Research Article / Araştırma Makalesi

Microorganisms Isolated from Respiratory Intensive Care Unit and the Change of Antibiotic Resistance Status By Years And Its Effect On Mortality

Solunumsal Yoğun Bakım Ünitesinde İzole Edilen Mikroorganizmalar ve Antibiyotik Direnç Durumlarının Yıllara Göre Değişimi ve Mortaliteye Etkisi

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Abstract

Background: Intensive care units (ICU) are multidisciplinary departments where patients with life-threatening diseases, major surgical interventions, respiratory failure, coma condition, hemodynamic insufficiency, and ≥1 organ failure are admitted for relevant diagnoses and treatment. The present study sought to investigate pathogens causing infections in patients admitted to our respiratory ICU and their antibiotic resistance patterns.
Materials and Methods: The antibiogram results and clinical data of all patient samples submitted between January 1, 2008, and December 31, 2010, were retrospectively reviewed. Ethics committee approval was obtained from Dicle University Faculty of Medicine.
Results: In total, 248 patients with 561 culture results were included in the study. Microbial growth was detected in the following samples: blood, 336 (59.9%); deep tracheal aspirate, 104 (18.6%); urine, 89 (15.9%); wound drain, 12 (2.1%); central venous catheter liquid, 7 (1.3%); phlegm, 10 (1.8%); Foley tip liquid, 1 (0.2%); and pleural effusion, and 1 (0.2%). Rapid growth was most frequently noted in the cultures of coagulase-negative staphylococci (25.3%), *Acinetobacter* spp. (23.1%), and *Escherichia coli* (12.6%).
Conclusions: the present study revealed microorganisms' resistance profiles similar to those of other relevant studies. The study provides important insights into the selection of empiric antibiotic therapy for patients admitted in intensive care unit.

Key Words: Respiratory intensive care unit, Intensive care infections, Antibiotic resistance, Antibiotic susceptibility

Öz

Amaç: Yoğun bakım üniteleri (YBÜ), yaşamı tehdit eden hastalıkları, büyük cerrahi girişimleri, solunum yetmezliği, koma durumu, hemodinamik yetmezliği ve ≥1 organ yetmezliği olan hastaların ilgili tanı ve tedavi için kabul edildiği multidisipliner bölümlerdir. Bu çalışma, solunum yoğun bakım ünitemize kabul edilen hastalarda enfeksiyonlara neden olan patojenleri ve antibiyotik direnç modellerini araştırmayı amaçladı.
Materyal ve Metod: 1 Ocak 2008 ile 31 Aralık 2010 tarihleri arasında sunulan tüm hasta örneklerinin antibiyogram sonuçları ve klinik verileri retrospektif olarak incelendi. Dicle Üniversitesi Tıp Fakültesinden etik kurul onayı alındı.
Bulgular: Toplamda 561 kültür sonucu olan 248 hasta çalışmaya dahil edildi. Aşağıdaki örneklerde mikrobiyal üreme tespit edildi: kan, 336 (%59,9); derin trakeal aspirasyon, 104 (%18.6); idrar, 89 (%15.9); yara drenajı, 12 (%2,1); santral venöz kateter sıvısı, 7 (%1,3); balgam, 10 (%1.8); Foley uçlu sıvı, 1 (%0,2); ve plevral efüzyon ve 1 (%0.2).
Hızlı üreme en sık olarak koagülaz negatif stafilokok (%25,3), Acinetobacter spp. (%23,1) ve Escherichia coli (%12,6).
Sonuç: Sonuç olarak, bu çalışma mikroorganizmaların direnç profillerini ilgili diğer çalışmalara benzer şekilde ortaya koymuştur. Çalışma, yoğun bakım ünitesine kabul edilen hastalar için ampirik antibiyotik tedavisinin seçimine ilişkin önemli bilgiler sunmaktadır.

