



Evaluation of Nosocomial Infections and Antimicrobial Resistance Profiles in the Intensive Care Units: Nine Years Experience

Yoğun Bakım Ünitesinde Nozokomiyal Enfeksiyonlar ve Antimikrobiyal Direnç Profillerinin Değerlendirilmesi: Dokuz Yıllık Deneyim

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ABSTRACT

Objective: The aim of this study is to identify nosocomial infections and causative mikroorganisms in adult intensive care units of hospital and also to investigate the changes in antimicrobial resistance profiles over a nine-year period.

Methods: The infection control committee surveillance data of 29318 patients hospitalized in adult intensive care units between 01 January 2010 and 31 December 2018 were evaluated retrospectively.

Results: A total of 29318 patients were followed up in adult intensive care units of hospital in nine-year period and nosocomial infection was detected in 2593 patients (8.8%). The most common infections were; ventilator-associated pneumonia (34.1%), catheter-related urinary tract infection (21.8%), primary bacteremia (17.1%), central venous catheter-related bloodstream infection (14.7%) and pneumonia (8.5%). The most common causative agents were Gram-negative bacteria (72.9%; 2056/2822). Carbapenem resistance in gram negative bacteria responsible for nosocomial infections was 33% in 2010 and reached 75% in 2018. Colistin resistance of *Klebsiella* spp. strains reached up to 34% in 2018.

Conclusion: In Turkey, nosocomial infections in intensive care units are an important problem as well as in the world. With increasing antibiotic resistance, treatment of infections is becoming difficult. Therefore; each center should follow its own infectious

ÖZ

Amaç: Bu çalışmanın amacı, hastanemiz erişkin yoğun bakım ünitelerinde gelişen hastane enfeksiyonlarını ve etken mikroorganizmaları tanımlamak, ve ayrıca dokuz yıllık süreçte antimikrobiyal direnç profillerindeki değişimi araştırmaktır.

Yöntemler: 01 Ocak 2010-31 Aralık 2018 tarihleri arasında erişkin yoğun bakım ünitelerinde yatan 29318 hastanın enfeksiyon kontrol komitesi süreyans verileri retrospektif olarak değerlendirildi.

Bulgular: Hastanemiz erişkin yoğun bakım ünitelerinde toplam 29318 hasta takip edildi, bunların 2593'ünde (%8,8) nozokomiyal enfeksiyon gelişti. En sık görülen hastane enfeksiyonları sırası ile ventilatör ilişkili pnömoni (%34,1), kateter ilişkili üriner sistem enfeksiyonu (%21,8), primer bakteremi (%17,1), santral venöz kateter ilişkili kan dolaşımı enfeksiyonu (%14,7) ve pnömoni (%8,5) idi. Nozokomiyal enfeksiyon etkeni olarak en sık gram negatif bakteriler (%72,9; 2056/2822) izole edildi. Nozokomiyal enfeksiyonlardan sorumlu olan gram negatif bakterilerde karbapenem direncinin 2010 yılında %33 iken 2018 yılında %75'e ulaştığı saptandı. Kolistin direncinin ise 2018 yılında *Klebsiella* spp. suşlarında %34'e kadar ulaştığı tespit edildi.

Sonuç: Yoğun bakım ünitelerinde gelişen nozokomiyal enfeksiyonlar tüm dünyada olduğu gibi Türkiye'de de önemli bir sorundur. Artan antibiyotik direnci ile enfeksiyonların tedavisi giderek

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agent distribution and antibiotic susceptibility, empirical treatment should be selected appropriate to the flora of the intensive care unit and the broad use of broad spectrum antibiotics should be limited.

Keywords: Antibiotic resistance, nosocomial infections, intensive care unit

zorlaşmaktadır. Bu nedenle; her merkezin kendi etken dağılımı ve antibiyotik duyarlılıklarını takip etmesi, empirik tedavide yoğun bakım ünitesinin florasına uygun antibiyotik seçilmesi ve geniş spektrumlu antibiyotiklerin yaygın kullanımının kısıtlanması gereklidir.

Anahtar Sözcükler: Antibiyotik direnci, hastane enfeksiyonları, yoğun bakım

Introduction

Patients who are followed up and treated in intensive care units (ICUs) in hospitals are at risk for the development of nosocomial infections due to the long hospitalization period and invasive procedures such as intubation, mechanical ventilation, tracheostomy and urinary catheterization (1).

