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Evaluation of Healthcare-Associated Infections in Intensive Care Units

Yoğun Bakım Ünitelerinde Sağlık Hizmetiyle İlişkili Enfeksiyonların Değerlendirilmesi

Murat Aydın[1], Nurten Nur Aydın[1], Gülseren Savaş[1], Sibel İba Yılmaz[1], Dursun Murat Alada[2]

1 Erzurum Regional Education and Research Hospital, Department of Infectious Diseases and Clinical Microbiology, Erzurum, Türkiye

[2] Erzurum Regional Education and Research Hospital, Medical Microbiology Laboratory, Erzurum, Türkiye

ORCID ID: Murat Aydın: https://orcid.org/0000-0002-0167-0802, Nurten Nur Aydın: https://orcid.org/0000-0003-4138-2490 Gülseren Savaş: https://orcid.org/0009-0003-1902-7641, Sibel İba Yılmaz: https://orcid.org/0000-0002-4123-0828, Dursun Murat Alada: https://orcid.org/ 0000-0002-7429-7471

***Sorumlu Yazar / Corresponding Author:** Murat Aydın , **e-posta / e-mail:** kibamurat61@hotmail.com

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Abstract

Aim The aim of this study was to determine the healthcare-associated infections (HAIs), causative microorganisms and antibiotic resistance profiles in the tertiary intensive care unit of our hospital and, based on the results, to contribute to the rational administration of antibiotics.

Material and Method The study included patients who were followed up in the tertiary intensive care unit between January 2023 and December 2023 and were diagnosed with HAI. Patient data were obtained retrospectively from infection control nurse records and patient files.

Results During the study period, 107 HAI episodes were identified in 99 of 2296 patients. The incidence rate of HAI was 4.7% and the incidence density was 5.2 per thousand. Central line-associated bloodstream infections (43%) were the most common HAI associated with invasive devices. The next most common were ventilator-associated pneumonia (42%) and catheter-associated urinary tract infection (15%). Gram negative bacteria were isolated in 83.2%, fungi in 10.3%, and gram positive bacteria in 6.5% of patients diagnosed with HAI. The most common gram negative bacteria were Acinetobacter baumannii (34.6%) and Pseudomonas aeruginosa (19.6%). A colistin resistance rate of 8.1% was determined for Acinetobacter baumannii. Carbapenem resistance was 91.9% for Acinetobacter baumannii and 76.2% for Pseudomonas aeruginosa. Methicillin resistance was found in 66.7% of Staphylococcus aureus, the most commonly isolated gram positive bacterium.

Conclusion Monitoring HAIs, causative microorganisms and antibiotic resistance rates in intensive care units is of great importance for both infection prevention and the rational use of antibiotics.

Keywords Antimicrobial resistance, healthcare associated infection, intensive care unit

Özet

Amaç *Bu çalışmada, hastanemizin üçüncü basamak yoğun bakım ünitesinde gelişen sağlık hizmetiyle ilişkili enfeksiyonların (SHİE), etken mikroorganizmaların ve antibiyotik direnç profillerinin belirlenmesi ve bulgular ışığında akılcı antibiyotik uygulanmasına katkı sağlanması amaçlanmıştır.*

Gereç ve Yöntem *Çalışmaya Ocak 2023-Aralık 2023 tarihleri arasında üçüncü basamak yoğun bakım ünitesinde takip edilen ve SHİE tanısı koyulan hastalar dahil edilmiştir. Hasta verileri, enfeksiyon kontrol hemşireleri tarafından tutulan kayıtlardan ve hasta dosyalarından retrospektif olarak elde edilmiştir.*

