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Original Article

Six-year evaluation of device-associated nosocomial infections in intensive care units

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Abstract

Introduction: Invasive device-associated nosocomial infections commonly occur in intensive care units (ICUs). These infections include intravascular catheter-related bloodstream infection (CRBSI), ventilator-associated pneumonia (VAP), and catheter-associated urinary tract infection (CAUTI). This study aimed to evaluate the factors associated with invasive device-associated nosocomial infections based on the underlying diseases of the patients and antibiotic resistance profiles of the pathogens causing the infections detected in the ICU in our hospital over a five-year period.

Methodology: Invasive device-associated infections (CRBSI, VAP, and CAUTI) were detected retrospectively by the laboratory- and clinic-based active surveillance system according to the criteria of the US Centers for Disease Control and Prevention (CDC) in patients hospitalized in the ICU of the tertiary hospital between 1 January 2018 and 30 June 2023.

Results: A total of 425 invasive device-associated nosocomial infections and 441 culture results were detected (179 CRBSI, 176 VAP, 70 CAUTI). Out of them, 57 (13.4%) patients had hematological malignancy, 145 (34.1%) had solid organ malignancy, and 223 (52.5%) had no histopathologic diagnosis of any malignancy. An increase in extended-spectrum beta lactamase (ESBL) and carbapenem resistance in pathogens was detected during the study period.

Conclusions: Antibiotic resistance of the Gram-negative bacteria associated with invasive device-associated infections increased during the study period. Antimicrobial stewardship will reduce rates of nosocomial infections, reduce mortality, and shorten hospital stay. Long-term catheterization and unnecessary antibiotic use should be avoided.

Key words: CRBSI; VAP; CAUTI; intensive care unit.

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Introduction

Invasive device-associated nosocomial infections are common in intensive care units (ICUs). These infections include intravascular catheter-related bloodstream infection (CRBSI), ventilator-associated pneumonia (VAP), and catheter-associated urinary tract infection (CAUTI).

Arterial and central venous catheters are frequently used in ICU patients due to the need for hemodynamic monitoring and intravenous treatment. Bloodstream infections involving these catheters are common and cause significant morbidity and mortality [1].

VAP is an infection of the lung tissue that develops within ≥ 48 hours after intubation for mechanical ventilation in patients. Nosocomial pneumonia often occurs as a result of endotracheal intubation and mechanical ventilation [2].

Urinary tract infections (UTIs) are the most common nosocomial infections in ICUs [3]. Although the majority of CAUTIs do not cause significant morbidity and mortality, the cumulative effect of these infections is large [4]. CAUTIs are the second most common cause of nosocomial bloodstream infection, causing 15–25% mortality [5-9].

Diseases that suppress the immune system, such as hematological and solid organ malignancies increase the incidence of invasive device-related infections. In

addition, the increase in invasive procedures in this patient group leads to increase in these infections [9].

This study aimed to evaluate the factors associated with invasive device-related nosocomial infections based on the underlying diseases of patients, and antibiotic resistance profiles of the pathogens associated with the infections detected in anesthesia and internal medicine ICUs between 1 January 2018 and 30 June 2023.

Methodology

Study design

This study was a retrospective study. The study was approved by the Clinical Research Ethics Committee of the Hospital (date: 5 October 2023 and decision No: 2023-10/74).

Patients aged ≥ 18 years who were hospitalized in anesthesia and/or internal medicine ICUs between 1 January 2018 and 30 June 2023 were included in the study. Patients who were under the age of 18 years and who were not hospitalized in anesthesia and/or internal medicine ICUs were not included in the study.

CRBSI was detected by laboratory and clinic-based active surveillance systems according to the US Centers for Disease Control and Prevention (CDC) criteria. The BacT/Alert® 3D (bioMérieux, Marcy l'Etoile, France) automated culture device was used for blood cultures. BacT/Alert bottles were incubated for 5 days. When growth was detected in the bottle, it was subcultured on 5% sheep blood agar, eosin methylene blue agar, and chocolate agar in accordance with the semiquantitative culture technique, and incubated at 37 °C for 24–48 hours. Growth of >15 CFU in semiquantitative culture was considered significant. When there was growth, identification of the strain was performed by matrix-assisted laser desorption ionization mass spectrometry (MALDI-TOF MS, Bruker, Germany).

VAP was detected by laboratory and clinic-based active surveillance system according to criteria of the CDC [10]. The pathogens isolated from deep tracheal aspirate cultures were recorded.

