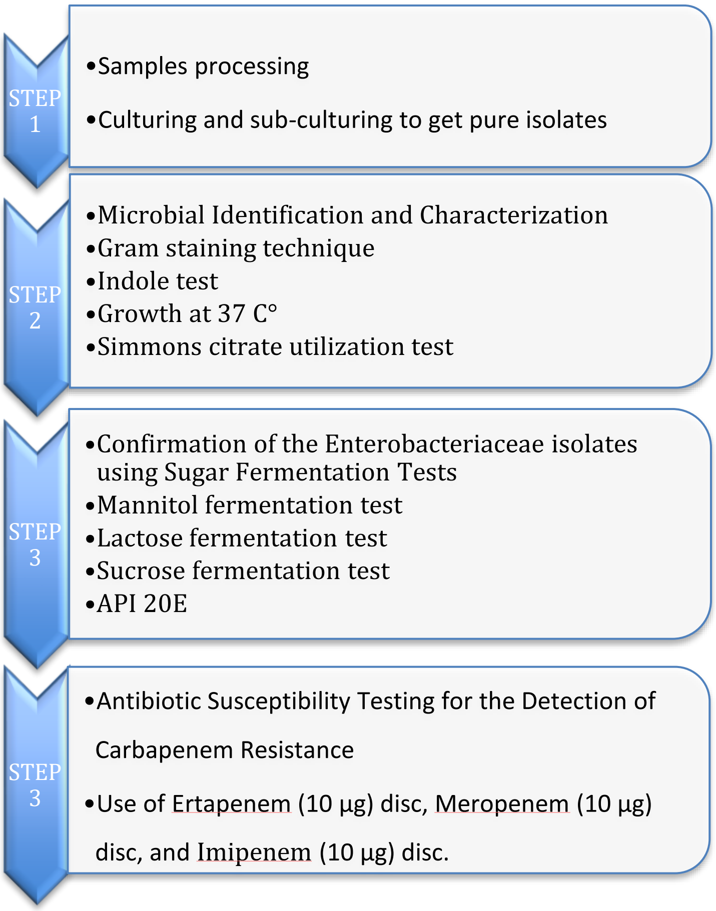

Figure 1. A flowchart of the detection of the Carbapenem-Resistant Enterobacteriaceae.

Statistical analysis

Statistical analyses were done by using SPSS. Microsoft Office Excel 2019 was used for entry data. The results were expressed as percentages and proportions. The Chi-square test was performed. The Value of P≤0.05 was used as a significant level for association in comparison.

Results

Description of study sample

All samples were collected from patients, were recruited and collected from Intensive Care Units (ICUs) at the Medical Center of Tobruk. A total of 119 investigated patients belonged to four ICUs vis: ICU=32, CCU=32, PICU=32, and NICU=23 (Figure 2).