Bulgular *Çalışma boyunca 2296 hastanın 99'unda 107 SHİE epizodu tanımlanmıştır. SHİE insidans hızı %4,7, insidans dansitesi binde 5,2 olarak olarak saptanmıştır. İnvazif araçla ilişkili SHİE içerisinde santral venöz kateter ilişkili kan dolaşımı enfeksiyonu (%43) ilk sırada yer almıştır. İkinci sıklıkta ventilatör ilişkili pnömoni (%42) ve sonrasında kateter ilişkili üriner sistem enfeksiyonu (%15) saptanmıştır. SHİE tanısı alan hastalardan %83,2'sinde gram negatif bakteriler, %10.3'ünde funguslar, %6.5'inde gram pozitif bakteriler izole edilmiştir. Gram negatif bakterilerden en sık Acinetobacter baumannii (%34,6) ve Pseudomonas aeruginosa (%19.6) saptanmıştır. Acinetobacter baumannii için kolistin direnci %8,1 olarak bulunmuştur. Karbapenem direnci Acinetobacter baumannii için %91,9, Pseudomonas aeruginosa için %76,2 olarak saptanmıştır. En sık izole edilen gram pozitif bakteri olan Staphylococcus aureus'un %66,7'sinde metisilin direnci tespit edilmiştir.*

Sonuç *Yoğun bakım ünitelerinde SHİE'lerin, etken mikroorganizmaların ve antibiyotik direnç oranlarının takip edilmesi ve hem enfeksiyonların önlenmesi hem de akılcı antibiyotik kullanımı açısından büyük önem taşımaktadır.*

Anahtar Kelimeler *Antimikrobiyal direnç, sağlık hizmeti ilişkili enfeksiyon, yoğun bakım ünitesi*

INTRODUCTION

Healthcare-associated infections (HAIs) represent an important health problem in intensive care units due to increasing mortality, impaired quality of life, increasing treatment costs, developing antibiotic resistance and placing additional burden on healthcare services.[1, 2]

Intensive care units (ICUs) are multidisciplinary units prepared for patients requiring specialized care and continuous follow-up in situations requiring advanced support. The incidence of HAI is higher than in other wards and ranges from 11% to 60%.[3] This difference is due to the presence of various risk factors that are unequally distributed in the healthcare system. The reasons for the high incidence of nosocomial infections, especially in ICUs, include the high frequency of invasive procedures, various comorbidities, suppression of the immune system and longer hospital stays.[4]

Nosocomial infections vary between different hospitals and units and these differences are due to various factors such as infectious agents and antibiotic resistance. Each hospital should identify the microorganisms and antibiotic resistance patterns that characterize its unique nosocomial flora. This information can be obtained through surveillance programs to determine the frequency and pathogens of infections.[5] In ICUs, the development of HAI is a dynamic process that changes continuously over time and requires constant monitoring. Therefore, it is crucial for each center to know the HAI rates, the causative microorganisms and antibiotic resistance profiles in their ICUs. This information can improve the treatment of nosocomial infections by enabling the development of infection control practices, the correct use of antibiotics, and a continuously informed approach.

The aim of this study was to identify the HAIs, causative microorganisms and antibiotic resistance profiles that developed in the intensive care unit of our hospital and to contribute to rational antibiotic administration according to these findings.

MATERIALS and METHODS

Among the 2296 patients followed up in the tertiary ICU of Erzurum Regional Training and Research Hospital between January 1, 2023 and December 31, 2023, patients aged 18 years and above who were diagnosed with HAI during their hospitalization were included in the study. Patients not diagnosed with HAI in ICUs and patients under 18 years of age were excluded from the study.

The 2017 National HAI Surveillance Guidelines, adapted from Centers for Disease Control and Prevention (CDC) criteria, were used to diagnose patients with HAIs.[6] Patient information was obtained retrospectively from infection control nurse records and patient files between the specified dates.

To identify and determine the antibiotic susceptibility of the infectious microorganisms isolated from the patients, conventional methods and the automated system VITEK 2 Compact (bioMérieux, France) were used.

The Phoenix ESBL test used five wells containing fixed concentrations of the following drugs or drug combinations: cefpodoxime, ceftazidime, ceftazidime plus clavulanic acid (CA), cefotaxime plus CA, and ceftriaxone plus CA. After inoculation with each of the isolates, the panel was placed in the instrument and continuously monitored for growth. At each decision point, the growth curve derived from each well was evaluated. Growth curves were evaluated using a series of functions describing their intensity and shape. A series of mathematical functions were used to determine a positive or negative growth response to a threshold; if the decision point was at the terminal node, the results were reported.