Nosocomial infection (NI) is defined as the infection that develops 48-72 hours after the patient's hospitalization (2). While pneumonia is the most common NI in ICUs, urinary infections are in the first order in hospital units other than ICU (3). At least one antibiotic is given to an average of 80% of the patients in the ICU (4,5). Therefore, ICUs are hospital units with the highest antibiotic resistance. The distribution of microorganisms that cause NI varies between units of the hospital as well as between different centers.

Increasing resistance against antibiotics creates a problem in the selection of empirical treatment of critically ill patients, especially those in the ICU. Infections caused by multi-antibiotic resistant microorganisms cause an increase in morbidity and mortality, prolongation of hospital stay, an increase in costs and the emergence of serious complications (6).

It is only possible to determine the frequency of NI and the distribution of agents, to detect developing epidemics, to evaluate whether infection control measures are applied effectively, and to monitor the infection rates of our hospital, with continuous and effective infection surveillance. Surveillance studies are guiding in identifying real problems and evaluating the effectiveness of infection control policies (7).

In this study, we aimed to examine the developing nosocomial infections, causative microorganisms and antimicrobial resistance profiles in the ICUs of our hospital between January 2010 and December 2018.

Method

Our hospital is a tertiary training and research hospital serving an average of 71767 inpatients and an average of 5278 ICU patients in a year. Until 2016, adult ICU had consisted of 4 separate units and 49 beds in total; after 2016, it started to serve with 9 units and a total of 83 beds. Active, patient and laboratory-based surveillance is carried out by the Infection Control Committee (ICC) in ICUs in our hospital. Surveillance data are evaluated by the infection control physician and the infection control nurse.

In our study, the ICC surveillance data of 29318 patients hospitalized in the ICU between January 2010 and December 2018 were retrospectively evaluated. The diagnosis of NI was made based on the definitions of the Ministry of Health National Nosocomial Infections Surveillance Network (UHESA). Typing of the causative microorganisms and their antibiotic susceptibilities were done with the Phoenix automatized system (BD Diagnostic Systems, USA). Infection rate was calculated with the formula (NI number/patient number)X100 and NI Density was calculated with the formula (NI number/patient day)X1000. In the calculation of invasive device-related infection rates, the invasive device-associated NI number/invasive device use day \times 1000 formula was used.

The study was approved by the Antalya Training and Research Hospital Ethics Committee (Date: 30-03-2017, number: 6/03).

Results

In the course of nine years, a total of 29318 patients were followed up in all ICUs, and NE developed in 2593 (8.8%) of them. The distribution of NI by years is given in Table 1. When the distribution of NI according to systems was examined; ventilator-associated pneumonia (VAP) was found the most (34.1%) in ICUs. The second most common was catheter-associated urinary tract infection (CAUTI) (21.8%), followed by primary bacteremia (17.1%), central venous catheter-related bloodstream infection (CRBSI) (14.7%), and pneumonia (8.5%).

The most common NE agents were gram negative bacteria (2056/2822) with a rate of 72.9%. The distribution of causative microorganisms is given in Table 3.

Carbapenem resistance in gram-negative bacteria responsible for NI between 2010 and 2018, were found as 33%, 48%, 57%, 46%, 52%, 68%, 60%, 72% and 75%, respectively. The increase in carbapenem resistance among especially in strains of *Klebsiella* spp. was remarkable. While there was no carbapenem resistance in 2010, this rate reached 83% in 2018 (Table 4).

The rate of detection of extended spectrum beta-lactamase (ESBL) in gram-negative bacteria, which were nosocomial infectious agents, was 20%, 55%, 41%, 27%, 40%, 38%, 38%, 21% and 27%, respectively between 2010 and 2018 (Table 5).

It was noteworthy that colistin resistance in strains of *Acinetobacter* spp., *Pseudomonas* spp. and *Klebsiella* spp. which were included in the study increased over the years. Colistin resistance reached up to 34% in strains of *Klebsiella* spp. It was

determined that piperacillin-tazobactam resistance increased in strains of *Klebsiella* spp. over the years. These high resistance rates cause serious problems in treatment planning and treatment success, especially in infections caused by gram-negative bacteria (Table 6).

