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Original Article

Intensive care units-acquired urinary tract infections: a 5-year multicenter retrospective study in Istanbul

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Abstract

Introduction: Urinary tract infection (UTI) is the most common hospital-acquired infection worldwide. Nosocomial UTI develops due to swelling of the urinary catheter. This study was conducted to determine the pathogens associated with catheter-associated urinary tract infection (CAUTI), identify these microorganisms, and investigate antimicrobial resistance patterns in intensive care units-acquired CAUTIs of two hospitals during 5 years.

Methodology: Semiquantitative culture of urine samples was done in both hospitals. Identification and sensitivity of microorganisms were made using conventional methods and automated systems. Susceptibility testing was performed according to Clinical and Laboratory Standards Institute (CLSI) standards and European Committee on Antimicrobial Susceptibility Testing (EUCAST). All 24,882 patients were admitted to the intensive care units (ICUs) at both hospitals.

Results: A total of 677 microorganisms were isolated from 580 patients. The CAUTI rate observed in patients was 580/24,882 (2.33%). The most common microorganisms isolated were *E. coli* (184; 27.18%), *K. pneumoniae* (128; 18.9%), and enterococci (104; 15.36%). Vancomycin resistance was noted in 10.6% of all enterococci. Staphylococci were not resistant to vancomycin. The most effective antibiotics for Gram-negative bacteria were colistin (90.5%), followed by amikacin (77.4%), meropenem (66.6%), and imipenem (66.4%). High rates of extended-spectrum beta lactamase (ESBL) was noted in 54.3% and 69.5% of *E. coli* and *K. pneumoniae*, respectively.

Conclusions: Universal recommendations on the use of catheters should be carefully applied to prevent the development of the infection. Patients who are infected by multidrug resistant (MDR) microorganisms should be followed carefully. Both centers should develop their own policies on this issue.

Key words: urinary tract infection; intensive care units; antimicrobial resistance; ESBL.

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Introduction

Urinary tract infection (UTI) is among the most frequent nosocomial infections in intensive care unit (ICU) patients. Urinary catheterization is applied in 15–25% of hospitalized patients. The most common infections that occur as a result of urinary catheter application are bacteriuria and catheter-associated UTI (CAUTI). CAUTI may lead to various complications such as endocarditis, bacteremia, meningitis, osteomyelitis, and septic arthritis. These pathologies result in prolongation of hospital stay. However, the most important risk factors are the duration of catheterization and indwelling catheter [1–4]. Most of these microorganisms are part of patients' endogenous bowel flora, but they can also be acquired from the hospital environment. They are responsible for approximately 20–30% of nosocomial infections in ICUs [1,3].

Prolonged catheterization is the most important risk factor in ICU patients. When an indwelling urinary catheter remains in place for more than 7 days, up to 25% of patients develop bacteriuria or funguria [1–4]. Common microorganisms for CAUTI are *Escherichia coli*, *Klebsiella pneumoniae*, *Enterobacter* spp., *Proteus mirabilis*, *Pseudomonas aeruginosa*, enterococci, staphylococci, and *Candida* species. Moreover, CAUTIs constitute probably the largest institutional reservoir of nosocomial antibiotic resistant organisms; the most important of these are multidrug resistant (MDR) microorganisms. Microorganisms gain access through direct inoculation during catheterization or through extraluminal contamination, which may occur later by microorganisms rising from the perineum. Also, the use of broad-spectrum antibiotics in ICUs leads to the spread of drug-resistant microorganisms, and MDR bacteria are more frequent in ICUs than in wards [4–6].

This study aimed to determine the microorganisms associated with CAUTI and investigate their susceptibility to the antimicrobial agents used in the

ICU patients in the Institute of Cardiology and Istanbul Training and Research Hospital over 5 years.

Methodology

Study design

This retrospective study was approved by the Ethical Committee of the Istanbul Training and Research Hospital, University of Health Science, Istanbul, Turkey (Date: 19 February 2021 and No: 2735).

The study was conducted in the 12-bed surgical ICU and 10-bed coronary ICU in a 100-bed cardiac center, and a 93-bed general ICU in a 610-bed research hospital. A total of 24,882 ICU patients were treated in the ICUs at the Institute of Cardiology and Istanbul Training and Research Hospital between January 2015 and December 2019. The age of the patients was in the range of 19–106 years. The length of stay of patients in ICUs was 8–126 days. All of the patients admitted to the ICUs for more than 48 hours were included in the present study. Patient's clinical and demographic data, including date of hospitalization and discharge, age, gender, causes of admission to ICU, length of hospitalization, underlying disease, duration of catheterization, and use of antibiotics, were recorded. Successive cultures from the same patient were excluded to avoid duplication of data.