The Phoenix™ CPO Detection Test (BD), a qualitative, confirmatory, growth-based test aimed at phenotypically detecting carbapenemase enzyme expression in Entero-

bacteriaceae, P. aeruginosa, and A. baumannii, was used. Colistin resistance was determined by microdilution method (0.25-8).

The incidence rate of HAIs = (number of HAIs/number of patients) × 100, the incidence density = (number of HAIs/ number of patient days) × 1000 were calculated using the formula.

As part of the invasive device-related HAI rates, the rate of ventilator-associated pneumonia (VAP), the rate of central line-associated bloodstream infections (CLABSI) and the rate of catheter-associated urinary tract infections (CAUTI) were evaluated. VAP rate = number of VAPs / ventilation days x 1000, CLABSI rate = number of CLABSI / central line days x 1000, CAUTI rate = number of CAUTIs / urinary catheter days x 1000 were calculated using the formula. The formula was used to calculate the device usage rate = number of device days / patient days.

Ethical approval of this study was granted by the Ethics Committee of Erzurum Regional Training and Research Hospital (Decision No: 2024/01-06).

Statistical analysis

The statistical package program IBM SPSS 23.0 was used for data analysis. In the descriptive statistics of the evaluation results, numerical values (n) and percentage values (%) were given for categorical variables as well as mean and standard deviation (SD) values for numerical variables.

RESULTS

The study retrospectively analyzed 20,444 hospitalization days of 2296 patients followed up in the tertiary ICU over a one-year period. During this period, 107 HAI episodes were detected in 99 patients. Of the patients diagnosed with HAI, 59 (55%) were female and 48 (45%) were male. The mean age of the patients was 74.1 ± 14.4 years. Data on the patients' demographic characteristics, reasons for hospitalization, and comorbidities are shown in Table 1.

Table 1. Patient demographic characteristics, reasons for hospitalization, and comorbidities

	n	%
Male	48	45
Female	45	55
Mean age ± SD	74.1 ± 14.4	
Comorbidities		
Hypertension	48	44.9
Diabetes mellitus	27	25.2
Chronic obstructive pulmonary disease	15	14.0
Coronary artery disease	18	16.8
Congestive heart failure	11	10.3
Chronic kidney disease	9	8.4
Cerebrovascular disease	14	13.1
Alzheimer's disease	7	6.5
Malignancy	4	3.7
Reasons for hospitalisation		
Cerebrovascular accident	37	34.6
Acute coronary syndrome	9	8.4
Pulmonary causes	33	30.9
Trauma	16	15.0
Cardiac arrest	9	8.4
Other causes	16	15.0
Mean length of hospitalisation (days) ± SD	40.4 ± 41.7	

The incidence rate of HAI was 4.7% and the incidence density was 5.2 per thousand. The mechanical ventilator use rate was 56%, the VAP rate was 4 per thousand; the rate of urinary catheter use was 94%, the rate of CAUTI was 1 per thousand; The rate of central line use was 84% and the rate of CLABSI was 2.7 per thousand. The most common HAI associated with invasive devices was CLABSI (n: 46, 43%), followed by VAP (n: 45, 42%) and CAUTI (n: 16, 15%), respectively (Table 2).

Table 2. Days of invasive device use, frequency of invasive device use, and infection rates					
	Days of invasive device use	**Frequency of invasive device use (%)**		**Number of infections**	**Infection rate (per thousand)**
Central line	17.323	84	**CLABSI**	46	2.7
MV	11.505	56	**VAP**	45	4
UC	19.363	94	**CAUTI**	16	1

Th e causative agents of HAI and their distribution are listed in Table 3. Gram negative bacteria were isolated in 89 (83.2%), fungi in 11 (10.3%), and gram positive bacteria in 7 (6.5%) patients. *Acinetobacter baumannii* (n:37, 34.6%) and *Pseudomonas aeruginosa* (n:21, 19.6%) were the most commonly isolated gram negative bacteria. Staphylococcus aureus (n:6, 5.6%) was the most commonly isolated gram positive bacterium. *A. baumannii* (n:25, 55.6%) and *P. aeruginosa* (n:11, 24.4%) were the most common pathogens in VAP, *A. baumannii* (n:8, 17.4%) and *P. aeruginosa* (n: 5, 31.3%) were the most common pathogens in CAUTI.