Coagulase negative staphylococci constituted the majority of gram positive bacteria which were NI agents. Methicillin resistance was quite high in coagulase-negative staphylococci (100%, 92%, 85%, 95%, 84%, 87%, 88%, 100%, 100%, respectively by years).

Vancomycin resistance was detected in 20 (11.3%) of a total of 177 *Enterococcus* strains isolated as NI agents between 2010-2018 in ICUs. Although vancomycin resistance seemed to increase in recent years, it should be kept in mind that there might be strains naturally resistant to vancomycin such as *E. gallinarum* in this group (Table 7).

Discussion

NI increases the length of hospital stay, leading to labor loss and increased treatment costs. Morbidity and mortality rates are higher than other infections. While the incidence of NI is

between 3.6% and 12% in high-income countries, this rate varies between 5.7% and 12% in low and middle-income countries (8).

Prematures and newborns whose immune system is not sufficient, elderlies, those with underlying chronic diseases, those who have undergone an operation, those diagnosed with cancer, traumatic patients, and patients with metabolic disorders constitute the risk group for the development of NI. In addition, long-term follow-up and treatment of patients in the ICU increase the risk of colonization of these patients with microorganisms and subsequent infection development. Multiple antibiotic treatments used because of the high infection rate in the ICU lead to the emergence of resistant microorganisms. As a result, problems arise in empirical antibiotherapy response.

Microorganisms and antibiotic susceptibilities that develop in ICUs differ between countries, regions, hospitals, and even ICUs in the same hospital (9,10). In order to achieve success in NI treatment and to determine the infection control measures that should be applied, it is necessary to continuously monitor the specialized units of the hospital and crowded ICUs for the infections that occur, the microorganisms that cause infections and the antibiotic susceptibility of microorganisms (11). For this

Table 1. Nosocomial infections developing in ICUs between 2010-2018

	Number of hospitalized patients	Patient day	Nosocomial infection n (%)	Nosocomial infection density
2010	2,295	11,051	179 (7.84)	16.29
2011	2,952	12,456	144 (4.95)	11.72
2012	3,124	12,463	183 (5.86)	14.78
2013	3,178	12,561	189 (5.95)	15.05
2014	3,517	13,847	393 (11.1)	28.3
2015	2,573	12,664	425 (16.5)	33.5
2016	2,911	14,216	436 (14.9)	30.6
2017	4,123	20,827	360 (8.7)	17.2
2018	4,645	24,721	411(8.8)	16.8
Total	29,318	134,806	2,593 (8.8)	19.2

Table 2. Distribution of nosocomial infections in ICUs between 2010-2018 by systems

	CAUTI n (%)	Respiratory system infections n (%)		Bloodstream infection n (%)		Other n (%)	Total
		Pneumonia	VAP	CRBSI	Primary bacteremia		
2010	42 (4.82)	12 (1.44)	37 (3.57)	42 (5.21)	46 (4.89)	-	179
2011	16 (2.30)	4 (0.50)	18 (2.54)	27 (3.71)	73 (10.01)	6 (0.50)	144
2012	41 (5.57)	12 (1.62)	51 (6.88)	20 (2.50)	54 (7.34)	5 (0.66)	183
2013	47 (3.74)	11 (0.88)	41 (3.26)	26 (2.07)	53 (4.22)	11 (0.9)	189
2014	104 (26.4)	37 (9.4)	118 (30.0)	66 (16.8)	57 (14.5)	11 (2.9)	393
2015	106 (25.0)	38 (9.0)	169 (39.7)	50 (11.7)	44 (10.3)	18 (4.3)	425
2016	108 (24.8)	42 (9.6)	173 (39.6)	52 (11.9)	44 (10.1)	17 (4.0)	436
2017	74 (20.6)	41 (11.4)	147 (40.8)	41 (11.4)	47 (13.0)	10 (2.8)	360
2018	54 (13.1)	36 (8.8)	174 (42.3)	74 (18.0)	49 (12.0)	24 (5.8)	411

VAP: Ventilator-associated pneumonia, CAUTI: Catheter-associated urinary tract infection, CRBSI: Central venous catheter-related bloodstream infection