Anahtar Kelimeler: Solunum yoğun bakım ünitesi, Yoğun bakım enfeksiyonları, Antibiyotik direnci, Antibiyotik duyarlılığı

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Introduction

Intensive care units (ICU) are multidisciplinary departments where patients with life-threatening diseases, major surgical interventions, respiratory failure, coma condition, hemodynamic insufficiency, and ≥1 organ failure are admitted for relevant diagnoses and treatment. Although the patients admitted to ICUs (5%–10%) constitute only a small group of all the inpatients, 25% of the cases of nosocomial infections and approximately 45% of all cases of nosocomial bacteremia and pneumonia are associated with ICU admission. All of the study show that he average duration of ICU stay is 39.7 days(1-2-5-7-8-9). The prevalence of nosocomial infections in the ICU is 5–10 times higher than that of other surgical and internal medicine wards.(1 -2)

The empirical use of antibiotics can be associated with cross-drug reactions, colonization, superinfection caused by opportunistic pathogens, and drug-resistant infections. Infections caused by antibiotic-resistant microorganisms not only increase the morbidity and mortality rates but also are associated with prolonged hospitalization, increased financial burden, and various health complications(3 -4)

Although Gram-positive bacteria are more common in hospital infections (HE) today, Gram-negative bacteria continue to be important. As Gram-negative bacteria develop resistance to antibiotics, the importance of HE caused by them increases and the treatment of these infections with existing antibiotics becomes difficult(5-6). Multi-drug resistance (MDR) becomes more important in NI, especially in intensive care units, as the use of high-dose, broad-spectrum paraenteral antibiotics is required. Infections caused by a resistant bacteria cause increased mortality, prolonged hospital stay and increased cost. In general, infections that occur within 48–72 hours of hospital admission and within 10 days of discharge are considered hospital-acquired(8).

In this study, we examined the pathogens causing infection and their antibiotic resistance patterns in patients hospitalized in our respiratory intensive care unit during January 2008 and December 2010. Thus, we tried to establish the surveillance of our intensive care unit.

Materials and Methods

This study included patients who were admitted to the Respiratory Intensive Care Unit of Chest Diseases Department, Dicle University Faculty of Medicine, Turkey, between January 2008 and December 2010 and exhibited positive culture results of their samples. Ethics committee approval was obtained from Dicle University Faculty of Medicine.

Patient data were retrieved by reviewing the patients' files and medical records. Data on age, sex, isolated microorganism species, antibiotic susceptibility, infection/colonization foci, duration of ICU stay, diagnoses, antibiotics administered, and patient outcomes (alive/dead) were collected using patient record forms prepared for the purpose of this study.

Bedside blood samples (8–10ml) were collected from both arms of the patients. The blood samples were collected in BD BACTEC plus + Aerobic/F 30-ml blood culture tubes and sent to the laboratory without delay. The samples were cultured using BACTEC 9240 or BACTEC 9120 devices. The incubation period lasted a maximum of 7 days. The tubes with positive growth signal were removed from the device, and the culture was inoculated onto eosin–methylene blue (EMB) agar, blood agar, and Sabouraud dextrose agar (SDA) media. The respiratory tract samples were carefully collected in into deep tracheal aspirate (DTA) sample tubes while maintaining sterilized conditions to avoid contamination. Urine samples were collected from the patients' existing Foley catheters with due care to maintain sterilized conditions in sterile disposable injectors. Furthermore, wound swabs were collected with sterile swabs and cultured directly using EMB agar, blood agar, and SDA growth media. All growth media were maintained in an incubator (Bimderz® or Heraew®) at 35°C for 18–24 h. Subsequently, antibiogram was generated for microorganism colonies using the Phoenix 100 device.

The exclusion criteria for culture results are mentioned below.

1. Culture results that were not compatible with the clinical and laboratory results of the patient were excluded from the study.
2. If blood samples collected simultaneously from both arms were positive, only one was considered to avoid duplication.
3. If the antibiogram patterns of the same pathogens that showed positive results in two different cultures (e.g., blood and tracheal aspirate) were also the same, only the result that clinically suggested the focus of infection was included in the study.
4. If the culture results of blood samples collected from both arms were positive for different factors and were not compatible with the clinic findings, the results were excluded from the study.

Statistical analysis

Descriptive statistics for continuous variables were expressed as means and standard deviations. The intermittent variables were converted into cross-tables and analyzed using Fisher's exact and Pearson's chi-square tests. The normal distribution of the study data was assessed using Kolmogorov–Smirnov test. The mean values of the variables were analyzed using Student's *t*-test. Bidirectional hypotheses were used, and a p-value of <0.05 was considered statistically significant. The IBM Statistical Package for the Social Sciences Ver. 18.0 for Windows (SPSS Inc., Chicago, IL, USA) software was used for statistical analyses.