CAUTI was defined according to the Centre for Disease Control and Prevention's (CDC) criteria [7]. ICU-acquired CAUTI was detected as a urinary infection identified at least 48 hours after ICU admission and confirmed by bacteriuria $\geq 10^5$colony forming units/mL (CFU/mL).

Urine specimen collection and microbiological examination

Urine specimens were collected aseptically before catheter change or removal from each patient, using a sterile syringe from the distal edge of the catheter tube into a sterile universal tube and sent to the microbiology laboratory for examination. The samples were investigated using the standard microbiological procedures that included microscopy, culture identification, and antibiotic susceptibility testing. All specimens were inoculated on blood agar and MacConkey agar (Oxoid, UnipathLtd, Basingstoke, UK) for isolating the urinary pathogens.

A semi-quantitative method of urine culture was followed. A sterile calibrated loop was used to deliver a loopful (0.01 mL) of urine onto each culture media. All the culture plates were incubated at 35 °C aerobically for 18–24 hours and Gram staining was performed on positive culture of the organism likely to be present and counted in CFU/mL. The culture-positive isolates were identified using the standard microbiologic laboratory tests and automated systems (Vitek 2; Biomerieux, Marcy I'Etoile, France; and BD Phoenix, BD, Franklin Lakes, USA; identification and susceptibility testing). Microorganisms were identified using the Vitek 2 GP and 2 GN Cards (Biomerieux, Marcy I'Etoile, France) between 2015 and 2017. The microorganisms were also identified by Phoenix 100 ID panels (Becton Dickinson, Franklin Lakes, USA) between 2018–2019.

Antibiotic susceptibility

Susceptibility testing for enterococci, staphylococci, and Gram-negative rods (GNRs) was performed using the Kirby-Bauer disk diffusion method on Mueller Hinton Agar (MHA) (Oxoid, Unipath Ltd, Basingstoke, UK), and automated test systems and E-test (AB Biodisk, Solna, Sweden), in accordance with the manufacturer's instructions [8], Clinical and Laboratory Standards Institute (CLSI) standards, and European Committee on Antimicrobial Susceptibility Testing (EUCAST) standards (2016) [9]. Data from 2015–2016 was evaluated according to CLSI, and 2017–2019 according to EUCAST criteria (2016). Susceptibility testing for all isolates were performed using Vitek 2 AST N261, AST N262, AST P592, and AST P619 (Biomerieux, Marcy I'Etoile, France) between 2015 and 2017. The microorganisms were also perfomed by Phoenix AST panels (Becton Dickinson, Franklin Lakes, USA) between 2018–2019.

A colistin susceptibility test was performed using the broth microdilution method (Micronaut Colistin MIC Strip, Merlin, Germany). The minimum inhibitory concentration (MIC) was interpreted as the point at which the inhibition ellipse intersected with the E-test strip edge in the E-test. Extended-spectrum beta lactamase (ESBL) production for *E. coli* and *K. pneumoniae* was investigated using the E-test method (AB Biodisk, Solna, Sweden). Ceftazidime-clavulanate was used for the ESBL E-test. ESBL production was detected by a ceftazidime MIC $\geq$ 2 µg/mL, which decreased more than 4-fold in the presence of clavulanate [8].

Each *Enterococcus* spp. was tested for in vitro susceptibility to penicillin, ampicillin, gentamicin, and vancomycin. Each *Staphylococcus* spp. was tested for in vitro susceptibility to erythromycin, penicillin, tetracycline, rifampicin, trimethoprim-sulphametoxazol, cefoxitin, vancomycin, and teicoplanin. Each GNR was tested for in vitro

susceptibility to colistin, imipenem, meropenem, cefotaxime, ceftazidime, cefepime, ciprofloxacin, levofloxacin, piperacillin-tazobactam, gentamicin, and amikacin.

Staphylococcus aureus ATCC 29213, *E. coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 27853, and *K. pneumoniae* BCC 1395 were used as control strains.

Statistical analysis

Descriptive statistics expressed as percentages were used to evaluate the incidence of CAUTI in ICUs and to detect the antimicrobial resistance patterns of isolated microorganisms. Categorical variables (gender, age groups) were compared between MDR (+) and MDR (–) patients using Fisher's exact test due to small expected cell counts. Since age was non-normally distributed, group comparisons were performed using the Mann-Whitney U test. A binary logistic regression model was applied to evaluate the association between MDR status (dependent variable) and the predictors: gender, age group, and bacterial species (independent variables). Categorical predictors were included using dummy coding, with female gender, the 18–39 years' age group, and *Acinetobacter baumannii* as reference categories.

All statistical analyses including descriptive statistics, Chi-square, and Fisher's exact tests were performed using Python (version 3.10). Logistic regression modeling was conducted using the Statsmodels library (version 0.14). A p value of less than 0.05 was considered statistically significant.

