TÜBİTAK

ORIGINAL ARTICLE

Turk J Med Sci
2009; 39 (2): 295-304
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E-mail: medsci@tubitak.gov.tr
doi:10.3906/sag-0806-4

The Problem of Antimicrobial Resistance in Nosocomial Medical and Surgical Intensive Care Units Infections in a University Hospital; a Two-Year Prospective Study

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Received: June 09, 2008
Accepted: November 13, 2008

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Aim: To determine the frequency of nosocomial infections (NIs) and the antimicrobial resistance of pathogens isolated from patients admitted to 4 intensive care units (ICUs) at a university hospital.

Materials and Methods: The patients were prospectively followed over 2 years in medical, surgical, and reanimation ICUs. The isolates were collected from patients with NI determined by the Center for Diseases Control and Prevention criteria. The identification was performed and susceptibility to antibiotics was determined in an automated system Sceptor (Becton Dickinson) as described by the CCLS.

Results: Among the 3962 patients in the ICUs, total NI incidence was 6.9%, with the highest rate in the reanimation ICU (14.7%) and the lowest rate in the surgical ICU (2.5%). In all, 492 NI episodes were diagnosed in 272 patients. The incidence of NIs was 13.1 per 1000 patient days. The NIs were urinary tract infections (32%), primary blood stream infections (24%), pneumonia (20%), surgical-site infections (13%), and other infections (11%). Pneumonia was the most common NI in the reanimation ICU (54%). The pathogens were 39% gram-positive bacteria, 52% gram-negative bacteria, and 9% *Candida* species. *S. aureus* (18%) was the most frequently isolated bacteria, followed by *P. aeruginosa* (16%), *Acinetobacter* spp. (10%), coagulase negative staphylococcus (CNS) (10%), *Klebsiella* (9%), *E. coli* (9%), and *Enterococcus* spp. (9%). Resistance to methicillin was 90% in *S. aureus* isolates and was 95% in the CNS isolates; no resistance was detected to vancomycin in *S. aureus* and CNS isolates. Eight percent of *Enterococcus* isolates were resistant to vancomycin. Against the gram-negative bacteria the carbapenems were most active, followed by amikacin and ciprofloxacin. Five percent of *P. aeruginosa* and 15% of *Acinetobacter* spp. were resistant to all antibiotics. The most active antimicrobial agents against *Acinetobacter* spp. were imipenem (73%) and tobramycin (46%); against Pseudomonas spp. were ticarcillin/clavulanate (56%), piperacillin (44%), and imipenem (33%); against *Klebsiella* spp. was imipenem (92%); against *E. coli* were imipenem (94%), amikacin (94%), and ciprofloxacin (74%); and against *Enterobacter* spp. were ciprofloxacin (89%) and imipenem (78%).

Conclusions: The high rates of resistant pathogens responsible for NI in ICUs suggest that infection preventive procedures should be implemented and antimicrobial agents must be used appropriately.

Key Words: Nosocomial infections, intensive care units, antimicrobial resistance

Bir Üniversite Hastanesi Medikal ve Cerrahi Yoğun Bakım Üniteleri Nozokomiyal İnfeksiyonlarında Antimikrobiyallere Direnç Problemi, 2 Yıllık Prospektif Çalışma

Amaç: Bir üniversite hastanesinde dört yoğun bakım ünitesinde yatan hastalarda nozokomiyal infeksiyonların sıklığı ile izole edilen patojenlerde antimikrobiyallere direnci belirleme.

Yöntem ve Gereç: Medikal, cerrahi ve reanimasyon yoğun bakım ünitelerinde yatan hastalar prospektif olarak izlendi. İzolatlar CDC kritelerine göre belirlenen nozokomiyal infeksiyonlardan toplandı. İzolatların tanımlanması ve antibiyotiklere duyarlılığı Sceptor (Becton Dickinson) otomatize sistemle CCLS kriterlerine göre yapıldı.