Table 3. Microorganisms causing nosocomial infections in ICUs between 2010-2018

Microorganism n (%)	2010	2011	2012	2013	2014	2015	2016	2017	2018	
Gram-negative	<i>A. baumannii</i>	21 (11.9)	31 (20.9)	38 (20.4)	41 (20.0)	108 (24.0)	133 (31.9)	111 (34.2)	122 (32.9)	174 (32.1)
	<i>Acinetobacter spp.</i>	21 (11.9)	10 (6.7)	21 (11.3)	1 (0.5)	2 (0.6)	2 (0.4)	7 (2.2)	-	3 (0.6)
	<i>P. aeruginosa</i>	23 (13.1)	14 (9.4)	22 (11.8)	28 (13.6)	64 (14.2)	55 (13.2)	41 (12.6)	50 (13.5)	93 (17.2)
	<i>Pseudomonas spp.</i>	5 (2.8)	-	1 (0.5)	2 (1.0)	5 (1.1)	-	3 (0.9)	3 (0.8)	-
	<i>K. pneumoniae</i>	5 (2.8)	11 (7.4)	14 (7.5)	34 (16.5)	50 (11.1)	66 (15.9)	60 (18.5)	67 (18.1)	95 (17.5)
	<i>Klebsiella spp.</i>	9 (5.1)	7 (4.8)	1 (0.5)	-	3 (0.6)	1 (0.2)	2 (0.6)	1 (0.3)	4 (0.7)
	<i>E. coli</i>	11 (6.3)	6 (4.0)	12 (6.5)	14 (6.8)	15 (3.3)	11 (2.7)	14 (14.3)	13 (3.5)	25 (4.6)
	<i>Enterobacter spp.</i>	4 (2.2)	3 (2.0)	4 (2.1)	7 (3.3)	18 (4.0)	11 (2.7)	5 (1.5)	9 (2.4)	11 (2.0)
	<i>Others</i>	2 (1.1)	4 (2.8)	5 (2.7)	3 (1.4)	26 (5.8)	28 (6.8)	16 (4.9)	29 (7.8)	65 (12.0)
	Total	101 (57.2)	86 (58.0)	118 (63.3)	130 (63.1)	291 (64.7)	307 (73.8)	259 (79.7)	294 (79.3)	470 (86.7)
Gram-positive	<i>S. aureus</i>	5 (2.8)	5 (3.4)	5 (2.7)	6 (2.9)	12 (2.6)	7 (1.7)	2 (0.6)	10 (2.7)	10 (1.8)
	CNS	28 (15.9)	12 (8.1)	15 (8.1)	24 (11.7)	37 (8.2)	15 (3.5)	10 (3.1)	1 (0.2)	8 (1.4)
	<i>Enterococcus spp.</i>	13 (7.5)	18 (12.1)	13 (7.0)	13 (6.3)	35 (7.8)	25 (5.9)	16 (4.9)	19 (5.1)	25 (4.6)
	<i>Streptococcus spp.</i>	1 (0.6)	-	-	1 (0.5)	-	1 (0.2)	-	-	-
	<i>Others</i>	-	2 (1.3)	-	1 (0.5)	1 (0.2)	1 (0.2)	-	-	-
	Total	47 (26.8)	37 (24.9)	33 (17.8)	45 (21.9)	85 (18.8)	49 (11.5)	28 (8.6)	30(8.0)	43 (7.8)
Fungus	<i>C. albicans</i>	9 (5.1)	8 (5.5)	6 (3.3)	11 (5.3)	24 (5.3)	22 (5.3)	25 (7.8)	21 (5.7)	11 (2.0)
	<i>C. tropicalis</i>	5 (2.8)	1 (0.7)	3 (1.7)	7 (3.3)	33 (7.3)	22 (5.3)	4 (1.2)	10 (2.7)	4 (0.7)
	<i>C. parapsilosis</i>	1 (0.6)	4 (2.8)	4 (2.1)	5 (2.4)	7 (1.5)	4 (0.9)	3 (0.9)	6 (1.6)	7 (1.3)
	<i>Candida spp.</i>	13 (7.5)	12 (8.1)	22 (11.8)	4 (2.0)	2 (0.6)	7 (1.7)	1 (0.3)	-	-
	<i>Others</i>	-	-	-	4 (2.0)	8 (1.8)	6 (1.5)	5 (1.5)	10 (2.7)	8 (1.5)
	Total	28 (16.0)	25 (17.1)	35 (18.9)	31(15.0)	74 (16.5)	61 (14.7)	38 (11.7)	47 (12.7)	30 (5.5)
	Grand total	176 (100)	148 (100)	186 (100)	206 (100)	450 (100)	417 (100)	325 (100)	371 (100)	543 (100)