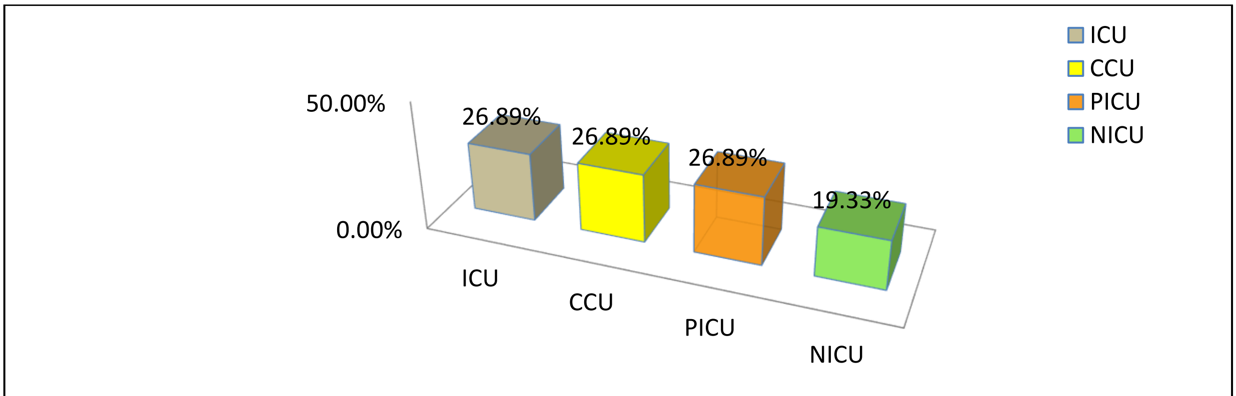

Figure 2. Case distribution by the Medical Center of Tobruk

Age and Gender

Of the 119 patients included in this study, the patients were found in the age range from 1 day to 95 years. The patients were grouped into pediatric patients, who were younger than 15 years, and accounted for about 46.2%, while adult patients, those who were older than 15 years, accounted for about 53.8% (Figure 3). On the other hand, patients were classified according to gender, into male patients were 55% (65) and female patients were 45% (54) (Figure 4).

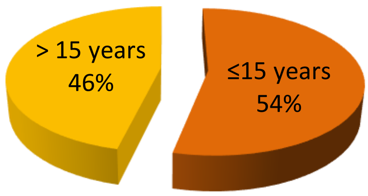

Figure 3. Patient distribution by age

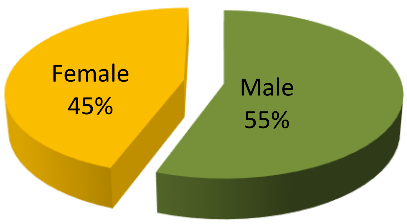

Figure 4. Patient distribution by Gender

Distribution of samples according to type

The study included eighteen types of samples taken from patients. The most of which were blood samples (33), followed by urine samples (22), sputum (17), pus (11), then nasal swabs (7) and endotracheal intubation (6), vaginal and throat samples were (4), CSF and Ear both (3), and the other was nasogastric tube (1), stool (1), cintral line (1), colostomy (1), umbilical (1), suction (1), nasopharngeal swab (1), wound swab (1) and chest tube (1) (Table 1) (Figure 5).

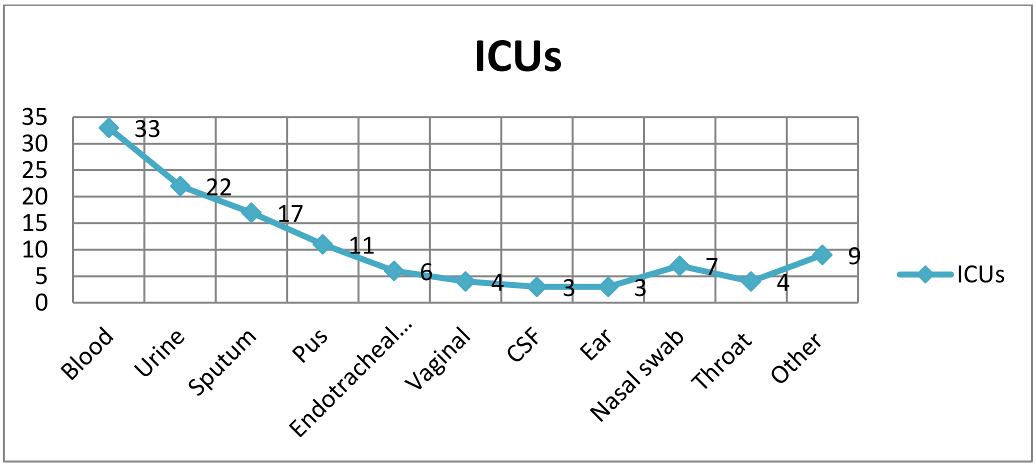

Figure 5. Distribution of patients' samples according to type of sample

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Antimicrobial susceptibility testing