Results

A total of 24,882 ICUs patients were treated at the Institute of Cardiology and Istanbul Training and Research Hospital between January 2015 and December 2019. A total of 677 microorganisms were isolated from 580 patients with CAUTI (317, 54.66% female and 263, 45.34% male), and the median age of these patients was ± 74.31 (± 74.12 female and ± 74.51 male). The CAUTI rate was 580/24,882 (2.33%). The culture showed bacterial growth in 529 patients, while in 51 patients it showed fungal growth. Polymicrobial growth was determined in 49 patients.

Among all microbial growth, 498 (73.56%) were Gram-negative bacteria, 128 (18.9%) were Gram-positive bacteria, and 51 (7.54%) were fungi. *E. coli* was the most frequently identified microorganism (27.18%), followed by *K. pneumoniae* (18.9%), enterococci (15.36%), *Acinetobacter baumannii* (8.86%), *Pseudomonas aeruginosa* (8.56%), *Candida* spp. (7.53%), *P. mirabilis* (4.43%), *Staphylococcus* spp. (3.54%), *Enterobacter* spp., (1.92%), and *Acinetobacter* spp. (1.5%) (Table 1). *Enterococcus* spp. was not resistant to vancomycin, but the resistance rates of *E. faecalis* and *E. faecium* to vancomycin were 8.6% and 25.8%, respectively. The overall resistance of all enterococci to vancomycin was 10.6% (Table 2). Staphylococci were not resistant to vancomycin and teicoplanin (Table 3). 50% of *S. aureus* were methicillin-resistant and 83.33% of coagulase-negative staphylococci were also methicillin-resistant. All Gram-negative bacteria, except for *K. pneumoniae*, were susceptible to colistin, followed by amikacin (77.4%), meropenem (66.6%), imipenem (66.4%), and piperacillin-tazobactam (60.1%) (Table 4). Colistin resistance in *K. pneumoniae* was 33.6%. High rates of ESBL of *E. coli* and *K. pneumoniae* were found; 54.3 and 69.6%, respectively. The sensitivity of ESBL positive microorganisms—especially *K. pneumoniae* to ciprofloxacin, levofloxacin, and cefepime—was also very low. But, *A. baumannii* was the bacterium with the lowest susceptibility rates, except to colistin (Table 4).

The rate of MDR was 29/184 (15.7%) in *E. coli*, 18/128 (14%) in *K. pneumoniae*, and 10/60 (16.7%) in

Table 1. Microbial etiologies of intensive care unit (ICU)-acquired urinary tract infections.

Microorganism	n	%
Escherichia coli	184	27.18
Klebsiella pneumoniae	128	18.9
Enterococci	104	15.36
Acinetobacter baumannii	60	8.86
Pseudomonas aeruginosa	58	8.56
Candida spp.	51	7.53
Proteus mirabilis	30	4.43
Staphylococcoccus spp.	24	3.54
Enterobacter spp.	13	1.92
Acinetobacter spp.	10	1.5
Providencia spp.	4	0.6
Morganella morgagni	3	0.44
Serratia marcescens	3	0.44
Burkholderia cepacia	3	0.44
Citrobacter freundii	2	0.3
Total	677	100.0

Table 2. Antimicrobial susceptibility of enterococci isolates.

Antibiotics	Microorganisms (n; %)		
	Enterococcus spp. n: 38	*E. faecium* n: 31	*E. faecalis* n: 35
Ampicillin	19; 50	14;45.2	17; 48.6
Gentamicin	11; 29	8; 25.8	10; 28.6
Penicillin	28; 73.7	22; 71	28; 80
Vancomycin	38; 100	23; 74.2	32; 91.4

Table 3. Antimicrobial susceptibility of staphylococci isolates.

	***S. aureus* (n: 12)**		**Coagulase negative staphylococci (n: 12)**	
	n, %	**n, %**	**n, %**	**n, %**
Staphylococci	MRSA (6)	MSSA (6)	MRCNS (10)	MSCNS (2)
Antibiotics				
Erythromycin	*0*	*0*	*0*	*1;50*
Penicillin	*0*	*5; 83.3*	*0*	*2; 100*
Tetracycline	*1; 16.6*	*5; 83.3*	*4; 40*	*2; 100*
Rifampicin	*4; 66.6*	*6; 100*	*5; 50*	*2; 100*
Trimetoprim-sulfametoxazol	*1; 16.6*	*4; 66.6*	*4; 40*	*2; 100*
Vancomycin	*6; 100*	*6; 100*	*10; 100*	*2; 100*
Teicoplanin	*6; 100*	*6; 100*	*10; 100*	*2; 100*

MRSA: methicillin resistant *S. aureus*; MSSA: methicillin susceptible *S. aureus*; MRCNS: methicillin resistant coagulase negative *staphylococci*; MSCNS: methicillin susceptible coagulase negative *staphylococci.*

Table 4. Susceptibility of Gram-negative bacteria isolated from urinary tract infections.