CNS: Coagulase negative staphylococci

reason, active and patient and laboratory-based surveillance is carried out by ICC in ICUs and specialized units of our hospital, and agent microorganisms and antibiotic susceptibilities are regularly reported to the relevant departments. Defining NIs in ICUs is necessary for determining local epidemiological features and empirical treatment approach (12).

In studies conducted in our country, the NI rate has been reported between 5.3% and 56.1% (13). Karahocagil et al. reported the NI rate as 3.5% throughout the hospital and 18.3% in the ICU (14). On the other hand, Öncül et al. reported the NE rate as 9.1% in ICU (15). In our study, we found the rate of NI in the ICU as 8.8%.

Table 4. Carbapenem resistance in agent microorganisms in ICUs between 2010-2018

		Total number of agents	Number of agents resistant to carbapenem (%)
2010	<i>A. baumannii</i>	21	19 (90)
	<i>P. aeruginosa</i>	23	3 (13)
	<i>Klebsiella spp.</i>	9	-
	<i>E. coli</i>	11	-
2011	<i>A.baumannii</i>	31	29 (94)
	<i>P. aeruginosa</i>	14	3 (21)
	<i>Klebsiella spp.</i>	18	1 (6)
	<i>E. coli</i>	6	-
2012	<i>A.baumannii</i>	38	38 (100)
	<i>P. aeruginosa</i>	22	11 (50)
	<i>Klebsiella spp.</i>	15	1 (7)
	<i>E. coli</i>	12	-
2013	<i>A.baumannii</i>	41	37 (90)
	<i>P. aeruginosa</i>	28	11 (39)
	<i>Klebsiella spp.</i>	34	6 (18)
	<i>E. coli</i>	14	-
2014	<i>A.baumannii</i>	108	96 (89)
	<i>P. aeruginosa</i>	64	23 (36)
	<i>Klebsiella spp.</i>	53	5 (9)
	<i>E. coli</i>	15	-
2015	<i>A.baumannii</i>	132	121 (92)
	<i>P. aeruginosa</i>	101	51 (50)
	<i>Klebsiella spp.</i>	67	36 (54)
	<i>E. coli</i>	11	3 (27)
2016	<i>A.baumannii</i>	111	92 (83)
	<i>P. aeruginosa</i>	43	13 (67)
	<i>Klebsiella spp.</i>	62	31 (50)
	<i>E. coli</i>	14	1 (7)
2017	<i>A.baumannii</i>	122	113 (93)
	<i>P. aeruginosa</i>	50	18 (36)
	<i>Klebsiella spp.</i>	68	48 (71)
	<i>E. coli</i>	13	4 (31)
2018	<i>A.baumannii</i>	122	113 (93)
	<i>P. aeruginosa</i>	50	18 (36)
	<i>E. coli</i>	13	4 (31)

ICUs: Intensive care units

The most common NI in ICUs is pneumonia (16,17). The most important risk factor for the development of nosocomial pneumonia is intubation and mechanical ventilation. Therefore, VAP constitutes the majority of pneumonia in ICUs. Akin et al. reported the rate of pneumonia as 41% (18). In our study, the VAP rate was found to be 34.1%.