Results

A total of 2,028 patients were admitted to the Respiratory Intensive Care Units(ICU) of Dicle University Education and Research Hospital between January 1, 2008, and December 31, 2010. This study included a total of 746 positive culture results obtained from 248 patients using their samples collected during hospitalization and the period of elevated infection markers. In total, 64 positive culture results were excluded from this study because of the fact that the microorganisms cultured were incompatible with the clinical findings of the patient. Only one of the simultaneous blood culture results was included in the study because 97 positive culture results were based on the samples collected from both arms. Furthermore, owing to the lack of antibiogram data, culture samples from 24 patients were excluded from this study. Thus, a total of 185 samples were excluded from the study. Finally, a total of 561 culture samples obtained from 248 patients were included in this study.

Within 48 h, growth was detected in the culture results of 5 out of 248 patients but not in the results of the remaining 243 patients. Upon a review of these samples, five culture results of these five patients suggested community-acquired infection. Infections in the other 243 patients met the criteria for HAIs (patients were referred to our hospital after they were hospitalized in another institute; infections occurred during the patients' stay in our respiratory ICU). Thus, the rates of community-acquired infections and HAIs were 2% and 98%, respectively.

The participants included in the study comprised 147 men (59.2%) and 101 women (40.8%). No significant differences were noted in terms of patient sex (p=.30). The mean age of patients who were followed up in respiratory ICU during the 3-year period was 63.56±19.930 years . The analysis of the association between age and mortality indicated that the mean age of dead patients was 66.29±18.03 years, whereas that of the survivors was 59.83±21.79 years. A statistically significant relationship was detected between the patients' age and mortality. Mortality increased with increasing age (p= 0.016).

No statistically significant difference was noted between male and female patients in terms of mortality (p=0.30). The mean duration of ICU stay was 23.95±22.95 days. Year-wise analysis revealed that the mean durations of hospital stay for 2008, 2009, and 2010 were 24.55±22.94, 19.66±16.99, and 29.40±28.78 days, respectively. Separate analysis of the duration of hospital stay per year showed a significant difference in the duration of hospital stay between 2009 and 2010 (p<0.05). The mean duration of hospital stay for female and male patients was 23.86±21.927 and 24.11±23.800 days, respectively. Male patients had longer durations of hospital stay than female patients, and the difference was statistically significant (p=0.013). The mean durations of ICU stay of the dead and discharged patients were 24.11±23.79 and 23.73±21.85 days, respectively. There was no statistically significant difference in the mean duration of stay ICU between the dead and discharged patients (p=0.89).

The analysis of the data of inpatients according to year revealed a significant increase in the rate of respiratory ICU admission of women (p=0.013). The mortality rate was 57.7% (143 patients), whereas 42.3% (105 patients) patients were discharged from the ICU after full recovery (p>0.05;).

The analysis of the association between mortality and patient sex showed that the mortality rates in female and male patients were 57.7% and 60.5%, respectively (p>0.05) and there was no statistically significant difference in mortality rates according to years (p=0.83).

Pneumonia was the most common reason for ICU admission (55.6%). Sepsis was the most common cause of death in the ICU (30.2%)(Table 1).

Table 1. Diagnosis at admission(the share of sub-crimes in disease percentages is given)

Diagnosis	Number	Percentage (%)
Pneumonia and comorbid diseases	**134**	**55.6**
Pneumonia	35	14.1
Pneumonia+Sepsis	41	16.5
Pneumonia+Neurological diseases	26	10.5
PE+Pneumonia	9	3.6
Pneumonia+ARDS	8	3.3
COPD+Pneumonia	15	6
Sepsis	**85**	**34.3**
Sepsis	48	19.4
Sepsis+MODS	11	4.5
COPD+Sepsis	15	6
Urosepsis	2	0.8
Sepsis+TB	2	0.8
Sepsis+ILD	2	0.8
COPD attack	**5**	**2**
Others	**12**	**4.8**
Total	**248**	**100**

MODS, multiorgan dysfunction syndrome; PE, pulmonary embolism; ILD, interstitial lung disease; Tb, tuberculosis; COPD, chronic obstructive pulmonary disorder.

Microbial growth was detected in the following samples: blood, 336 (59.9%); DTA, 104 (18.6%); urine, 89 (15.9%); wound drain, 12 (2.1%); phlegm, 10 (1.8%); central venous pressure catheter liquid, 7 (1.3%); Foley tip liquid, 1 (0.2%); and pleural effusion, 1 (0.2%).