Bulgular: YBÜ'lerinde yatan 3962 hastada, nozokomiyal infeksiyon insidansı % 6,9; en yüksek oran reanimasyon YBÜ'nde (% 14,7), en düşük oran cerrahi YBÜ'nde (% 2,5) olarak belirlendi. 272 hastada 492 Nİ epizodu belirlendi. Nİ insidansı 1000 hasta gününe 13,1 olarak saptandı. Nİ oranları, üriner sistem (% 32), primer bakteriyemi (% 24), pnömoni (% 20), cerrahi alan (% 13) ve diğer infeksiyonlar % 11 bulundu. Pnömoni Reanimasyon YBÜ'nde en sık saptanan (% 54) Nİ idi. Etkenlerin % 39'u gram pozitif, % 52'si gram negatif bakteri, % 9'u *Candida* türleri idi. En sık izole edilen bakteri *S. aureus* (% 18); bunu *P. aeruginosa* (% 16), *Acinetobacter* spp. (% 10), koagülaz negatif stafilokok (KNS) (% 10), *Klebsiella* (% 9), *E. coli* (% 9), ve *Enterococcus* spp. (% 9) izlemekteydi. *S. aureus* türlerinde metisilin direnci % 90, KNS larda % 95, *S. aureus* ve KNS larda vankomisine direnç saptanmadı. Enterokokların % 8'i vankomisine dirençli idi. Gram negatiflere en etkili antibiyotik karbapenemi, amikasin ve siprofloksasin izlemekteydi. *P. aeruginosa* suşlarının % 5'i ile *Acinetobacter* türlerinin % 15'i tüm antibiyotiklere dirençli bulundu. *Acinetobacter* türlerine en etkin antibiyotikler imipenem (% 73), tobramisin (% 46); Pseudomonas türlerine tikarsilin/klavulanat (% 56), piperasilin (% 44), imipenem (% 33); *Klebsiella* türlerine imipenem (% 92), *E. coli* suşlarına imipenem (% 94), amikasin (% 94), siprofloksasin (% 74); *Enterobacter* türlerine siprofloksasin (% 89), imipenem (% 78) idi.

Anahtar Sözcükler: Nozokomiyal infeksiyon, yoğun bakım üniteleri, antimikrobiyal

Introduction

Nosocomial infections (NIs) cause increased mortality and morbidity as well as extended periods of hospitalization and increased cost of treatment (1-3). Hospital infections constitute a major problem in Turkey, as in all other countries (4-7). The prevalence of NIs is higher in intensive care units (ICUs) than in general hospital wards (8,9). Although these patients constitute approximately 10%-15% of all inpatients, about 25% of NIs and 45% of all pneumonia and bacteremia cases are detected in ICUs (10,11). Factors such as invasive interventions for diagnosis and treatment purposes, disturbed defense of the host due to an underlying condition, inappropriate uses of antibiotics, and type of the ICU also contribute in varying degrees (9,10,12-14) to NIs.

Although the rate of infection is related to the type of ICU, respiratory tract infections and urinary tract infections are the most common (12,15). In addition, the incidence of microorganisms accounting for NIs and their susceptibility to antibiotics differ from hospital to hospital and among different departments. In the same hospital setting, there might be some differences associated with time. Moreover, factors accounting for NI present different characteristics than community acquired infections (10). Resistance against microorganisms develops more rapidly in the hospital environment and multidrug resistant bacteria are more frequent (8,16).

In this study, types of NIs, pathogens and antimicrobial resistance patterns were detected in patients admitted to ICUs. The objectives of the study were to contribute to empirical therapy offered by our ICUs based on the most prevalent infection type(s) and antimicrobial resistance pattern that we observed.

Materials and Methods

Over a 2-year period, all patients who stayed for ≥48 h at 1 of 4 ICUs in a university hospital were enrolled in this study. The ICUs were the medical ICU, surgical ICU (General Surgery and Neurosurgery), and reanimation ICU.

This university hospital is a 1100 bed tertiary care referral center for our region, serving a population of approximately 5 million. In our university, all ICUs patients were consulted by the Infectious Disease department every day. The study was conducted prospectively; laboratory and patient-based active surveillance methods were used.