CAUTI was detected by laboratory and clinic-based active surveillance system according to the criteria of the CDC. The pathogens isolated from urine cultures taken from the catheter were recorded. The definitions in the Infectious Diseases Society of America guide were used for diagnosis of CAUTI [11].

Table 2. Numbers and percentages of catheter related blood stream infections (CRBSI) pathogens between 2018–2023.

Pathogens	n	%
Gram-negative bacteria		
Klebsiella pneumoniae	43	22.9
Acinetobacter baumannii	36	19.1
Pseudomonas aeruginosa	6	3.2
Enterobacter cloacae	5	2.6
Escherichia coli	5	2.6
Serratia marcescens	4	2.1
Proteus mirabilis	2	2.3
Stenotrophomonas maltophilia	1	0.5
Sphingomonas paucimobilis	1	0.5
Chryseobacterium indologenes	1	0.5
Gram-positivebacteria		
Enterococcus faecalis/faecium	25	13.3
Coagulase-negative staphylococci	18	9.6
Staphylococcus aureus	3	1.6
Fungus		
Candida parapsilosis/albicans	37	19.7
Geotrichum spp.	1	0.5
Total	188	100

Statistical analysis

The data were analyzed using the Statistical Package for the Social Sciences (SPSS, IBM, Chicago, IL) version 23 software package. Distribution of continuous data was described by median and minimum/maximum, and categorical data by number and percentage.

Results

A total of 425 invasive device-related nosocomial infections and 411 culture results from 425 patients were analyzed. 57 (13.41%) patients had hematological malignancy, 145 (34.11%) patients had solid organ malignancy, and 223 (52.47%) patients did not have any histopathological diagnosis of malignancy (Table 1).

CRBSI was detected in 179 (42.1%) patients. 31 (17.3%) patients had hematological malignancy; 58

Table 1. Underlying diseases in invasive device-associated nosocomial infections detected in intensive care units.

Years	Number of patients with hematological malignancy	Number of patients with solid organ malignancy	Number of patients without malignancy	Total
2018	19	32	26	77
2019	5	29	39	73
2020	9	17	34	60
2021	15	30	38	83
2022	8	20	58	86
06/30/2023	1	17	28	46
Total	57	145	223	425

Table 3. Resistance profiles of catheter related blood stream ınfections (CRBSI) pathogens between 2018–2023.

Years	ESBL positive	Carbapenem resistant	Colistin resistant	MRCNS	MRSA	VRE
2018	3	8	2	3	0	2
2019	5	16	4	3	0	0
2020	2	12	3	2	0	0
2021	12	15	10	5	0	1
2022	9	10	1	4	0	0
06/30/2023	2	5	3	1	0	0
Total	33	66	23	18	0	3

EBSL: extended spectrum beta-lactamase; MRCNS: methicillin-resistant coagulase-negative *Staphylococcus*; MRSA: methicillin-resistant *Staphylococcus aureus*; VRE: vancomycin-resistant enterococci.

(32.4%) patients had solid organ malignancy; and 90 (50.3%) patients did not have any malignancy.

A total of 188 positive blood culture results were detected in patients with CRBSI. 104 (55.3%) of this were Gram-negative bacteria, 46 (24.5%) were Gram-positive bacteria, and 38 (20.2%) were fungi. The most frequently isolated Gram-negative bacteria was *Klebsiella pneumoniae* (43 (22.9%)) and *Acinetobacter baumannii* (36 (19.1%)), respectively. The most frequently isolated Gram-positive bacteria was *Enterococcus faecalis/faecium* (25 (13.3%)) and coagulase-negative staphylococci (18 (9.6%)). The most common fungal agent was *Candida* spp. (37 (19.7%); Table 2). Over the years, an increase in extended spectrum beta lactamase (ESBL) and carbapenem resistance was detected in pathogens. The highest increase in resistance was seen in carbapenem resistance. The resistance profiles of the pathogens are shown in Table 3.

A total of 182 positive culture results were detected in 176 patients who developed VAP. 20 (11.4%) patients had hematological malignancy and 62 (35.2%) patients had solid organ malignancy. 94 (53.4%) patients did not have any malignancy.

The most frequently isolated agents in VAP were *A. baumannii* (87 (47.8%)), *K. pneumoniae* (51 (28%)), and *Pseudomonas aeruginosa* (20 (11%)), respectively (Table 4). An increase in ESBL and carbapenem resistance in the pathgens has been recorded over the years. The resistance profiles of the pathogens were shown in Table 5.