Table 3. Healthcare-associated infectious agents and their distribution					
Microorganism	**VAP**	**CLABSI**	**CAUTI**	**Total number (n)**	**%**
Gram negative bacteria	**43**	**31**	**15**	**89**	**83.2**
Acinetobacter baumannii	25	8	**4**	37	34.6
Pseudomonas aeruginosa	11	5	**5**	21	19.6
Klebsiella pneumoniae	5	7	**2**	14	13.1
Pseudomonas putida	0	4	**0**	4	3.7
Escherichia coli	0	0	**4**	4	3.7
Stenotrophomonas maltophilia	1	3	**0**	4	3.7
Enterobacter cloacae	1	1	**0**	2	1.9
Klebsiella oxytoca	0	1	**0**	1	0.9
Moraxella species	0	1	**0**	1	0.9
Cedecea davisae	0	1	**0**	1	0.9
Gram positive bacteria	**2**	**4**	**1**	**7**	**6.5**
Staphylococcus aureus	2	4	**0**	6	5.6
Enterococcus faecium	0	0	**1**	1	0.9
Fungi	**0**	**11**	**0**	**11**	**10.3**
Candida albicans	0	6	**0**	6	5.6
Candida glabrata	0	2	**0**	2	1.9
Candida tropicalis	0	2	**0**	2	1.9
Candida parapsilosis	0	1	**0**	1	0.9
CAUTI: Catheter-associated urinary tract infections, CLABSI: Central line-associated bloodstream infections, VAP: Ventilator-associated pneumonia					

Extended spectrum beta-lactamase (ESBL) positivity for *Klebsiella pneumoniae* and *E. coli* was found to be 100%. Carbapenem resistance was 91.9% for *A. baumannii,* 76.2% for *P. aeruginosa* and 92.9% for *K. pneumoniae,* while no carbapenem resistance was detected in *Escherichia coli.* A colistin resistance rate of 8.1% was determined for *A. baumannii*. Susceptibility to ceft azidime-avibactam was examined in 46 bacteria and resistance to ceft azi-dime-avibactam was found in 28.3% of them. Th e most eff ective antibiotics according to susceptibility in gram negative bacteria were colistin for *Acinetobacter* spp. and *Pseudomonas* spp.; colistin, ceft azidime-avibactam and aminoglycosides for *Klebsiella* spp.; Carbapenems for E. coli and trimethoprim sulfamethoxazole for *Stenotrophomonas maltophilia*. Antimicrobial resistance rates of gram negative pathogens are shown in Table 4.

Table 4. Antimicrobial resistance rates of gram negative pathogens (%)

Antibiotic	A. baumannii (n: 37)	P. aeruginosa (n: 21)	K. pneumoniae (n: 14)
Ceftazidime	100.0	71.4	100.0
Ceftriaxone	-	-	100.0
Cefepime	-	90.4	92.9
Piperacillin tazobactam	100.0	81.0	85.7
Meropenem	91.9	76.2	92.9
Imipenem	91.9	76.2	92.9
Amikacin	83.8	33.3	35.7
Gentamicin	94.6	33.3	57.1
Ciprofloxacin	97.3	90.5	78.6
Levofloxacin	97.3	85.7	85.6
Trimethoprim-sulfamethoxazole	94.6	61.9	71.4
Colistin	8.1	9.5	21.4
Ceftazidime avibactam	-	23.8	35.7

Table 5: Antimicrobial resistance rates of gram positive pathogens (%)

Antibiotic	***S. aureus*** (n: 6)	***E. faecium*** (n: 1)
Oxacillin	66.7	-
Moxifloxacin	33.3	-
Trimethoprim sulfamethoxazole	16.7	-
Clindamycin	33.3	-
Linezolid	0	0
Teicoplanin	0	0
Vancomycin	0	0

S. aureus was the most commonly isolated gram positive bacterium and 66.7% were methicillin-resistant *S. aureus* (MRSA). 66.2% of *S. aureus* strains were isolated from blood and 33.3% from tracheal aspirate. The most eff ective antibiotics against gram positive bacteria were linezolid, vancomycin and teicoplanin. Antimicrobial resistance rates of gram positive pathogens are shown in Table 5.