Determination of the hospital infections was based on criteria for NIs by the Center for Diseases Control and Prevention (CDC) (17). The data collected on each infection included the date, site of infection, and patient demographics. NIs were considered ICU-associated if they developed in the ICU (48 h after admission to the ICU, unless the evidence strongly suggested otherwise). The isolates were collected from patients with NI. Identification of isolates was performed and susceptibility to antibiotics was determined in the Central Laboratory of our University Hospital with automated system Sceptor (Becton Dickinson) MIC/ID panels as described by the NCCLS. The distinction of *Candida albicans* from other types of *Candida* was done by germ tube test, a morphological test.

Statistical analysis of this study was performed using SPSS 9.

Results

Study population

During the 2-year study period, 3962 patients admitted to the ICUs were prospectively followed. NIs were determined in 272 (69%) of these patients. Of the 272 patients enrolled in the study 160 (59%) were male and 112 (41%) were female. Mean age was 45.93 ± 19.56 years (range 1-85). Reasons for hospitalization in the medical ICU were gastrointestinal (20%) bleeding, uremic coma, acute renal failure, hepatic coma (12.0%), congestive heart failure (7.2%), diabetic ketoacidosis coma, and others.

Reasons for hospitalization in the neurosurgical ICU mainly included hemorrhage of the central nervous system (43.2%), postoperative complications (30.9%), and trauma (25.9%). The reason for hospitalization in the surgical ICU was postoperative complications in about half of the patients (48.5%).

In the reanimation ICU, more than half of the patients had been hospitalized due to ARDS, respiratory failure, or trauma.

Underlying diseases among the patients with NIs are shown in Table 1. It was found that 143 patients (53%) had chronic diseases, with 29 patients (11%) having multiple diseases. In the medical ICU at least one underlying disease was determined in 76.8% of patients.

Mean duration of hospitalization in our patients was 19.99 (± 13.90 SD) days. The maximum mean duration of hospitalization for the patients in the neurosurgery ICU was 26.30 ± 14.82. It was also reported that 55.6% of the patients in this unit and 42.4% of the patients in the reanimation ICU were hospitalized for more than 20 days.

Table 1. Underlying disease in patients with nosocomial infection.

Disease	Patient numbers (n: 272)	Rate (%)
Hypertension	36	13.2
Diabetes mellitus	34	12.5
Chronic liver disease	33	12.1
Intracranial mass	19	7
COPD	16	5.9
Chronic renal disease	15	5.5
Solid neoplasia	14	5.2
Chronic cardiac insufficiency	12	4.4
Autoimmune diseases (SLE, RA, PAN)	9	3.3
Leukemia/Lymphoma	4	1.5
Other	7	2.6

APACHE II score was over 15 in 6.9% of the patients in the medical ICU and in 75.8% of the patients in the reanimation ICU. The proportions of patients with APACHE II scores over 15 in the neurosurgery and surgical ICUs were 19.8% and 27.3%, respectively. Fifty-three percent of 136 patients with APACHE II scores over 15 died. The mortality rate was high in patients hospitalized for 20 or more days (27.5%). The highest rates of mortality were found in the reanimation (54.5%) and the medical ICUs (43.2%).

Frequency and distribution of nosocomial infections

The total incidence of NI was 6.9% (272/3962), with the highest rate among patients in the reanimation ICU (14.7%) and the lowest in the surgical ICU (2.5%). The incidence of NIs was 13.1 per 1000 patient days. In all, 272 had a total of 492 documented NIs; 147 patients had 1, 66 patients had 2, and 59 patients had 3 infections. Table 2 shows the distribution of patients according to ICUs and rates of NIs. Types of NI according to ICUs are shown in Table 3.

Three major NI sites represented 76% of all reported infections in the ICUs; urinary tract infection (32.3%) was the most frequent, followed by bloodstream infection (23.8%) and pneumonia (20.3%).

Table 2. Nosocomial infection rates in intensive care units.