The number of positive culture results was 173 in 2008, 221 in 2009, and 166 in 2010. There was no statistical difference between the samples collected according to years and microorganisms cultured (p=0.10). Most frequent growth in blood culture was noted for CoNS. Year-wise analysis also indicated that *CoNS* showed the most frequent growth. These were for CoNS (25.3%), *Acinetobacter* spp. (23.1%), and *E. coli* (12.6%) in this order(Table 2). The analysis of pathogen distribution according to year indicated that the most frequent growth in urine was noted for *E. coli*. Considering the 3-year period, the most frequent growth was also noted for *E. coli* (in 30 patients).

The most frequent growth in DTA and phlegm samples obtained from the lower respiratory tract was noted for *Acinetobacter baumannii*, which was followed by that for *Pseudomonas* spp. (13%). *S. aureus* was the third most frequently present microorganism (6.14%).

Table 2. Microorganisms and their cultures from different samples according to years

Microorganisms	Year	Blood	Urine	DTA	Catheter	Wound drain	Foley	Phlegm	Total
Acinetobacter spp.	2008	20	2	21	1	1			45
	2009	18	5	19	1	2			45
	2010	19	4	15	2	0			40
	Total	57	11	55	4	3			130
Pseudomonas spp.	2008	0	0	1	0	0		3	4
	2009	5	0	8	1	2		2	19
	2010	3	5	1	0	1		0	10
	Total	8	5	10	1	3		5	33
Staphylococci	2008	12		5	1	0	0	0	18
	2009	11		0	1	0	1	1	13
	2010	14		1	0	2	0	0	17
	Total	27		6	2	2	1	1	38
Escherichia Coli	2008	10	8	8		1			27
	2009	9	16	2		0			27
	2010	9	6	2		0			17
	Total	28	30	12		1			71
Coagulase Negative Staphylococcus	2008	44	0	1	0				45
	2009	57	1	1	1				60
	2010	35	1	1	0				37
	Total	136	2	3	1				142
Enterococci	2008	6	0						6
	2009	11	1						12
	2010	14	4						18
	Total	31	5						36
Klebsiella spp.	2008	6	0						6
	2009	11	1						12
	2010	14	4						18
	Total	31	5						36
Enterobacter spp.	2008	0	1	0					1
	2009	1	2	1					4
	2010	4	0	0					4
	Total	5	3	1					9
Others	2008	1	0	0		0		0	1
	2009	3	2	3		2		1	11
	2010	3	0	2		0		0	5
	Total	7	2	5		2		1	17
Candida spp.	2008	4	4			0		1	9
	2009	12	5			1		0	18
	2010	5	10			0		0	15
	Total	21	19			1		1	42
Streptococci	2008	3		1				0	4
	2009	2		0				0	2
	2010	2		0				1	3
	Total	7		1				1	9

The analysis of microbial growth according to year indicated a decrease in the growth of *Acinetobacter* spp., cagulase-negative staphylococci (CoNS), *E. coli*, and *S. aureus*. However, the growth of *Candida* and enterococci was increased (p= 0.013).(Figure 1)