All 11 fungal strains were isolated from blood. Of the Candida strains, 6 (%) were *C. albicans*, 2 (%) *C. tropicalis,* 2 (%) *C. glabrata* and 1 (%) *C. parapsilosis*.

DISCUSSION

In ICUs, where high-risk patients are followed for a long period of time and hospitalizations are frequent, nosocomial infections are common and become a serious problem. Nosocomial infections, particularly in ICUs, are known to increase the morbidity and mortality of patients in these units, prolong hospital stays and increase hospital costs.1 In our country, nosocomial infection rates in ICUs are related to surveillance methods, training status of staff, and compliance with infection control measures. The infection rates can vary between 5.3% and 88.9%.7,8 In our study, the rate and incidence density of HAI was found to be lower than national and international data. This reflects the eff ectiveness of the infection control measures implemented in our hospital. In the study by Çalangu et al. the nosocomial infection rate in ICU was reported as 16.8% and the incidence density as 25.9 per thousand.[9] Eggiman

et al. reported a nosocomial infection rate of 15.5% and an incidence density of 13.5 per thousand in 311 ICUs from 18 European countries.[10] Th ese results show that our hospital's infection control measures meet national and international standards and that these measures reduce the risk of infection.

Th e infectious agents of HAIs can vary from hospital to hospital and vary over time in the same department of the same hospital. In our study, gram negative bacteria were most frequently isolated among the HAI pathogens. In the study by Yılmaz et al. 82.8% of nosocomial infectious agents were gram negative bacteria.8 Köksaldı Motor et al. showed that 51% of the causative microorganisms were gram negative bacteria.[11] In the EPIC study, which analyzed ICU infections in 18 countries, it was reported that 53.1% of pathogens were gram negative, 49.2% were gram positive and 17.1% were fungal.[12] Th e EPIC II study reported that 62% of the causative agents of ICU infections were gram negative, 47% were gram positive bacteria, and 19% were fungi.[13] In our study, gram negative bacteria were found in 83.2%, fungi in 10.5%, and gram positive bacteria in 6.3%. Th ese results show that gram negative bacteria are an important pathogen group in ICUs and infection control measures for these bacteria should be strengthened.

Th e most frequently isolated agent among all microorganisms was *A. baumannii* (34.6%), followed by *P. aureginosa* (19.6%) and *K. pneumoniae* (13.1%). Leblebicioğlu et al. reported that 36.6% of nosocomial infection agents were caused by *A. baumannii.*[14] In the study conducted by Balın et al. *Acinetobacter* spp. (29.9%) was found to be the most common microorganism.[15] According to these results, it is thought that A. baumannii is a resistant pathogen frequently seen in ICUs and the choice of empirical treatment of moderate and serious infections developing in ICU should include especially gram negative bacteria and the antibiotic that acts on *Acinetobacter* spp. strains should be selected.

Th e prevalence of gram positive bacteria as pathogens of nosocomial infections in ICUs varies. Aly et al. report-ed that 27% of culture-confirmed nosocomial infections were caused by gram positive bacteria.[16] Similarly, Ak et al. reported that 68.8% of the isolates were gram negative bacteria and 27.6% were gram positive.[17] Doyle et al. reported that resistant *S. aureus* was reported less frequently compared to multidrug-resistant gram negative bacteria.[17] Th e se studies indicate that both gram positive and gram negative bacteria can be important causative agents of HAIs. Qadeer et al. reported that *Enterococcus* and MRSA were the two most common gram positive bacteria.[18] In our study, gram positive bacteria were observed at a rate of 6.5%, with *S. aureus* being the most commonly found. Th e frequency of active ingredients in HAIs also varies depending on the invasive instrument used. In the study by Ak et al. S. aureus was found to be the most common path-ogen in bloodstream infections, *P. aureginosa* in pneumonia, and *E. coli* in urinary tract infections.[17] In the study by Köksaldı Motor et al. *A. baumannii* was found to be the most common agent in VAP, Candida spp. for urinary tract infections and bloodstream infections.[11] In our study, *A. baumannii* was the most common pathogen in VAP and CLABSI, while *P. aureginosa* was the most common path-ogen in CAUTI.