		No. of beds	All patients	Patients with nosocomial infection (n)	Episodes of infection (n)	Incidence of NI %
ICU	Medical	12	1520	125	193	8.2
	Neurosurgery	17	892	81	166	9
	Reanimation	10	224	33	74	14.7
	Surgical	18	1326	33	59	2.5
Total		57	3962	272	492	6.9

Table 3. Nosocomial infection types in ICUs.

Type of infection	Intensive Care Units				
	Medical	Surgical	Neurosurgery	Reanimation	Total
	(n) (%)	(n) (%)	(n) (%)	(n) (%)	(n) (%)
Urinary tract infection	74 (38.3)	13 (22)	59 (35.5)	13 (17.6)	159 (32.3)
Bloodstream infection	48 (24.9)	18 (30.5)	35 (21.1)	16 (21.6)	117 (23.8)
Pneumonia	38 (19.7)	5 (8.5)	17 (10.2)	40 (54.1)	100 (20.3)
Surgical site infection	14 (7.3)	21 (35.6)	24 (14.5)	5 (6.8)	64 (13)
CNS infection		1 (1.7)	27 (16.3)		28 (5.7)
Decubitus infection	9 (4.7)	1 (1.7)	5 (2.3)		15 (3)
GIS infection	9 (4.7)				9 (1.8)

In all, 607 pathogens from patients with 492 documented NIs were isolated. In 383 cultures 1 pathogen was grown, in 108 cultures 2, and in 1 culture 3 different pathogens were grown. Among these isolated pathogens 238 (39.2%) were gram-positive bacteria, 313 (51.5%) were gram-negative bacteria, and 56 (9.3%) were *Candida* species. *S. aureus* (18%) was the most commonly isolated gram-positive bacteria; among the gram-negative bacteria, *Pseudomonas* spp. (16.3%) and *Acinetobacter* spp. (10.4%) were the most common pathogens.

The pathogens isolated from hospital infections in ICUs are shown in the Figure.

Isolated pathogens from types of NI are shown in Table 4.

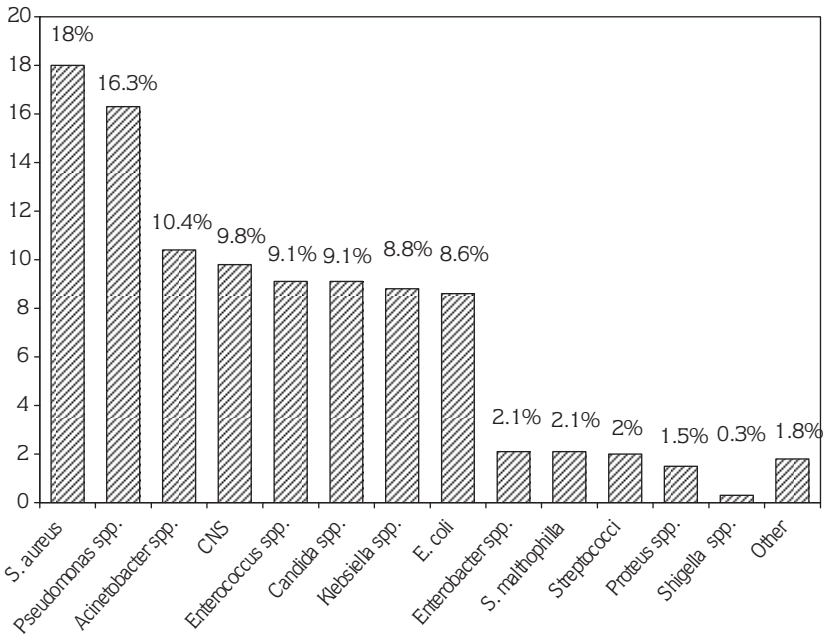

Figure. Isolated pathogens from patients with nosocomial infections.

Table 4. Types of nosocomial infections and the most commonly isolated pathogens.