A total of 71 positive culture results were detected in 70 patients who developed CAUTI. Six (8.6%) of the cases were patients with hematological malignancy, 25 (35.7%) were patients with solid organ malignancy, and 39 (55.7%) were patients without malignancy. The most frequently detected agents were *K. pneumoniae* (21 (29.6%)), *Escherichia coli* (16 (22.5%)), *A. baumannii* (8 (11.3%)), and *P. aeruginosa* (8 (11.3%)) (Table 6).

Discussion

Central venous catheters (CVC) are the most important cause of healthcare-associated bacteremia [12]. The presence of growth in blood cultures taken simultaneously from the periphery and CVC was used in the diagnosis of catheter-related blood stream infections [12]. A time difference exceeding two hours indicated catheter-related bacteremia [12].

Table 4. Numbers and percentages of ventilator associated pneumoniae (VAP) pathogens between 2018–2023.

Pathogens	n	%
Gram-negative bacteria		
Acinetobacter baumannii	87	47.8
Klebsiella pneumoniae	51	28
Pseudomonas aeruginosa	20	11
Proteu smirabilis	6	3.3
Stenotrophomonas maltophilia	5	2.7
Enterobacter cloacae	4	2.2
Serratia marcescens	4	2.2
Escherichia coli	2	1.1
Sphingomonas paucimobilis	1	0.5
Gram-positive bacteria		
Corynebacteria spp.	1	0.5
Kocuria spp.	1	0.5
Total	182	100

Table 5. Resistance profiles of ventilator associated pneumoniae (VAP) pathogens between 2018–2023.

Years	ESBL positive	Carbapenem resistant	Colistin resistant	MRCNS	MRSA	VRE
2018	2	33	2	0	0	2
2019	2	14	1	0	0	0
2020	1	13	3	2	0	0
2021	19	29	18	0	0	0
2022	11	31	7	0	0	0
06/30/2023	9	16	0	1	0	0
Total	44	136	31	3	0	2

EBSL: extended spectrum beta-lactamase; MRCNS: methicillin-resistant coagulase-negative *Staphylococcus*; MRSA: methicillin-resistant *Staphylococcus aureus*; VRE: vancomycin-resistant enterococci.

The most important factors that determine the risk of developing CRBSI are chronic diseases, bone marrow transplantation, immunosuppressive treatment, malignancy, neutropenia, nutritional deficiency, total parenteral nutrition, advanced age, low previous body mass, and deterioration of skin integrity such as burns [13,14]. In this study, 49.7% of patients with CRBSI had hematological or solid organ malignancy.

In a report prepared by the US CDC National Health Safety Network from 2011 to 2017, Enterobacteriaceae and *Candida* species were reported as the most common pathogens in CRBSI [15]. Gram-negative bacilli may account for 16–31% of CRBSIs. The most frequently isolated organisms included *E. coli*, *K. pneumoniae*, *Pseudomonas aeruginosa*, *Enterobacter* spp, *Serratia* spp, and *Acinetobacter baumannii* [16]. Gram-negative pathogens were dominant causative agents of CRBSI in patients with malignancy [17]. Bloodstream infections caused by multidrug-resistant (MDR) Gram-negative bacilli were very important due to increased treatment failure and mortality rates.

In this study, Gram-negative bacteria were detected in 55.3% of CRBSIs, Gram-positive bacteria were detected in 24.5%, and fungi were detected in 20.2%. Thus, the most isolated agents were Gram-negative bacteria. As the years progressed, resistance rates in Gram-negative bacteria increased. Almost half of the patients had malignancies, all patients were hospitalized in the ICU, and there was low rate of Gram-positive bacterial growth in the hospital. These may have contributed to the predominance of Gram-negative bacteria.

Fungi, especially *Candida* spp, accounted for 27% of CRBSIs. Patients receiving intravenous hyperalimentation fluid are at a higher risk of the developing CRBSI [15]. *Candida* infections detected in CVC are more common in patients with suppressed immune systems and those receiving multiple antibiotic treatments [18]. Analysis of hospitals surveillance data, distribution of isolated agents, and knowledge of risk factors are very important for the prevention and successful treatment of CRBSI.

VAP is a hospital-associated pneumonia that develops 48 hours after endotracheal intubation. The most common organisms causing VAP are *Staphylococcus aureus* and *P. aeruginosa*. Other common causes include aerobic Gram-negative bacilli (*E. coli*, *K. pneumoniae*, *Enterobacter* spp., *Acinetobacter* spp.) and Gram-positive cocci (*Streptococcus* spp.) [19,20].