Microorganisms	**n**	**%**	**GM**	**AMK**	**PTZ**	**CL**	**CP**	**LV**	**CFT**	**CAZ**	**CPM**	**IMP**	**MP**
E. coli	184	37.0	66.8	91.8	76	100	51.4	54	45.6	45.6	56.7	91.1	92.9
K. pneumoniae	128	25.8	55.3	69.7	38.9	66.4	36.6	36.6	30.5	30.5	39.8	62.5	60.8
A. baumannii	60	12.0	33.3	50	30	100	30	33.3	-	20	30	10	10
P. aeruginosa	58	11.6	67.9	70.3	84.2	100	69.2	69.2	-	54.5	55.1	55.1	55.1
P. mirabilis	30	6.0	66.6	-	-	-	-	-	-	-	-	-	-
Enterobacter spp.	13	2.6	69.2	100	69.2	100	61.5	61.5	76.9	76.9	69.2	76.9	76.9
Acinetobacter spp.	10	2.0	50	90	60	100	60	60	-	20	60	50	50
Providencia spp.	4	0.8	25	25	75	-	75	75	-	75	50	75	75
Serratia marcescens	3	0.6	100	100	0	-	100	100	0	0	100	0	0
Morgenalla morganni	3	0.6	66.6	100	100	-	33.3	66.6	-	100	100	100	100
Burkholderia cepacia	3	0.6	-	-	-	-	66.6	66.6	-	66.6	66.6	-	66.6
Citrobacter freundii	2	0.4	100	100	100	100	50	50	50	50	100	100	100
Total	498	100	59.6	77.4	60.1	90.5	47.7	49.4	40.5	40.5	49.6	66.4	66.6

GM: gentamicin; AMK: amikacin; PTZ: piperacillin-tazobactam; CL: colistin; CP: ciprofloxacin; LV: levofloxacin; CFT: cefotaxime; CAZ: ceftazidime; CPM: cefepime; IMP: imipenem; MP: meropenem.

Table 5. Demographic distribution of Gram-negative rods.

Characteristics	**Total patients**	**MDR (+); %**	**MDR (–);%**	***p* value**
Gender				$p = 1.000$*
Male	169	26 (7.0 %)	143 (38.4%)	
Female	203	31 (8.3%)	172 (46.3%)	
Total	**372**	57 (15.3%)	**315 (84.7%)**	
Age (min–max)	25–103	41–101	25–103	
Age Mean ± SD	77.2 ±14.6	72.6 ± 17.3	74.4 ± 15.9	$p = 0.436$ †
Median (IQR)	78 (65–85)	76 (62–85)	78 (65–85)	$p = 0.34$
Age group	Total (n = 372)	MDR (+);%	MDR (-);%	$p = 0.112$*
18–39	6 (1.6%)	0	6 (1.9%)	
40–59	47(12.6%)	11 (19.3%)	36 (11.4%)	
60–74	71 (19.1%)	6 (10.5%)	65 (20.6%)	
≥ 75 years	248 (66.7%)	40 (70.28%)	208 (66.0%)	
Total	**372**	**57 (15.3%)**	**315 (84.7%)**	

MDR (+) and MDR (-) GN (*Acinetobacter baumannii, Klebsiella pneumaniae* and *E. coli*); n = 372. MDR: multi drug resistant; GN: Gram negative. *Fisher's exact test; †Independent t-test; ‡Mann-Whitney U test.

A. baumannii (Tables 5 and 6).

No significant differences were observed in gender distribution between MDR (+) and MDR (–) patients (Fisher's exact test, $p = 1.000$), with males comprising 7.0% (26/372) of MDR (+) cases and females 8.3% (31/372) (Table 5). Age did not differ significantly between groups, whether analyzed as a continuous variab le (MDR (+) mean age: 72.6 ± 17.3 years vs. MDR (–): 74.4 ± 15.9 years; p= 0.436, t-test) or as a categorical variable. When age was stratified into < 60 vs. ≥ 60 years, Fisher's exact test revealed no association with MDR status ($p = 0.413$). A sensitivity analysis retaining all four age groups (18–39, 40–59, 60–74, ≥75 years) with Monte Carlo simulation similarly showed no significance ($p = 0.112$; Table 5). Out of the 372 isolates analyzed, 57 (15.3%) were classified as MDR-positive, while 315 (84.7%) were MDR-negative. The distribution of MDR-positive isolates by species was as follows: *Acinetobacter baumannii* (10/60, 16.7%), *Klebsiella pneumoniae* (18/128, 14.1%), and *Escherichia coli* (29/184, 15.8%). In terms of age groups, MDR-positive isolates were more frequently observed in patients aged ≥ 75 years (31/162, 19.1%), followed by the 60–74 years age

Table 6. Distribution of MDR-positive and MDR-negative isolates according to gender and age group.