The results of this study showed that the total percentage of Gram-negative bacteria isolated from patient samples was 66.4%, while the total percentage of Gram-positive bacteria was 24.4%. The *Candida albicans* accounted for 5%, and the percentage of samples with no bacterial growth was 4.20%. In the ICU unit, Gram-negative bacteria constituted 29% compared to 27.6% of Gram-positive bacteria, but the CCU unit showed a higher percentage of Gram-positive bacteria 31% compared to Gram-negative bacteria 26.6%. The percentages of Gram-negative bacteria in both the PICU and NICU units were 25.3% and 19%, respectively. The results of the chi-square test showed a significant (X^2=25.36; P<0.01) association between the intensive care unit and type of isolated microorganism from patients (Table 2).

Table 1: The distribution of samples according to type

Specimen	ICU N(%)	CCU N(%)	PICU N(%)	NICU N(%)	Total N(%)
Blood	5(15.6)	6(18.8)	12(37.5)	10(43.5)	33(27.7)
Urine	3(9.4)	7(21.9)	5(15.6)	7(30.4)	22(18.5)
Sputum	8(25)	9(28.1)	0(0)	0(0)	17(14.3)
Pus	1(3.1)	4(12.5)	3(9.4)	3(13)	11(9.2)
Endotracheal intubation	4(12.5)	1(3.1)	1(3.1)	0(0)	6(5)
Vaginal	3(9.4)	1(3.1)	0(0)	0(0)	4(3.4)
CSF	0(0)	0(0)	1(3.1)	2(8.7)	3(2.5)
Nasogastric tube	0(0)	0(0)	1(3.1)	0(0)	1(0.84)
Stool	0(0)	0(0)	1(3.1)	0(0)	1(0.84)
Central Line	1(3.1)	0(0)	0(0)	0(0)	1(0.84)
Colostomy	0(0)	1(3.1)	0(0)	0(0)	1(0.84)
Umbilical	0(0)	0(0)	0(0)	1(4.3)	1(0.84)
Suction	1(3.1)	0(0)	0(0)	0(0)	1(0.84)
Nasopharyngeal swab	1(3.1)	0(0)	0(0)	0(0)	1(0.84)
Wound swab	1(3.1)	0(0)	0(0)	0(0)	1(0.84)
Nasal swab	4(12.5)	3(9.4)	0(0)	0(0)	7(5.9)
Ear	0(0)	0(0)	3(9.4)	0(0)	3(2.5)
Throat	0(0)	0(0)	4(12.5)	0(0)	4(3.4)
Chest tube	0(0)	0(0)	1(3.1)	0(0)	1(0.84)
Total	32(26.89)	32(26.89)	32(26.89)	23(19.32)	119(100)

Table 2: Distribution of Gram-negative and Gram-positive bacteria among isolates from patients' samples

Units	Gram-negative bacteria N(%)	Gram-positive bacteria N(%)	Candida albican N(%)	No growth bacteria N(%)	Total N(%)
ICU	23(29)	8(27.6)	1(16.7)	0(0)	32(26.89)
CCU	21(26.6)	9(31)	2(33.3)	0(0)	32(26.89)
PICU	20(25.3)	9(31)	3(50)	0(0)	32(26.89)
NICU	15(19)	3(10.3)	0(0)	5(100)	23(19.33)
Total	79(66.4)	29(24.4)	6(5)	5(4.20)	119(100)
Chi-square test	X2=25.36; P<0.01				

Out of 119 samples isolated from patients from various ICUs, 79 isolated samples were found to be Enterobacteriaceae and gram-negative bacterial infections. The results also showed that the percentage of Gram-negative bacteria isolated was the highest among males 62% (49/79), while among females it was 38% (30/79) (Table 3). On the other hand, out of a total of 29 isolated samples, the gram-positive bacteria were higher among females, 55.2% (16/29), when compared

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with males, 44.8% (13/29). The results explained that insignificant (X2=6.38; P>0.05) association between the sex of the patient and the type of isolated microorganism (Table 3).