Table 5. Positivity Rate of Extended Spectrum Beta-Lactamase (ESBL) in gram-negative microorganisms in ICUs between 2010-2018

		Total number of agents	Number of agents with ESBL (%)
2010	<i>E. coli</i>	11	2 (18)
	<i>K. pneumoniae</i>	5	3 (60)
	<i>Klebsiella spp.</i>	9	-
2011	<i>E. coli</i>	6	3 (50)
	<i>K. pneumoniae</i>	11	7 (64)
	<i>Klebsiella spp.</i>	7	2 (29)
2012	<i>E. coli</i>	12	4 (33)
	<i>K. pneumoniae</i>	14	7 (50)
	<i>Klebsiella spp.</i>	1	-
2013	<i>E. coli</i>	14	9 (64)
	<i>K. pneumoniae</i>	33	3 (9)
	<i>Klebsiella spp.</i>	1	1 (100)
2014	<i>E. coli</i>	15	7 (47)
	<i>K. pneumoniae</i>	50	20 (40)
	<i>Klebsiella spp.</i>	3	0
2015	<i>E. coli</i>	11	7 (64)
	<i>K. pneumoniae</i>	66	23 (35)
	<i>Klebsiella spp.</i>	1	-
2016	<i>E. coli</i>	11	4 (36)
	<i>K. pneumoniae</i>	48	17 (35)
	<i>Klebsiella spp.</i>	2	2 (100)
2017	<i>E. coli</i>	13	3 (23)
	<i>K. pneumoniae</i>	66	14 (21)
	<i>Klebsiella spp.</i>	2	-
2018	<i>E. coli</i>	25	9 (36)
	<i>K. pneumoniae</i>	95	24 (25)
	<i>Klebsiella spp.</i>	4	-

ICUs: Intensive care units

The first three NI types vary in studies from different regions of Turkey (14,19,20,21,22). In our study, in order of frequency, the most common NI was VAP (34.1%), followed by CAUTI (21.8%), primary bacteremia (17.1%), CRBSI (14.7%) and pneumonia (8.5%).

The causative microorganisms in NI may differ between hospitals and in-hospital units, as well as vary according to the systems in which they are infectious. Gram negative bacteria are the most common agents in VAP and urinary tract infections. Gram-positive bacteria are more frequent agents in bloodstream and surgical site infections (9,23). In our study, the most common agents in VAP and urinary tract infections were gram negative bacteria, primarily *Acinetobacter spp.* While gram-negative bacteria were detected as the causative agent in 57.2% of all NIs in 2010, this rate increased over the years and reached 86.7%

Table 6. Antimicrobial resistance of gram-negative bacteria causing nosocomial infection between 2010-2018 in ICUs

		Resistance (%)								
		2010	2011	2012	2013	2014	2015	2016	2017	2018
Acinetobacter spp.	Piperacillin-tazobactam	81	100	100	98	98	78	100	100	100
	Amikacin	95	79	97	96	97	92	98	75	99
	Ceftriaxone	100	100	100	100	100	100	100	100	100
	Ciprofloxacin	95	97	98	99	100	100	100	100	100
	Colistin	-	-	-	-	-	2	1	1	2
Pseudomonas spp.	Piperacillin-tazobactam	24	20	67	57	21	9	44	38	70
	Amikacin	41	10	47	38	15	3	23	24	64
	Ceftriaxone	100	100	100	100	100	100	100	100	100
	Ciprofloxacin	48	20	74	56	25	3	28	28	74
	Colistin	-	-	-	-	-	1	-	2	-
Klebsiella spp.	Piperacillin-tazobactam	30	60	43	52	55	76	81	82	87
	Amikacin	50	41	57	48	7	6	76	48	36
	Ceftriaxone	100	82	86	75	34	50	85	57	74
	Ciprofloxacin	60	65	79	78	47	55	98	71	96
	Colistin	-	-	-	-	-	1	3	10	34

ICUs: Intensive care units

Table 7. Vancomycin resistance in causative enterococci in ICUs between 2010-2018

	Number of agents	Number of agents resistant to vancomycin (%)
2010	13	0
2011	18	2 (11)
2012	13	3 (23)
2013	13	3 (23)
2014	35	3 (9)
2015	25	3 (12)
2016	16	5 (31)
2017	19	-
2018	25	1 (4)

ICUs: Intensive care units

in 2018. In the "European Prevalence of Infection in Intensive Care (EPIC II)" study, which examined data from 1265 ICUs from 75 countries, 62% of the causative microorganisms were gram negative bacteria, 47% gram-positive bacteria and 19% candida (24). In a study conducted in Brazil, it was found that gram negative bacteria were causative agents in 28.1% of NIs, gram positive bacteria in 7.8%, and fungi in 1.6% (25).7