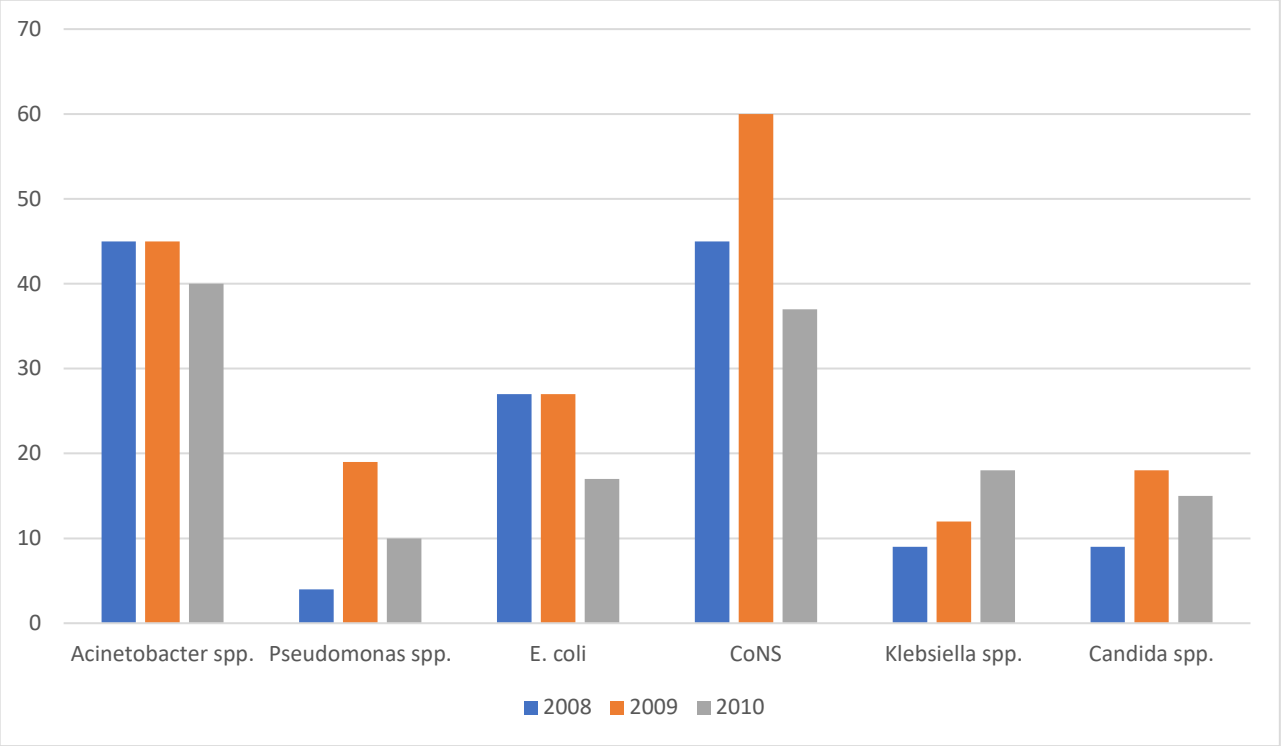

Figure 1. Percentage of microbial growth according to year

Year-wise drug susceptibility analysis revealed an increased amikacin resistance of *Acinetobacter* spp. Colistin susceptibility in 2008, 2009, and 2010 was 100%, 86%, and 96%, respectively. There was a rapid increase in the resistance of *Acinetobacter* spp. to cefoperazone/sulbactam according to year (p=0.016). Although *CoNS* and *S. aureus* remained susceptible to vancomycin, methicillin resistance remained prominent. All *Staphylococci* were susceptible to linezolid. *E. coli* remained susceptible to amikacin, imipenem, and meropenem for the 3 years; however, it showed resistance to ceftazidime and piperacillin–tazobactam. *Pseudomonas* spp. showed increased resistance to carbapenems .

Discussion

This study included patients who were admitted to the Respiratory Intensive Care Unit of Chest Diseases Department, Dicle University Faculty of Medicine, Turkey, between January 2008 and December 2010 and exhibited positive culture results of their samples. In total, 248 patients with 561 culture results were included in the study. Microbial growth was detected in the following samples: blood, 336 (59.9%); deep tracheal aspirate, 104 (18.6%); urine, 89 (15.9%); wound drain, 12 (2.1%); central venous catheter liquid, 7 (1.3%); phlegm, 10 (1.8%); Foley tip liquid, 1 (0.2%); and pleural effusion, and 1 (0.2%). Rapid growth was most frequently noted in the cultures of coagulase-negative staphylococci (25.3%), *Acinetobacter* spp. (23.1%), and *Escherichia coli* (12.6%). The present study revealed microorganisms' resistance profiles similar to those of other relevant studies. The study provides important insights into the selection of empiric antibiotic therapy for patients admitted in intensive care unit.

Owing to the advanced medical technology and intensive care services nowadays, many patients survive despite having previously fatal diseases. The factors that account for infection in Intensive Care Units (ICUs) include severe comorbidities, multiple diseases, complications, immune disorders, type of ICU where the patient is followed up, treatment, and invasive interventions. The patients admitted to ICUs may undergo diagnostic and treatment procedures for improved chances of survival. These procedures can be invasive; some of these procedures include mechanical ventilation, urinary catheterization, intravascular treatment, and cardiovascular monitoring, which increase patients' susceptibility to infections. In addition, the use of antacids, H_2-receptor antagonists, and İmmunosuppressive therapies increase metabolic requirements and total parenteral nutrition provided to avoid malnutrition significantly affect host defenses (5 -6.). Inadequate/compromised defense mechanisms may lead to a rapid host colonization of nosocomial pathogens (5).