Urinary tract infection n: 159	%	Bloodstream infection n: 117	%	Pneumonia n: 100	%	Surgical site infection n: 64	%
Candida	23	*S. aureus*	22	*Pseudomonas* spp.	37	*S. aureus*	24.7
E. coli	19	*Acinetobacter* spp.	10	*S. aureus*	21	*Pseudomonas* spp.	18
Enterococci	14.8	*Candida* spp.	5.8	*Acinetobacter* spp.	16.5	*Acinetobacter* spp.	14.6
Klebsiella spp.	13.8	*Enterococci*	7	*Klebsiella* spp.	8	*E. coli*	10.1
Pseudomonas spp.	10			*S. maltophilia*	5	*Enterococci*	7.9

S. aureus (n = 4) and *Acinetobacter* spp. (n = 3) were the most common pathogens isolated from nosocomial wound infections (n = 15). Other frequently isolated pathogens were *E. coli* (n = 2), *Pseudomonas* spp. (n = 2), and *Enterococci* (n = 2).

Pathogens and antimicrobial resistance

The frequency of methicillin resistance was 90% in *S. aureus* strains, no resistance was detected for vancomycin, and the susceptibility rate was 95% for trimethoprim-sulfamethoxazole (TMP-SMP).

Methicillin resistance was observed in 95% of the CNS. No resistance was detected to vancomycin in CNS strains. Table 5 presents antimicrobial susceptibility rates in *Staphylococci* strains.

The vancomycin resistance rate for *Enterococci* species was 7.7% (n = 5). In addition, 76.7% of the species established as the pathogens responsible for urinary infections were susceptible to nitrofurantoin. Resistance rates for *Enterococci* strains are presented in Table 6. The susceptibility to antibiotics for gram-negative bacteria is shown in Tables 7 and 8. The most susceptible antibiotic to all gram-negative microorganisms was imipenem (75%), followed by amikacin (47%), ticarcillin/clavulanic acid (42%), and ciprofloxacin (38%).

Imipenem resistance was established in 27% of *Acinetobacter* strains and in 66% of *Pseudomonas* strains. In addition, 14% of *Acinetobacter* strains and 5% of *P. aeruginosa* strains were resistant to all antibiotics studied.

The antibiotics having the highest susceptibility for *Acinetobacter* strains were imipenem (72.8%) and tobramycin (46.2%). The antibiotics having the highest susceptibility for *Pseudomonas* strains were ticarcillin/clavulanic acid (56.6%) and piperacillin (44.1%). The antibiotics having the highest susceptibility for *S. maltophilia* were ticarcillin/clavulanic acid (87.5%) and trimethoprim-sulfamethoxazole (TMP-SMP) (73.3%).

Table 5. Antimicrobial resistance in *Staphylococcus* spp. isolated from ICUs.

	CHO	CIP	CLIN	ERY	GM	NET	OFX	OXA	PEN	RIF	TET	TMX	VAN
S. aureus													
R/n	16/73	137/139	124/136	132/137	135/139	5/60	54/58	125/ 139	139/139	132/ 135	72/74	7/ 139	-/ 139
(%)	21.9	98.6	91.2	96.4	97.1	8.3	93.1	90	100	97.8	97.3	5	0
CNS													
R/n	29/43	60/69	64/73	67/72	64/69	2/22	17/23	67/71	70/71	53/62	12/38	56/72	-/ 72
(%)	67.5	86.9	87.7	93.1	92.7	9	73.9	94.4	98.6	75.5	31.6	77.8	0

Abbreviations: R: resistant, CHO: chloramphenicol, CIP: ciprofloxacin, CLIN: clindamycin, ERY: erythromycin, GM: gentamicin, NET: netilmicin, OFX: ofloxacin, OXA: oxacillin, PEN: penicillin, RIF: rifampin, TET: tetracycline, TMX: trimethoprim-sulfamethaxazole, VAN: vancomycin

Table 6. Antimicrobial resistance in *Enterococcus* spp. isolated from ICUs.