Table 3: Distribution of Gram-negative and Gram-positive bacteria between males and females among different ICUs

Units	Gram-negative bacteria (n=79)		Gram-positive bacteria (n=29)		Candida albican (n=6)		No growth bacteria (n=5)	
	Male N(%)	Female N(%)	Male N(%)	Female N(%)	Male N(%)	Femal e N(%)	Male N(%)	Female N(%)
ICU	16(50)	7(21.9)	5(15.6)	3(9.4)	0(0)	1(3.1)	0(0)	0(0)
CCU	13(40.6)	8(25)	4(12.5)	5(15.6)	0(0)	2(6.3)	0(0)	0(0)
PICU	11(34.4)	9(28.1)	3(9.4)	6(18.8)	2(6.3)	1(3.1)	0(0)	0(0)
NICU	9(39.1)	6(26.1)	1(4.3)	2(8.7)	0(0)	0(0)	1(4.3)	4(17.4)
Total	49(62)	30(38)	13(44.8)	16(55.2)	2(33.3)	4(66.7)	1(20)	4(80)
Chi-square test	X2=6.38; P>0.05							

Of the 79 Enterobacteriaceae and gram-negative bacterial infections, 48 (60.8%) displayed phenotypic carbapenem resistance, while 31 (39.24%) bacterial infections were carbapenem sensitive. Moreover, the results showed that 9 different bacterial species from 11 investigated species were carbapenem-resistant. Of these, *Klebsiella pneumoniae* (n = 18; 78.3%) displayed the highest levels of carbapenem resistance. The other strains detected include *Acinetobacter baumannii* (n = 9; 60%), *Escherichia coli* (n = 6; 50%), *Citrobacter freundii* (n = 4; 80%), *Pseudomonas aeruginosa* (n = 3; 60%), *Pantoea* sp. (n = 3; 42.9%), *Enterobacter cloacae* (n = 2; 50%), *Chryseomnasluteola* (n = 2; 66.7%), and *Serratia marcescens* (n = 1; 100%). The results of X^2 analysis explained that insignificant (X^2=12.34; P>0.05) association between the detected bacteria species and the carbapenem-susceptibility test (Table 4).

Table 4: Distribution of organisms isolated from patients during the study period

Organism	G- isolated; n(%=n/ total isolate)	Carbapenem-susceptibility	
		Sensitive; n (%=n/total organism)	Resistant; n (%=n/total organism)
Klebsiella pneumoniae	23(29.1)	5(21.7)	18(78.3)
Acinetobacter baumannii	15(19)	6(40)	9(60)
Escherichia coli	12(15.2)	6(50)	6(50)
Enterobacter cloacae	4(5.1)	2(50)	2(50)
Pseudomonas aeruginosa	5(6.3)	2(40)	3(60)
Citrobacter freundii	5(6.3)	1(20)	4(80)
Pantoea sp.	7(9)	4(57.1)	3(42.9)
Chryseomonas luteola	3(3.8)	1(33.3)	2(66.7)
Serratia marcescens	1(1.3)	0(0)	1(100)
Flavimonas oriyzihabitans	2(2.5)	2(100)	0(0)
Proteus vulgaris	2(2.5)	2(100)	0(0)
Total	79(100)	31(39.24)	48(60.76)
Chi-square test	X2=12.34; P>0.05		

The four most frequently recorded specimen sources from which the Enterobacteriaceae and gram-negative organisms were cultured include blood (n = 21; 26.6%), urine (n = 15; 17%), sputum (n = 15; 17%), and pus (n = 9; 11.4%) as summarized in (Table 5). The most abundant isolated organism in the blood sample was *Klebsiella pneumoniae* (6, 18.2%),

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and *Acinetobacter baumannii* (6, 18.2%), while in the urine samples was *Klebsiella pneumoniae* (5, 22.7%) and *Escherichia coli* (6, 27.3%) were found in the sputum sample was *Klebsiella pneumoniae* (6, 35.3%), and in the pus sample was *Klebsiella pneumonia* (3, 27.3%), *Acinetobacter baumannii* and *Pseudomonas aeruginosa* were all at 2, 18.2% (Table 6).