HAIs(patients were referred to our hospital after they were hospitalized in another institute; infections occurred during the patients' stay in our respiratory ICU) that are followed up in the ICU manifest in the form of pneumonia,

sepsis, surgical wound infection, and catheter infection. The European Prevalence of Infection in Intensive Care (EPIC) (7.) study reported the distribution of infection in general intensive care by order of frequency, which is as follows: Pneumonia (44.8%), lower respiratory tract infection (17.8%), urinary tract infection (17.6%), bacteremia (12%), and surgical wound infection (6.9%). HAI surveillance report published in the United States (National Nosocomial Infections Surveillance [NNIS] (8) in 1999 stated that the urinary tract infections (31%) were the most prevalent, followed by pneumonia (27%) and primary bloodstream infections (19%). However, very few studies have been conducted in the setting of respiratory ICU (10-11-12). In the present study, the most common causes of infection were pneumonia (49.9%), primary bloodstream infection (19.5%), and COPD (14%). The fact that the most frequent focus of infection was the lower respiratory tract in our ICU is consistent with the findings reported in the relevant literature. As expected, the prevalence of lower respiratory tract infections was higher in the present study than in other studies as the present study was conducted in the respiratory ICU of the chest diseases department.

A Turkish study conducted by Uzun et al. reported that microbial growth was most frequent in the cultures of the respiratory tract samples (45.9%) in a respiratory ICU, followed by in those of blood samples (37.6%) (10-11). Dundar et al. elucidated that the culture samples taken in the ICU that showed the most frequent microorganism growth were obtained from the respiratory system (40%), blood–catheter (23%), urogenital system (15%), and skin-soft tissue samples (14%) (12). In the present study, the distribution of pathogens according to culture samples was as follows: 59.9% in blood samples, 20.4% in respiratory samples, 15.9% in urine samples, and 2.1% in wound drain samples. There may be several reasons associated with the lower rate of respiratory tract samples in total growth. The most important reason is that samples from the lower respiratory tract were not collected from intubated patients because of the well-known restrictions(expectoration of non-intubated patients).

Previous studies that investigated the relationship between age and nosocomial infection risk and mortality reported inconsistent results.(13) Miller and Aube reported a direct proportional relationship between age and mortality (14-15). In the present study, the risk of mortality increased with increasing age ($p<0.05$). There was no significant difference in the duration of hospital stay and mortality of patients between the periods 2008–2009 and 2008–2010 ($p>0.05$). Nevertheless, there was a significant difference in the duration of hospital stay of the patients when considering the 2009–2010 period ($p<0.05$). In 2010, patients stayed for a long duration in the respiratory ICU. As the duration of ICU stay increases, the risk of infection increases and, in turn, infection significantly increases the duration of hospital stay (11 – 16). In a study by Aygen et al., the risk of HAIs increased as the duration of hospital stay in nosocomial infections increased (5). In the present study, the prolonged hospital stay was associated with the risk of HAIs in patients with comorbidities and the incidences of *Acinetobacter* spp., *Pseudomonas* spp., *Klebsiella* spp., and *S. aureus* infections were increased.

Co NS represented the most common pathogen in the present study (40.5%), followed by *Acinetobacter* spp. (17%), *Enterococcus* spp. (9.2%), *E. coli* (8.35%), and *S. aureus* (8.0%). Although the abovementioned results are consistent with those of the US NNIS report, *Acinetobacter* spp. was the second most common microorganism in the present study and grew in blood culture, which was not the case in the NNIS study. The frequency of growth of *Acinetobacter* in blood cultures in the present study was similar to that reported by Cetin et al. The number of *Acinetobacter* growths in blood culture was 336 (59.9%)in our study (17). Trouillet et al. conducted a study on ventilator-associated pneumonia and reported that the frequency of *P. aeruginosa* and *S. aureus* was 15.9% and 21.3%, respectively *P. aeruginosa*, *S. aureus*, *A. baumannii* were isolated at 33.9%, 15.9%, and 12.6% in a study conducted by Rello et al. on pneumonia-associated factors in the ICU (18). Namiduru et al. evaluated patients with ventilator-associated pneumonia (VAP) and identified the causative factors as *P. aeruginosa* (33.9%) in addition to *S. aureus* (30%) and *A. baumannii* (22%) (19). A study by Sevinç et al. reported that *P. aeruginosa* (36%), *Acinetobacter* (22.8%), and *S. aureus* (16.8%) were the most common microorganisms associated with hospital-acquired pneumonia(28%) (20). Cetin et al. reported that the most prevalent microorganism that grew in tracheal aspirate was *A. baumannii*, followed by *P. aeruginosa* and *Enterobacteriaceae* (21). In the present study, the pathogens that grew in the samples from the lower respiratory tract were *Acinetobacter* spp. (48.2%), *Pseudomonas* spp. (13.1%), *E. coli* (10.5%), and *Klebsiella* spp. (10.5%). The most prevalent microorganism was *Acinetobacter* spp., which was the most common cause of the HAIs. These results suggested that the healthcare professionals who were instrumental in patient-to-patient transmission failed to maintain the simplest hand-washing behavior to protect the patients against HAIs.