Isolates	Total (n)	MDR Conditions			
Acinetobacter baumannii	**60**	**MDR (+)10**		**MDR (-)50**	
Age group (years)		Male (n; 4) Female (6)	Female (n; 6)	Male (n; 35)	Female (n; 15)
18-39	4	0	0	4	0
40-59	8	2	1	1	4
60-74	13	0	0	11	2
≥ 75 years	35	2	5	19	9
Klebsiella pneumoniae	**128**	**MDR (+) (18)**		**MDR (-) (110)**	
Age group (years)		Male (n; 11)	Female (n; 7)	Male (n; 44)	Female (n; 66)
18–39	1	0	0	0	1
40–59	18	0	3	7	8
60–74	27	4	1	9	13
≥ 75	82	7	3	28	44
Escherichia coli	**184**	**MDR (+) (29)**		**MDR (-) (155)**	
Age group (years)		Male (n; 11)	Female (n; 18)	Male (n; 64)	Female (n; 91)
18–39	1	0	0	1	0
40–59	21	2	3	8	8
60–74	31	1	0	11	19
≥75 years	131	8	15	44	64

MDR: multi-drug resistant. Fisher's exact test was used due to small cell counts (<5 in some groups). OR >1 indicates higher odds in the first group listed (e.g., female vs. male).

group (6/64, 9.4%), 40–59 years group (8/66, 12.1%), and 18–39 years group (2/13, 15.4%). Regarding gender, MDR-positive rates were similar between males (26/136, 19.1%) and females (31/236, 13.1%). No predictor variable showed statistical significance ($p < 0.05$), suggesting that MDR status could not be predicted based on these demographic or microbiological factors alone (Table 7). Logistic regression analysis revealed no statistically significant associations between MDR positivity and gender (OR: 0.99, $p = 0.976$), age groups ($p > 0.8$ for all), or bacterial species ($p > 0.5$ for *K. pneumoniae* and *E. coli* compared to *A. baumannii*) (Table 8).

In the case of *A. baumannii*, females had 3.5× higher odds of MDR than males, though not statistically significant ($p = 0.097$). In the case of *K. pneumoniae*, males showed 2.4 × higher odds of MDR ($p = 0.099$, borderline significance). Fisher's exact tests revealed trends toward higher MDR risk in females with *A. baumannii* (OR=3.50, $p = 0.097$) and males with *K. pneumonia* (OR=2.38, $p = 0.099$), though these did not reach statistical significance. No age group showed significantly elevated MDR risk across pathogens. There were no significant age group differences for any pathogen (all $p > 0.05$) (Tables 6 and 8).

Table 7. Statistical analysis of patients according to their characteristics.

Predictors	Test used	*p* value
Female vs.male	Chi-square	0.0852
Age (18–39 years vs. others)	Fisher's exact	0.7278
Age (75+ years vs. others)	Chi square	0.0001
K. pneumoniae vs *A. baumannii*	Chi square	0.0109
E. coli vs *A. baumannii*	Chi square	0.0000

Discussion

UTI is one of the most common infections in humans worldwide. Nosocomial UTI accounts for approximately 30–40% of nosocomial infections and is a significant cause of morbidity, mortality, prolonged hospital stay, and increased costs [1,2]. About 11 million individuals in the USA are affected by UTIs each year, with associated costs predicted to be 5 billion USD annually. The most important risk factor for these infections is urinary catheter application. UTI also accounts for 36% of all healthcare-associated infections (HAI) and approximately 60% to 80% of them are catheter-associated [1,2]. An individual's susceptibility to CAUTI is associated with several risk factors, including female gender, advancing age, impaired immunity, and diabetes mellitus. The majority of UTIs are associated with indwelling urinary catheters. It is estimated that 70% of UTIs develop in patients with

Table 8. Logistic regression analysis of predictors of multi drug resistant (MDR) positivity.

Predictors	β coefficient	Standard error	Odds ratio (OR)	95% CI for OR	*p* value
Gender					
Male (vs. female)	–0.009	0.299	0.99	0.55–1.78	0.976
Age group (years)					
40–59 (vs. 18–39)	0.023	1.159	1.02	0.11–9.94	0.984
60–74 (vs. 18–39)	0.092	1.145	1.10	0.12–10.35	0.936
≥75 (vs. 18–39)	0.238	1.116	1.27	0.14–11.31	0.831
Bacterial species					
E. coli vs. *A. baumannii*	–0.152	0.416	0.86	0.38–1.94	0.715
K. pneumoniae vs. A. baumannii	–0.281	0.443	0.76	0.32–1.80	0.526

urinary catheters and 95% of UTIs occur in ICU patients with urinary catheters [1,2,10].