Table 5: Distribution of organisms across clinical specimens from patients

Source of specimen	Type of organisms	
	All Enterobacteriaceae and gram-negative bacteria; n (%=n/total isolates)	Carbapenem-resistant (CRE) isolates; n (%=n/number of isolates in specimen)
Blood	21(27)	18(85.7)
Urine	15(17)	9(60)
Sputum	15(17)	9(60)
Pus	9(11.4)	6(66.7)
Endotracheal intubation	6(7.6)	1(16.7)
Vaginal	3(3.8)	3(100)
CSF	3(3.8)	1(33.3)
Nasogastric tube	1(1.3)	0(0)
Stool	1(1.3)	0(0)
Central Line	1(1.3)	0(0)
Colonstomy	1(1.3)	1(100)
Umbilical	2(2.5)	0(0)
Suction	1(1.3)	0(0)
Total	79(100)	48(60.77)

Table 6: The bacterial strains isolated from samples

Sample Bacteria strain	Blood n=33	Urine n=22	Sputum n=17	Pus n=11	Other n=36	Total n=119
Klebsiella pneumoniae	6(18.2%)	5 (22.7%)	6 (35.3%)	3 (27.3%)	3(8.3%)	23(19.3%)
Acinetobacter baumannii	6 (18.2%)	0(0%)	2 (11.8%)	2(18.2%)	5(13.9%)	15(12.6%)
Escherichia coli	2 (6%)	6 (27.3%)	0 (0%)	1(9%)	3(8.3%)	12(10%)
Enterobacter cloacae	1 (3%)	2 (9%)	0 (0%)	0 (0%)	1(2.8%)	4 (3.4%)
Pseudomonas aeruginosa	0(0%)	0(0%)	1(5.9%)	2(18.2)	2(5.6%)	5 (4.2%)
Citrobacter freundii	2(6%)	2(9%)	0(0%)	0 (0%)	1 (2.8%)	5 (4.2%)
Pantoea sp.	2(6%)	0(0%)	1(5.9%)	0 (0%)	4 (11%)	7 (5.9)
Chryseomonas luteola	1(3%)	0(0%)	1(5.9%)	0 (0%)	0 (0%)	3 (2.5%)
Serratia marcescens	1(3%)	0(0%)	0(0%)	0(0%)	0 (0%)	1 (0.8%)
Flavimonas oriyzihabitans	0(0%)	0(0%)	2(11.8%)	0(0%)	0 (0%)	2 (1.7%)
Proteus vulgaris	0(0%)	0(0%)	2(11.8%)	0(0%)	0 (0%)	2 (1.7%)

Table 7: The antibiotic susceptibility pattern of carbapenem-susceptible bacteria from patients

Bacteria strain	Number of CRE isolates	ERT	EME	IMP
Klebsiella pneumoniae	18	R	R	R
Acinetobacter baumannii	9	R	R	R
Escherichia coli	6	R	R	R
Enterobacter cloacae	2	R	R	R
Pseudmonas aeruginosa	3	R	R	R

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Citrobacter freundii	4	R	R	R
Pantoea sp.	3	R	R	R
Chryseomonas luteola	2	R	R	R
Serratia marcescens	1	R	R	R

(ETP = Ertapenem, IMP = Imipenem, EME= Meropenem)