Enterococcus spp.	AMP	CHO	CIP	GM	NF	NOR	PEN	TET	TMX	VAN
R/ n	46/65	52/65	33/37	6/6	7/30	47/64	51/65	30/65	32/65	5/65
(%)	68.7	80	89.2	100	23.3	73.4	76.11	44.8	49.2	7.7

Abbreviations: AMP: ampicillin, CHO: chloramphenicol, CIP: ciprofloxacin, GM: gentamicin, NET: netilmicin, NOR: norfloxacin, PEN: penicillin, TET: tetracycline, TMX: trimethoprim-sulfamethaxazole, VAN: vancomycin

Table 7. Antimicrobial resistance in non-fermentative bacteria isolated from ICUs.

	AM	AZ	CF	CFT	CAZ	CFZ	CAX	CIP	GM	IMP	PIP	TIC	TIM	TM	TMX
Pseudomonas spp.	79/113	77/118	83/105	107/112	87/112	73/74	108/110	80/110	84/110	80/120	66/118	80/111	50/115	93/117	108/113
R/n %	69.9	65.3	79	95.5	74.4	98.6	98.2	72.7	76.4	66.7	55.9	72.1	43.5	79.5	95.6
Acinetobacter spp.	73/81	88/88	30/31	77/80	38/41	5/6	79/81	69/82	73/81	25/92	90/92	22/24	66/79	49/91	70/82
R/n %	90.1	100	96.7	96.2	92.7	83.3	97.5	84.1	90.1	27.2	97.8	91.7	83.5	53.8	85.4
S. maltophilia	14/16	15/16	12/13	15/16	11/13	9/10	15/16	12/15	16/16	14/17	14/17	12/13	2/16	1717/	4/15
R/n %	87.6	93.8	82.3	97.7	84.6	90	93.7	80	100	82.4	82.4	92.3	12.5	100	26.7

Abbreviations: R: Resistant

AM: Amikacin, AZ: Aztreonam, CF: Cefoperazone, CFT: Cefotaxime, CAZ: Ceftazidime, CFZ: Ceftizoxime, CAX: Ceftriaxone, CIP: Ciprofloxacin, GM: Gentamicin, IMP: Imipenem, PIP: Piperacillin, TIC: Ticarcillin, TIM: Ticarcillin/clavulanate, TM: Tobramycin, TMX: Trimethoprim/Sulfamethaxazole

Table 8. Antimicrobial resistance in *Enterobacteriaceae* isolated from ICUs.

	AM	AMP	AMP/S	AZ	CEF	CT	CAX	CFU	CIP	GM	IMP	N	NOR	PIP	TIC	TIM	TM	TMX	
E. coli	R/n	14/64	63/64	31/39	34/49	42/55	5/38	37/65	26/34	18/65	35/64	4/48	14/25	8/26	41/46	27/28	26/36	27/45	34/59
(n:64)	(%)	21.9	98.4	79.5	69.4	76.3	13.1	66.9	76.5	27.2	54.7	8.4	56	30.8	89.1	96.5	72.2	60	57.6
Klebsiella	R/n	4/65	52/65	28/32	16/35	27/63	5/33	25/65	26/44	35/62	17/64	2/35	8/36	21/37	26/31	29/44	19/31	14/35	51/64
(n: 65)	(%)	6.1	80	87.5	45.8	42.9	15.2	38.5	59.1	56.5	25.6	5.7	22.2	56.8	83.9	65.9	61.3	40	79.7
Enterobacter spp. *(n: 18)*	R/n	4/18	17/17	15/18	11/17	18/18	10/18	11/18	3/5	2/18	6/18	4/18			10/17	5/7	11/17	6/18	9/18
Proteus spp. *(n: 13)*	R/n	7/13	12/13	2/6	2/6	9/13	0/6	3/13	7/10	9/13	9/13	1/6	8/8	7/8	3/6	9/10	1/6	3/6	12/13