In this study, the rate of CAUTI was 2.33% (580/24,882). However, this CAUTI incidence is lower than that reported by other studies in Maharashtra 31% [11], Rawalpindi 33% [12], Assiut 11% [4], and Haryana 4.41% [1]. In the present study, there was a higher incidence of CAUTI in female patients (54.66%); the rate in male patients was 45.34%. These findings are in concordance with studies by Kakaria *et al.* (56.46%), Daniels *et al.* (61.3%), and Khan *et al.* (72%) that found a higher incidence of CAUTI in females [11–13]. However, this is not in harmony with observations by Sandhu *et al*., who reported a higher incidence (60.24%) of CAUTI in males [1]. In addition, Keten *et al*. also reported a higher incidence of CAUTI in males (51.5%) than females (48.5%) [14]. Females have a higher risk of bacteriuria than males. This is likely to be due to easier access of the perineal flora to the bladder along the outside of the catheter as it traverses the shorter female urethra. Heavy bacterial colonization of the perineum increases this risk. A woman's urethra is also closer to the anus. Therefore, microorganisms are more easily spread to her urethra and may cause an infection [10,11].

Several risk factors have been reported to be associated with CAUTI. Advanced age is among the risk factors [1–4,10], and is consistent with the findings of this study. Prolonged hospital stay and advanced age were reported to be risk factors of the patients with CAUTI [1–4,10]. In this study, the length of stay in the ICUs was 8–126 days, and median age was 74.31 years, which is compatible with the literature.

CAUTI accounts for a large proportion of hospital-acquired infections and is the most frequent cause of secondary bloodstream infections. The empirical and widespread use of broad-spectrum antibiotics in ICUs leads to the emergence of resistant microorganisms. Drug-resistant bacterial infections are difficult to treat [15,16]. The extended spectrum beta-lactamase (ESBL) producing strains of the Enterobacteriaceae, especially *E. coli* and *K. pneumoniae* strains, are emerging as a major problem for hospitalized patients and ESBL positive isolates are resistant to a broad range of beta lactam antibiotics, including third generation cephalosporins, carbapenems, and fluoroquinolones. Multidrug resistance (MDR) develops in these isolates and treatment options are limited. *Pseudomonas* and *Acinetobacter* spp. strains from hospital-acquired infections are resistant to a broad spectrum of agents [16–20]. Enterobacteriaceae are the most common pathogens associated with CAUTI; but in the ICU setting, *Candida* spp., (18%), *Enterococcus* spp., (10%), and *P. aeruginosa* (9%) become more prevalent. In addition, in recent decades, there has been an increase in antimicrobial resistance in CAUTI isolates from patients in ICU [10]. Data from the Centers for Disease Control and Prevention (CDC)'s National Healthcare Safety Network (NHSN) from 2006 to 2007 reported that 24.8% of all *E. coli* isolates from patients with CAUTIs were resistant to fluoroquinolones [21]. Many members of Enterobacteriaceae produced extended-spectrum beta-lactamases; and 21.2% of *K. pneumoniae* and 5.5% of *E. coli* isolates from patients with CAUTIs were resistant to ceftriaxone or ceftazidime. Even more concerning is that during this same time, 10.1% of all *K. pneumoniae* isolates from patients with CAUTIs were resistant to carbapenems [10].

Among all microbial growth in this study, 498 (73.56%) were Gram-negative bacteria (GNB), 128 (18.9%) were Gram-positive bacteria, and 51 (7.54%) were fungi. The most common bacterial pathogen isolated in this study was *E. coli* (184, 27.18%), followed by *K. pneumoniae* (128, 18.9%), *Enterococcus* spp. (104, 15.36%), *A. baumannii* (60, 8.86%), *P. aeruginosa* (58, 8.56%), *Candida* spp. (51, 7.53%), *P. mirabilis* (30, 4.43%), *Staphylococcus* spp. (24, 3.54%), *Enterobacter* spp. (13, 1.92%), and *Acinetobacter* spp. (10, 1.5%) (Table 1). Similarly, Khan *et al*. reported *E. coli* (69.7%), *K. pneumoniae* (21.2%), and *P. aeruginosa* (9.1%). In their work, *E. coli* infections in females were more than 4-fold of males. Also, *K. pneumoniae* infections were predominant in females (57.1%) [12]. Vyawahare *et al*. identified *E. coli* (57%), *Klebsiella* spp. (20%), and *Pseudomonas* spp. (7%) in CAUTI [3]. Kakaria *et al*. also identified *E. coli* (38.71%), *Pseudomonas* spp. (20.97%), *Klebsiella* spp. (17.74%), *Acinetobacter* spp. (6.45%), *Candida* spp. (4.84%), and *P. mirabilis* (8.06%) in patients with CAUTI [11]. Aly *et al*. identified *Klebsiella* spp. (50%), *Enterococcus* spp. (44%), and *S. aureus* (6%) [4]. However, Sandhu *et al*. identified *Candida* spp. (41.18%), *E. coli* (41.18%), *K. pneumoniae* (5.88%), and *S. aureus* (5.88%) in patients with CAUTI [1]. Keten *et al*. found *Candida* spp. (34.7%), followed by *E. coli* (20.6%), *Pseudomonas* spp. (14%), *Klebsiella* spp. (9.95%), and *Acinetobacter* spp. (8.2%) in a study conducted in Turkey [14]. Yadav *et al.* found the causative pathogens to be *Candida* spp., (n = 14), *E. coli* (n = 8), and *Enterococcus* spp., (n = 2), in patients with CAUTI; and the overall CAUTI incidence was 3.49% [22].