In two separate studies conducted by Küçükbayrak et al. (26) and Tanrıverdi Çaycı et al. (27), the most frequently isolated NI agents were *P. aeruginosa* and *Acinetobacter* spp. In the study of Kiremitçi et al. (11) the most frequently isolated microorganisms in the ICU were *Acinetobacter* spp. (28.4%), *S. aureus* (19.8%), *Candida* spp. (13.4%) and *P. aeruginosa* (8.1%). The most common gram negative bacteria isolated in our study were *Acinetobacter* spp. (30%), followed by *Klebsiella* spp. (15.2%), *Pseudomonas* spp. (14.4%), and *E.coli* (4.2%). Of Gram-positive bacteria, 5.3% were coagulase negative staphylococcus (CNS),

2.1% *S.aureus*, and 6.2% *Enterococcus* spp. *Candida* was observed at a rate of 13%. For this reason, empirical antibiotic should be chosen to cover gram-negative bacteria first in infections occurring in the ICU.

Studies have shown that methicillin resistance rate in staphylococci detected as infectious agents in ICUs, vancomycin resistance rate in enterococci and carbapenem resistance rate in gram negative bacteria are higher than those found in other parts of the hospital (9,22,28,29,30). In our study, carbapenem resistance in ICU was detected as 33% in 2010, but it gradually increased over the years and reached 75% in 2018. Especially, very high (90-100%) carbapenem resistance in *A. baumannii* strains has been interpreted as a result of intensive use of carbapenem against resistant gram-negative bacteria in ICUs in recent years. Similarly, the high rate of resistance to methicillin in coagulase-negative staphylococci and the use of glycopeptides in the treatment of infections caused by these bacteria cause the

risk of vancomycin resistance in gram positive bacteria. When the enterococcus strains included in our study were evaluated; vancomycin resistance was found in 11.2%.

Colistin resistance rates have increased in recent years as Acinetobacter-induced infection rates and colistin use have increased in ICUs. In our study, it was found that colistin resistance reached 2% in Acinetobacter and Pseudomonas and up to 34% in Klebsiella spp.

It has been reported that antibiotic resistance in microorganisms can be minimized with the proper and appropriate use of antibiotics in ICUs (31). In their study, Gruson et al. reported that providing the correct use of antibiotics in the ICU reduced the rate of VAP and resistant microorganisms (32).

With the use of antibiotics in combinations and sequentially, development of new resistance can be reduced. The choice of drugs to be used can be made depending on the microbiological flora detected in the ICU. To prevent microorganisms to develop resistance; unnecessary antibiotic use should be avoided, antibiotics should be used in appropriate dose and time according to the detected microorganism and the focus of infection, appropriate antibiotic combinations in empirical treatment should be selected for the microorganisms previously detected in the ICU, and appropriate isolation methods should be applied to patients who have developed NI caused by multi-drug resistant microorganisms. After empirical treatment, the treatment should be rearranged according to the agent reproducing.

Conclusion

As a result, NIs developing in ICUs are an important problem in our country as in the whole world. Many factors play a role in controlling NI. It is very important knowing the situations where hand washing is necessary, avoiding unnecessary antibiotic use, obeying the isolation rules, paying attention to the hospital cleaning rules, performing disinfection and sterilization processes properly and regularly, and performing surveillance studies properly. Surveillance studies help to reduce hospital infection rates, identify hospital outbreaks, and compare hospital infection rates. For this reason, all hospitals should know the factors causing NI and their sensitivity profiles; thus will contribute to the selection of appropriate antibiotics in empirical treatment, to decrease the unnecessary use of antibiotics, to decrease the cost and to prevent the emergence of resistant agents.

Ethics

Ethics Committee Approval: The study was approved by the Antalya Training and Research Hospital Ethics Committee (Date: 30-03-2017, number: 6/03).

Peer-review: Internally peer reviewed.

Authorship Contributions

Concept: A.K.S., F.K., K.D.Ö., N.Ö., Design: A.K.S., F.K., K.D.Ö., N.Ö., Data Collection or Processing: A.K.S., F.K., K.D.Ö., N.Ö., Analysis or Interpretation: A.K.S., F.K.,

K.D.Ö., N.Ö., Literature Search: A.K.S., F.K., K.D.Ö., N.Ö., Writing: A.K.S., F.K., K.D.Ö., N.Ö.

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