Abbreviations: R.: Resistance

AM: amikacin, AMP: ampicillin, AMP/S: ampicillin/sulbactam, AZ: aztreonam, CEF: cefazolin, CT: cefotetan, CAX: ceftriaxone, CFU: cefuroxime, CIP: ciprofloxacin, GM: gentamicin, IMP: imipenem, N: nitrofurantoin, NOR: norfloxacin, PIP: piperacillin, TIC: ticarcillin, TIM: ticarcillin/clavulanate, TM: tobramycin, TMX: trimethoprim/sulfamethaxazole,

Discussion

In our study, the incidence of NI was 6.9% in ICUs. Among the 4 ICUs, NI rate was highest in the reanimation ICU and lowest in the surgical ICU. Multiple traumas (63%) with life-threatening conditions, needs for respiratory support, and higher numbers of invasive interventions than the others for patients in the reanimation ICU were the most important contributory factors for the highest rate of infection observed.

A higher incidence of nosocomial infections has been determined in ICUs than in general hospital wards (9). In Turkey, it has been reported that the rate of hospital infection was 5.3%-39.0% in ICUs (4-7). The rate of hospital infections in a multicenter study from the USA carried out between 1992 and 1998 was reported to be 6.1%, whereas this rate was 20.6% in another multicenter study conducted in 1417 ICUs in 17 European countries (12,18).

In our study, the most frequent NI type was urinary tract infection (32.3%) in all units, except for the reanimation ICU (54%). Blood stream infection (BSI) was the second most frequent NI in all our ICUs. Pneumonia was the most commonly reported NI in other ICU studies (19), followed by urinary tract infections and other infections (12,18,20). The frequency of BSI in ICUs was high in several studies (10,12,21,22).

The frequency of the nosocomial pathogens may vary among hospitals and among different units within the same hospital (12,15,18). In studies conducted in ICUs in Turkey and other international multicenter studies conducted in ICUs, the most frequently isolated pathogens were *S. aureus* (11.8%-37.6%) and *P. aeruginosa* (11%-32%). *E. coli, Klebsiella* spp., *Acinetobacter* spp., and CNS followed them in various proportions (4,10,12,14,19-25). In our study, the most frequently observed pathogens were *S. aureus* (18.0%) and *P. aeruginosa* (16.3%), similar to the other studies.

The frequency of isolated pathogens varies depending on the type of NI. In urinary NI, most frequently observed pathogens were *Candida* spp., *E. coli*, *Enterococci* spp., and *P. aeruginosa* (10,12). In our study, *Candida* (23%) and *E. coli* (19%) were also the most frequently isolated pathogens.

In ICUs, *S. aureus* and *P. aeruginosa* are the most commonly determined pathogens responsible for nosocomial pneumonia, followed by *Enterobacter* species, *K. pneumoniae*, fungi, and *Acinetobacter* spp. (10,12,26). Similarly, in our study the most frequently isolated pathogens were *Pseudomonas* spp. (36.7%) and *S. aureus* (20.9%), followed by *Acinetobacter* spp. and *Klebsiella* spp.

The most common pathogens involved in BSI are CNS, *S. aureus* and less commonly species of *Enterococci* and *Candida* (21,27). It has been reported that gram-negative aerobic bacteria were isolated in lower frequencies (12,19,21,22). In this study, CNS (37.4%) and *S. aureus* (22.3%) were isolated most. However, *Acinetobacter* spp. (10.1%) were the third most commonly determined pathogen. In a multi-center European study (12) *Acinetobacter* spp. were isolated at a rate of 8%.

The most common causes of nosocomial surgical site infections are *S. aureus* and *P. aeruginosa,* similar to our study (10,12,18,21).

In our study, nosocomial central nervous system infections involved *S. aureus* (21.9%) and CNS (15.6%) pathogens most frequently. In a multicenter study, CNS (43%) and *Enterobacter* species (12%) were the most common pathogens (18).

Bacteria isolated from all nosocomial infection types in our study were similar to those isolated in other multi-center studies. However, the remarkable finding from our study was the high rate of *Acinetobacter* species in most of the NI types.

Most important problem concerning pathogens isolated from ICUs is their increasing resistance to several antibiotics. Antibiotic resistance is important in both gram-positive and gram-negative bacteria (9,26,28-32). Infections with resistant microorganisms and intensive antibiotic usage cause serious problems.