Enterococci are common pathogens causing

nosocomial infections. Vancomycin resistant enterococci (VRE) has increasing importance in UTI and is challenging to treat [23,24]. VRE prevalence was observed at a high rate in the European Antimicrobial Resistance Network (EARS-Net) [25]. Toner *et al.* reported vancomycin resistance as 9.8% in enterococci and they detected higher ampicillin resistance in vancomycin-resistant *E. faecium* than *E. faecalis* [23]. The 10-year surveillance of enterococcal nosocomial infections in Germany reported vancomycin-resistant enterococci in UTI to be 2.9–9.9% [24]. The VRE ratio was 0.16 in a study conducted in Hungary [26]. In the present study, no *Enterococcus* spp., were resistant to vancomycin, but 8.6% *E. faecalis* and 25.8% *E. faecium* were resistant to vancomycin. Resistance to vancomycin in all of enterococci was 10.6%. Ampicillin resistance was high in all enterococci. Gentamicin had lower susceptibility than ampicillin in all enterococci. *E. faecium* was more resistant to all antibiotics studied than *E. faecalis* (Table 2). The VRE ratio in this study was higher than the study conducted in Hungary [26] and was also consistent with the other studies [23–25].

Staphylococci are also among UTI agents. Methicillin-resistant *S. aureus* (MRSA) is clinically important among Gram positive cocci. An increase in the prevalence of MRSA leads to the use of vancomycin, which leads to the emergence of vancomycin-intermediate *S. aureus* (VISA) [10,26]. In a study conducted in Benin, all staphylococci grown in patients with UTI were resistant to penicillin and oxacillin [27]. In this study, the growth rate of staphylococci among all microorganisms was 3.54%, and 50% of *S. aureus* were methicillin resistant (MRSA) and 83.33% of coagulase-negative staphylococci were also resistant to methicillin. All MRSA, methicillin-susceptible *S. aureus* (MSSA), and methicillin-resistant coagulase-negative staphylococci (MRCNS) isolates were resistant to erythromycin. Also, MRSA and MRCNS had a lower level of susceptibility to tetracycline and trimethoprim/sulfametoxazole. MSSA and methicillin-susceptible coagulase-negative staphylococci (MSCNS) were also susceptible to trimethoprim/sulfametoxazole (66.6 and 100%, respectively). No resistance to vancomycin and teicoplanin was found in staphylococci (Table 3).

Nosocomial infections may lead to complications in 25–50% of ICU patients. The majority of ICU infections are device-associated infections, such as CAUTI, ventilator-associated pneumonia, and bloodstream infections. In recent years, there has been an increase in *Candida* spp., in CAUTI and bloodstream infections [28]. Deorukhkar *et al.* detected 31 *Candida* spp., out of 108 isolates in CAUTI [28]. *Candida* spp. (41.18%) and *E. coli* (41.18%) were predominant in a study conducted in India [1]. In this study, there were 51 (7.53%) *Candida* spp. in ICU patients with CAUTI (Table 1), while the present study found lower rates of *Candida* spp.

In this study, Gram-negative bacteria were sensitive to colistin, except for *K. pneumoniae*; followed by amikacin 77.4%, meropenem 66.6%, imipenem 66.4%, and piperacillin-tazobactam 60.1%. High rates of ESBL were noted in *E. coli* and *K. pneumoniae* (54.3 and 69.6%, respectively). The sensitivity of these ESBL positive microorganisms to ciprofloxacin, levofloxacin, and cefepime was also very low (Table 4). The rates of MDR recorded were 15.7% in *E. coli*, 14% in *K. pneumoniae*, and 16.7% in *A. baumannii* (Table 5). Carbapenems with a broad-spectrum of action are the first choice treatments in ESBL producing enteric bacteria. *K. pneumoniae* is the most commonly isolated agent in carbapenem-resistant enteric bacterial infections. Colistin is the last choice treatment alternative in the treatment of carbapenem-resistant *K. pneumoniae* infections. Colistin resistance has increased in *K. pneumoniae* strains as a result of the widespread use of colistin for carbapenem-resistant enteric bacteria [29]. In this study, the carbapenem resistance rates of *K. pneumoniae* isolates for imipenem and meropenem were 37.5% and 39.2%, respectively. The CAESAR 2019 report noted resistance percentages for ertapenem and imipenem/meropenem as 51% and 39 % in *K. pneumoniae* isolates obtained from blood and cerebrospinal fluid samples from Turkey, similar to the results obtained in this study [30]. In this study, colistin resistance was detected in 33.6% of *K. pneumoniae* isolates. The prevalence of colistin resistance (ColR) in enteric bacteria has been reported to be high in various studies in Turkey [29,31,32].