Discussion

Carbapenem is one of the antibiotics that offer broad-spectrum activity and is used as a last-line therapy for multidrug-resistant bacteria. The treatment of infections caused by drug-resistant bacteria is sometimes impossible and may lead to unexpected or bad complications. Antimicrobial resistance increases the cost of health care and the possibility of complications. Without effective antimicrobials for the prevention and treatment of CRE infections, medical procedures become very high-risk. The major worrisome, treatment of the infections caused by these multidrug organisms is extremely difficult, which may result in high mortality rates and healthcare costs. In intensive care units, hospitalized patients are more susceptible to nosocomial pathogens, especially multidrug-resistant bacteria. These bacteria can spread from patient care staff and medical equipment in intensive care units and vice versa, leading to nosocomial outbreaks through cross-infection and/or cross-contamination [8]. Therefore, the main objective of this study was to determine the MDR profile of pathogenic bacteria isolated from collected samples and their antibiotic susceptibility profiles in different intensive care units of Toburk City Medical Center.

Carbapenem-resistant Enterobacteriaceae and gram-negative infections have become a critical problem and a significant threat to global health, associated with a high morbidity and mortality rate [1,9,10]. High rates of carbapenem resistance, 28.6% of isolates have also been observed in Uganda [11]. In Tanzania, the prevalence of carbapenemase-producing isolates was 35% [12]. Carbapenem resistance in low and middle-income countries (LMICs) in Africa is likely to increase as a result of unrestricted usage of antibiotics, as the majority of the population consumes antibiotics without a clinical prescription [13]. This value higher than those reported in literature from other locations—Uganda (30.6%) [14], Tanzania (42.0%) [15], India (24.0%) [16], and also higher than that reported from south-west Nigeria (22%) [17], and from Tunisia (15.8%) [18]. Other studies from different locations in Nigeria have also reported varying numbers, with [19], who reported a prevalence of 6.8% from Northeast Nigeria, while [20] and [21], reported a prevalence of 36.8% and 27.4% respectively. The clinical samples from which the highest proportion of carbapenem-resistant isolates were cultured were blood (27%), urine culture (17%), sputum (17%), and pus (11.4%). These are similar to the results obtained in London by [22], where they found urine cultures (44.5%), sputum cultures (14.5%) were the most frequently recorded clinical specimens containing carbapenem-resistant Enterobacteriaceae and gram-negative bacterial infections.

Differences were also noticed in the proportion of carbapenem-resistant infections across clinical departments, with samples from patients on the intensive care unit ICU (29%), CCU (26.6%), PICU (25.3%), and NICU (19%) in displaying the highest proportions of carbapenem-resistance, a result which corresponds with that obtained in South Africa by [23], where the ICU (5%) and surgical wards (23%) reported the highest CRE prevalence. This difference could be explained by the critical nature of the illnesses that patients on these wards suffer and their requirement for prolonged hospitalization. This information related to different care units could be used to identify locations within the hospital requiring increased infection prevention and control measures to reduce the dissemination of CRE and gram-negative infections.

Another variable within which there were differences in proportion of carbapenem-resistant isolates was age, with the age over 15 years displaying the highest proportion (55.7%) of CRE infections and the age low than or equal 15 years displaying the lowest proportion (44.3%). This finding is commensurate with those from other studies, such as that from China [24] in which patients aged 50–64 years had the second highest rate of carbapenem-resistant infections (23.9%), while those aged 65–79 years had the highest rate (28.9%). However, a prospective, multicentre, observational study of hospitals in Ohio, Pennsylvania and Michigan, launched by the Consortium on resistance against carbapenems in Klebsiella and other Enterobacteriaceae (CRACKLE) found that the median age of patients enrolled in the study, with carbapenem-resistant K. pneumoniae infections was much higher at 70 years (interquartile range 58–81 years) [25]. A possible explanation for the higher predisposition of middle-aged and elderly patients to these infections could be the higher prevalence of co-morbidities such as: diabetes mellitus, hypertension, cardiovascular diseases, renal