Incidences of methicillin-resistant *S. aureus* (MRSA) vary among countries. A high rate (70%-90%) of MRSA was reported in studies conducted in ICUs in Turkey. The rate of MRSA ranges between 0% and 60% in European countries, while the Mediterranean countries seem to have a higher figure.

According to the NNIS report, 52% of *S. aureus* isolates and 87% of CNSs were methicillin-resistant and 25% of *Enterococci* were vancomycin-resistant in the USA in 1999 (29). In Taiwan, it was reported that 62% of *S. aureus* and 63% of CNS were oxacillin-resistant, and 2% of the *Enterococci* were vancomycin-resistant (36). *S. aureus* was reported to be the most commonly isolated

pathogen in Latin America, with the MRSA rate being 31% (37). In a study performed in the United States, the rate of CNS resistance to methicillin was determined to be 49% in ICUs (8).

In our study, although methicillin-resistance among CNS was above 95%, no resistance was detected to vancomycin. Susceptibility to trimethoprim-sulfamethoxazole (TMP-SMX) was high. In a multi-center European study (12), 70.1%, 3.5%, and 9.3% of the CNS isolates were resistant to methicillin, vancomycin, and teicoplanin, respectively.

Glycopeptide resistance of *Enterococci* has been rapidly increasing. According to CDC data, it has increased from 0.04% in 1989 to 13.6% in 1993 (38). In Reacher's study, vancomycin-resistant *E. faecium* was reported as 24% and *E. faecalis* 5% in patients with nosocomial bacteremia (33). In our study, 7.7% of the *Enterococcus* species were vancomycin-resistant. Of these strains 4 were *E. faecium* and 1 was *E. faecalis.* In another study from Turkey, vancomycin resistance was not determined in *Enterococcus* spp. (39).

When the antibiotic susceptibilities of all gram-negative bacteria were assessed, imipenem was found to be the most effective (74.6%), followed by amikacin, ticarcillin/clavulanic acid, and ciprofloxacin. It was also reported that amikacin, ciprofloxacin and cefepime were the other effective antibiotics. In our study, *Pseudomonas* spp. were highly resistant to antibiotics and showed the highest susceptibility to piperacillin and to ticarcillin/clavulanic acid. Imipenem susceptibility was only 33.3%. In the SENTRY study, the most active agents against *P. aeruginosa* were amikacin, cefepime, tobramycin, meropenem, and piperacillin/tazobactam (25).

In this study, *Acinetobacter* strains' resistance was high to all antibiotics, except imipenem and tobramycin. The most effective antibiotics against *Enterobacter* species were ciprofloxacin (89%), imipenem (78%), and amikacin (78%). The most effective antibiotic against *Klebsiella* species was imipenem (81.6%). The most effective antibiotics were imipenem (94%) and amikacin (94%) in *E. coli* strains. In multi-center studies (25,38,40) conducted in Turkey, amikacin, imipenem, and piperacillin-tazobactam were reported to have the highest activity against *P. aeruginosa*, while cefepime, ceftazidime, and ciprofloxacin were reported to have a efficacy rate of 43%. The most susceptible antibiotic for *Acinetobacter* species was imipenem; however, even for imipenem the rate of resistance was determined to be 44.5%. Imipenem was found to be very effective for *Klebsiella* strains, and cefepime, ciprofloxacin, and ceftazidime-clavulanate comprised the other active antibiotics.

In conclusion, the antimicrobial resistance rate is high in our ICUs. For this reason, every ICU must monitor its infection rates, distributions of the isolated microorganisms, and their antibiotic susceptibilities very closely. In ICUs, the use of antibiotics requires a multidisciplinary approach. In evaluating the epidemiology and risk factors, it should be taken into account that the policies regarding antibiotics use have a great impact on the epidemiology of infections. Limiting the inappropriate use of antibiotics and increasing the compliance to the infection control practices were suggested to be the most significant strategies for prevention of antimicrobial resistance in ICUs.

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