The antibiotic resistance rates are increasing among pathogens that cause HAIs (22-23-24).

Resistance data are important to inform treatment policies for ICU interventions (6). The most important factor that determines treatment success in HAIs is the timely initiation of adequate and appropriate antimicrobial therapy (24). Inappropriate, frequent, and prolonged use of broad-spectrum antibiotics may lead to an increased number of resistant microorganisms. HAIs caused by resistant gram-negative microorganisms are one of the most important problems encountered in ICUs. Kollef et al. (25).

) reported that a mortality rate of 12.2% based on the use of appropriate antibiotic therapy increased to 52.1% with inappropriate antibiotic use in the ICU(25). *Acinetobacter*

spp. and *Pseudomonas* spp., which are capable of developing MDR, can cause life-threatening infections. Some alternative methods used in the treatment of the abovementioned infections include a high dose of drugs, long-term infusion, and reuse of routine/traditional antibiotics. Colistin (polymyxin E) is one of the routine antibiotics that has been associated with new uses. A Palestinian study reported a high level of colistin resistance of *Acinetobacter* spp. (26). In the present study, the resistance of *Acinetobacter* spp. to amikacin, imipenem, meropenem, ceftazidime, piperacillin–tazobactam, levofloxacin, colistin was 70%, 85.3%, 86.0%, 98.4%, 97.6%, 81.3%, 94.8%, and 40.8%, respectively. In the present study, carbapenem resistance was high for *Acinetobacter* spp. We believe that the reason for this high resistance may be associated with the fact that the patients admitted to our respiratory ICU were chronic patients who were hospitalized in the chest disease or other wards within the past 3 months of study commencement and/or received antibiotic therapy in during this period.

Although NNIS identified *C. albicans* as the most prevalent pathogen in urinary tract infections, Cetin et al. suggested *E. coli*, followed by *Candida spp*. (8 -15). In the present study, the most common pathogens of the urinary tract were *E. coli* (33.7%), *Candida* spp. (21.3%), *Klebsiella* spp. (13.4%), and *Acinetobacter* spp. (12.3%). Year-wise analysis of the microorganisms cultured indicated no significant difference in terms of the sample locations (p>0.05).

The antibiotic resistance rate of *Pseudomonas* has been increasing over the past two decades. In a study by Trouillet et al., the prevalence of resistant *P. aeruginosa* was reported to be 17.7% for imipenem, 27.3% for quinolones, and 26.4% for third-generation cephalosporins (including ceftazidime) (18). The NNIS study reported the prevalence of imipenem-resistant *P. aeruginosa* to be 32% in patients admitted to ICUs. (8). Aksaray et al. stated that imipenem resistance was 52% in their study (27). In the present study, this rate was gradually increasing. Uzun et al. reported the meropenem resistance to be 63.3% and piperacillin–tazobactam resistance to be 83.3%. (10). Although several studies have identified *P. aeruginosa* as one of the most common pathogens of the lower respiratory tract, this microorganism was detected in only 10 tracheal aspirate and 5 phlegm samples, which varied from the findings of relevant studies. In the present study, the resistance against amikacin, carbapenem, ceftazidime, and piperacillin–tazobactam was 25.8%, 56.2%, 59.3%, and 59.3%, respectively. The results of the present study indicated high β-lactam resistance in the *Pseudomonas* strains in the respiratory ICU. The extensive use of penicillin and aminoglycoside is important for resistance development. Beta-lactamase-producing bacteria cannot be killed by antibiotics, and they exist as resistant mutants in the infectious environment. These strains intermingle and spread with the hospital microflora and contribute to the development of HAIs. (17).