The pathogens associated with 9,266 VAP cases reported by the CDC between 2015 and 2017 were *S. aureus* (28.8%), *P. aeruginosa* (12.9%), *Klebsiella* spp. (10.1%), *Enterobacter* spp. (8.4%), *Haemophilus influenzae* (5.9%), *Streptococcus* (5.7%), *E. coli* (5.6%), and *Acinetobacter baumannii* (3.2%) [21]. A study reported that *Acinetobacter* spp., *K. pneumoniae*, and *P. aeruginosa* were most frequently isolated as VAP agents [23]. In another study, the most frequently isolated agents were *Klebsiella* spp. (32.7%), *Acinetobacter* spp. (31.8%), and *Pseudomonas* spp. (12.7%) [24]. In this study, the most frequently isolated agents were *A. baumannii*, *K. pneumoniae*, and *P. aeruginosa*. This is in alignment with previous reports in the literature.

Table 6. Numbers and percentages of catheter associated urinary tract ınfections (CAUTI) pathogens between 2018–2023.

Pathogens	n	%
Gram-negative bacteria		
Klebsiella pneumoniae	21	29.6
Escherichia coli	16	22.5
Acinetobacter baumannii	8	11.3
Pseudomonas aeruginosa	8	11.3
Proteus mirabilis	7	9.8
Enterobacter cloacae	3	4.2
Serratia marcescens	1	1.4
Stenotrophomonas maltophilia	1	1.4
Gram-positive bacteria		
Enterococcus faecalis/faecium	6	8.4
Total	71	100

The 2016 VAP guidelines recommended that ≥ 95% of patients with VAP should receive empiric treatment against the most likely pathogens during the initial antimicrobial therapy [22]. Over the years, there has been an increase in carbapenem resistance of Gram-negative bacteria, especially *A. baumannii* and *K. pneumoniae*, that caused VAP in this study. Long-term hospitalization and recent antibiotic treatment are the most important risk factors for MDR pathogens associated with VAP [22]. In a meta-analysis that included 15 studies, factors that increase the risk of MDR VAP were determined to be intravenous antibiotic use in the last 90 days, hospitalization for ≥ 5 days before VAP, septic shock during VAP, acute respiratory distress syndrome before VAP, and renal replacement therapy before VAP [22].

Since recent antibiotic usage may have selected resistant pathogens, a drug from a different class should be chosen when empiric treatment is re-arranged. The development of antibiotic resistance can be reduced by discontinuing antibiotics or narrowing the regimen 48 to 72 hours after the start of treatment, based on appropriate culture results [25]. Strategies should be determined to reduce the development of VAP in ICUs. Empirical treatment should be selected according to the local microbiological data and antibiotic resistance profile of the unit. After the agent is isolated, treatment

should be revised ccording to the antibiotic sensitivity result.

Urinary catheters are inserted in 12–25% of hospitalized patients. Prolonged duration of catheter use is an important risk factor for CAUTI [26]. *E. coli* and other Enterobacteriaceae are common causative agents, but *P. aeruginosa*, enterococci, staphylococci and fungi are also important causes.

The most common pathogens identified in approximately 154,000 CAUTIs reported to the US National Healthcare Safety Network between 2011 and 2014 were *E. coli* (24%), *Candida* spp (24%), *Enterococcus* spp. (14%), *P. aeruginosa* (10%), and *Klebsiella* spp. (10%) [16]. In this study, *K. pneumoniae*, *E. coli*, and *A. baumannii* were isolated as the most common agents.

In a study where daily urinary catheter need was questioned and unnecessary catheters were removed, it has been shown that CAUTI decreased by 48–81%. Prolonged catheterization is associated with polymicrobial bacteriuria or altered urinary flora. Application of hand hygiene and precaution bundles has been found effective in preventing UTI [27].

There was an increase in the frequency of MDR Gram-negative bacteria as a causative agent of CAUTI. These infections are difficult to treat, so hand hygiene and precaution bundles should be followed; unnecessary antibiotic usage and long-term catheterization should be avoided.

There are often delays in initiating appropriate antibiotic treatment for MDR organisms [28]. These delays result in increased mortality rates due to infections caused by MDR pathogens [29]. In clinical studies, it is unclear whether poor outcomes are due to increased virulence of the organism or inappropriate antibiotic therapy administered to patients with MDR infection [30].

Conclusions

Resistant Gram-negative bacteria are being isolated with increasing frequency in invasive device-associated infections. Therefore, treatment of infections is difficult. Antibiotic stewardship will reduce rates of nosocomial infections and antibiotic expenditure without increasing mortality or prolonging hospital stay. It will also reduce the incidence of resistant bacteria. Long-term catheterization and unnecessary antibiotic use should be avoided.

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