Th e widespread use of antibiotics in the ICU leads to the colonization of resistant microorganisms in patients, resulting in treatment diffi culties and increased mortality rates in patients with infections. This problem is exacerbated by factors such as frequent use of antibiotics, prolonged ICU hospital stays, presence of comorbidities, lack of isolation practices, and easy spread of resistant pathogens, thereby increasing the burden of resistance in critically ill patients.[19] In the study by Gözütok et al. 82.7% of E. coli strains and 83.3% of *K. pneumoniae* strains were ESBL positive.[20] In the study conducted by Göktaş et al, ESBL positivity was found in 70% of *E. coli* and 93.7% of *Klebsiella* spp.[21] In our study, 100% ESBL positivity was found in E. coli and *K. pneumoniae*, and the carbapen-

em resistance rate was 92% for *A. baumannii,* 93% for *K. pneumoniae*, and 76% in P. aeruginosa. Th is situation is extremely worrying in the treatment of resistant gram negative bacteria and highlights the importance of new generation therapies. In the study by Gözütok et al. 96.6% of A. baumannii strains were resistant to imipenem and the most eff ective antibiotic was colistin, and no resistance to this antibiotic was detected.[20] In our study, carbapenem resistance was 91.9% and colistin resistance was 8.1% for A. baumannii. Furthermore, colistin was the most eff ective antibiotic against gram negative bacteria in our study. Th ese results indicate that carbapenem resistance is a serious treatment problem in intensive care units and the use of carbapenem should be limited and alternative antibiotics should be developed.

With the widespread use of antibiotics in ICUs, methicillin resistance rates in staphylococci are increasing. In previous studies, methicillin resistance in *S. aureus* was found to be 41.02% by Kula Atik et al. and 66.6% by Gözütok et al.[20,22] In our study, methicillin resistance was found to be 66.7%. Given that MRSA infections represent a serious treatment problem in ICUs, it should be borne in mind that measures such as MRSA screening, isolation and decolonization should be taken.

In the ICU, the frequency of fungal infections is increasing, which is associated with high mortality and morbidity. Candida species account for the majority of hospital-acquired fungal infections. Although C. albicans ranks fi rst among Candida species, there has been a recent increase in other Candida species.[23] In a study conducted in Turkey, *C. albicans* was reported to be the most frequently isolated, followed by *C. tropicalis* and *C. glabrata.*[24] Kerget et al. isolated C. parapsilosis most frequently in their study.[25] In our study, C. albicans was found most frequently.

In conclusion, the frequency, pathogens, and resistance profi les of H AIs developing in the ICUs of our hospital may diff er from similar studies in the literature. Th ese differences reflect our hospital's unique hospital flora, infection control practices, and antibiotic use policies. Therefore, each center should continuously monitor the development of nosocomial infections in its ICUs, determine the causative microorganisms and their antibiotic resistance profiles, develop infection control measures and ensure rational use of antibiotics. In this way, more successful results can be achieved in the prevention and treatment of HAIs.

Ethical Approval

Ethical approval of this study was granted by the Ethics Committee of Erzurum Regional Training and Research Hospital (Decision No: 2024/01-06).

Peer-review

Externally and internally peer-reviewed.

Author Contributions

Concept: M.A., N.N.A., Design: M.A., N.N.A., Data collection or Processing: G.S., N.N.A, Analysis or interpretation: M.A., S.İ.Y., D.M.A., Literature Search: M.A., N.N.A., Writing: M.A., N.N.A.

Conflict of Interest

No conflict of interest was declared by the authors.

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Informed Consent

Informed consent was not obtained since it was a retrospective study.

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