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insufficiency and cancer, which result is frequent hospitalization, long hospital stay and use of multiple antibiotics use, all of which predisposes them to the most severe forms of these infections [26,27].
Gender distribution in this study was 55%% males and the rest 45% females. Though the higher proportions of males 62% (49/79) of the subjects, were found to be Enterobacteriaceae and gram-negative bacterial infections, than females 38% (30/79). Regarding antibiotic susceptibility testing, all 60 CRE isolates from patients, healthcare workers, and surface swabs were highly resistant to Ertapenem, Imipenem, and Meropenem, with a 100% resistance rate. Other antibiotics such as Ceftazidime (93.3%), Cefoxitin, Amoxicillin, Clavulanic acid, and Cefepime also had a resistance rate (91.7%), and Ceftriaxone (90%), while Cefotaxime (88.3%), then Aztronam had less resistance compared to other antibiotics that were used in this study at a rate of (76.7%). In agreement with this observation, the previous studies also reported that 100% resistance of the carbapenem-resistant isolates were also found to be multidrug resistant (defined as non-susceptibility to at least one agent in three different antibiotic groups). These findings are in tandem with existing literature on the subject as reported by [24,17], where all carbapenem-resistant Enterobacteriaceae were also resistant to all Cephalosporins tested, and aminoglycosides possessed better activity compared with Fluoroquinolones.
The reason for this can be traced back to the mechanism of development of carbapenem-resistance, which is due to the development of extended spectrum-β-lactamases, and Cephalosporins, being β-lactam antibiotics themselves, would therefore be ineffective against CRE infections. Therefore, this study forms an opening to facilitate epidemiological studies. However, in addition to antibiotic combinations for the treatment of CRE, new treatment options using other antibiotics are gradually emerging. However, these all have their disadvantages, such as drug delivery and resistance. That is why this approach has not been successfully applied in practice. Moreover, the use of new antibiotics leads to different resistance mechanisms, and new resistance characteristics may appear. Therefore, the rational use of antibiotics in appropriate combinations is the only promising alternative for infections caused by CRE-like bacteria.
Of the 79 Gram-negative bacterial and Enterobacter infections, 79 (60.4%) were isolated from patients and showed apparent resistance to carbapenems. The study showed that *Klebsiella pneumoniae* (29.1%) had the highest levels of carbapenem resistance isolated from patients, as well as carbapenem-resistant *Klebsiella pneumoniae* isolated from healthcare workers (23.1%). This is consistent with a number of previous studies that the highest percentage of Enterobacteriaceae isolated was reported by Aya et al. (21%) [28], but was less than that reported by Deogratius et al., (52.2%) [29]. In our study, Acinetobacter was the second most common isolate with 19%, followed by *Escherichia coli* (15.2%). While the previous studies reported *Escherichia coli* was the second highest bacteria in other studies, such as Anita et al. [30].

Limitations
The analytical results presented in this study provide insight into the epidemiology of carbapenem-resistant Enterobacteriaceae and other Gram-negative bacteria in the healthcare setting studied. In addition, we demonstrated how routinely collected microbiology laboratory data can be used to gain insight into infectious disease trends and emerging threats; however, this study is not without limitations. First, we did not report the molecular epidemiology of carbapenem resistance mechanisms in the study population. This is important to understand the molecular basis for the emergence of these observed resistance characteristics. Second, we also did not report hospital-level carbapenem resistance rates nor the clinical characteristics of the patients from whom the study isolates were obtained. The reasons for this were that the required data could not be collected due to difficulties in collecting the necessary data, a lack of sufficient collaboration, and the absence of a centralized electronic health information management system at the study site. These data, if available, would provide insight into clinical risk factors associated with carbapenem resistance in the study population, which could inform health promotion efforts. Finally, due to the small sample size, we were unable to perform organism-level analyses to determine trends in carbapenem resistance among bacterial species and investigate possible differences or associations.

Conclusion
The study provided evidence of the presence of CRE infections among patients admitted to ICUs in the study centers. This underscores the need for effective infection prevention and control measures to avoid the spread of CRE in a hospital setting.

Conflict of interest. Nil

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