A. baumannii is an opportunistic pathogen that may cause healthcare-associated infections in ICUs. *A. baumannii* can survive for a long time in the hospital environment and easily develop antimicrobial resistance. Infections caused by carbapenem-resistant *A. baumannii* are considered challenging to treat [33–34]. In the CAESAR 2019 report, the resistance percentage for imipenem/meropenem was reported as 90% in *Acinetobacter* spp., isolates obtained from blood and cerebrospinal fluid samples from Turkey [30]. In this study, carbapenem resistance in *A. baumannii* was 90% (imipenem and meropenem) and resistance rates to the other antibiotics were also high

(Table 4). The findings of this study are compatible with the previous studies available in the literature.

The findings of this study are consistent with that of Sandhu *et al*., who observed that most of the Gram-negative bacteria were susceptible to amikacin (77.78%) and had decreased sensitivity to cefotaxime (55.56%) [1]. However, Kakaria *et al.* observed that among the Enterobacteriaceae, 79.54% isolates were ESBL producers, and *E. coli* had the highest resistance to cefotaxime (83.33%) [11]. Vyawahare *et al.* reported high resistance to cefotaxime (86%) among *Klebsiella* isolates [3]. Yadav *et al*. determined high resistance to all the antimicrobials in *Klebsiella* and *Citrobacter* isolates (100%), and *E. coli* isolates were moderately sensitive to imipenem (50%) and aminoglycosides (37.5%) [22]. Keten *et al*. observed ESBL positivity in *E. coli* and *Klebsiella* spp. (64% and 91.6%, respectively), and they were resistant to ceftazidime (72% and 100%, respectively) [14].

Many outbreaks of urinary pathogens have been caused by inadequate hand hygiene of healthcare workers. In addition, antimicrobial resistance in CAUTI isolates obtained from ICU patients has been increasing in the last decade. Hospitalized patients with urinary tract complaints, especially in ICU, constitute an important reservoir for MDR organisms [5,6]. Reducing the use of broad-spectrum antimicrobials and limiting the duration of use of urinary catheters is important to prevent the development of antimicrobial resistance associated with urinary catheters.

In this study, no gender-related differences in MDR infections were identified. Furthermore, contrary to some studies that have linked older age with an increased risk of MDR infections, there was no significant association in this cohort, possibly due to the widespread use of antibiotics among elderly patients [1,4,10,12].

The limitations of this study may include the absence of patients in the younger age group (18–39 years) and the low number of patients in other age groups, which may reduce the predictive power for MDR (+) patients.

Although *Acinetobacter baumannii* is often associated with high levels of resistance, the findings of this study did not demonstrate a significantly higher MDR rate compared to *E. coli* or *K. pneumoniae*. Similarly, MDR positivity was not significantly associated with older age groups or male gender, despite previous literature suggesting that advanced age and male gender may be risk factors for antimicrobial resistance. The lack of statistically significant associations in the regression model may be partly due to sample size limitations in certain subgroups, particularly among younger patients. Despite its limitations, this study highlights the continued threat of MDR GNB in ICU patients and the need for comprehensive surveillance systems that incorporate both clinical and microbiological data. Future studies with larger sample sizes and more detailed clinical parameters are warranted to better understand the risk factors of MDR colonization and infection in critical care settings.

Conclusions

CAUTI remains an important problem in ICUs. Recently, there has been an increase in resistance, especially MDR, in Gram-negative bacteria. What complicates the situation is that there are few treatment options for MDR microorganisms. Strict adherence to hand hygiene procedures is recommended for prevention of all healthcare associated infections, including CAUTI. Healthcare workers should pay attention to aseptic techniques, especially hygiene in urinary catheterization; and receive regular training on this subject. The infection prevention policies and the treatment protocols implemented in the ICUs of both the hospitals in this study should be reviewed, taking into account the antimicrobial resistance status, including MDR, of the institutions.

Authors' contributions

EK, AK, study conception and design, data collection, data analysis and interpretation; SA, data analysis and interpretation; all authors, manuscript draft, critical revision for important intellectual content. All authors gave approval for the submitted version of the manuscript and agree to be accountable for all aspects of the study.

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Conflict of interest

No conflict of interest is declared.

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