The patients in our study who were followed up at the respiratory ICU mostly had chronic diseases, experienced frequent hospitalizations, and received frequent antibiotic therapy; these factors accounted for the aforementioned resistance.

Kim et al. identified *S. aureus* as the most common causative agent of nosocomial infections in the ICU (20.8%) (28). Engin et al. conducted a study on anesthesia in ICU and found that methicillin resistance of *S. aureus* was 51% compared with the resistance of CoNS (69%) (29). According to the US NNIS report, methicillin resistance was reported for 55% of *S. aureus* and 87% of CoNS (8) The EPIC study revealed methicillin resistance to be 50% in *S. aureus* infections in all the countries across Europe (7). However, this rate greatly varied across countries. Several Turkish studies have reported the methicillin resistance of *S. aureus*, including studies that reported a resistance rate of 100%. In the present study, methicillin resistance was 85.7% for *S. aureus* and 94.2% for CoNS. In the present study, the methicillin resistance of *S. aureus* was 88% in 2008 and 71% in 2010. This rate was not statistically significant as there the number of patients with *S. aureus* was inadequate in 2010. This might be because of the uncontrolled reduction in empiric glycopeptide antibiotic therapy in our hospital. Unfortunately, this was not the case with CoNS. This might be because of the fact that growth was not considered contamination and revised appropriate treatments were not implemented considering that CoNS represent a member genus of the skin's normal flora. The vancomycin resistance of *S. aureus* was 8.1% in the present study compared with 3.6% for CoNS. Recent studies have reported low levels of glycopeptide resistance in several cases of infection associated with MRSA (11-30). Although it is good news that vancomycin resistance has not been noted for nearly half a century, a total of seven cases of vancomycin-resistant *S. aureus* have been reported in the United States between 2002 and 2006, suggesting the possibility of losing another important weapon in our battle against the staphylococci (25). Although all staphylococci were susceptible to linezolid in the present study, there exists a recent report on linezolid-resistant staphylococcal strains (31).

A Turkish study reported the antibiotic resistance rates of extended-spectrum beta-lactamase-positive *E. coli* strains as follows: netilmicin (6.6%), piperacillin–tazobactam (14.8%), amikacin (1,6%), and cefoperazone/sulbactam (4,8%) carbapenem(1,7%) (32). In Turkey, ciprofloxacin resistance in *E. coli* 44,2-57.4% (32-33). Another Turkish study conducted in a respiratory ICU setting found that *E. coli* was resistant to ciprofloxacin (83.3%), whereas its resistance to amikacin and meropenem was low at 9.1% (11-16-21).In the present study, the resistance against piperacillin–tazobactam, amikacin, ceftazidime, and carbapenem was 52.8%, 7.4%, 71.6%, and 1.4%, respectively; however, no statistical difference was detected when analyzing according to year. These results suggest that resistant strains of *E. coli* are developing in the respiratory ICU. Most of our

patients had started antibiotic therapy in have resulted from an inappropriate use of antibiotic therapy. Caution must be exercised regarding the use of beta-lactamase and carbapenem to prevent this issue.

Cetin et al. found the antibiotic resistance in *Klebsiella* strains was 60% to ceftazidime, 60% to ceftriaxone, and 6% to ciprofloxacin (17). In *Klebsiella* spp., the susceptibility to aminoglycosides ranges from 33.7% to 44.2% for hospital-derived isolates (26). The antibiotic resistance of *Klebsiella* strains in the present study was as follows: ceftazidime, 89%; imipenem, 19%, meropenem, 13%, and piperacillin, 87.1%. Antibiotic resistance was noted against ciprofloxacin and levofloxacin at the rates of 46% and 36%, respectively. This result is consistent with those of previous studies. However, the present study identified a total of 23 growth during the 3-year period.

Upon antibiogram analysis, the antibiotic therapy was modified or expanded in 47% of the cases where microbial growth was noted in the patient samples. It is a well-established fact that the timely initiation of an effective antibiotic therapy is associated with decreased morbidity, mortality, and hospital-associated financial burden (34-35). Therefore, the initial antibiotic therapy must be introduced considering all relevant patient factors and also the findings of the present study. Investigating the infection risk factors in each hospital and understanding the prominent factors combined with studies investigating such factors and antibiotic susceptibility patterns would ensure that more appropriate, center-specific infection control measures are implemented. This may be possible through the establishment and functioning of an infection control committee.

Conclusion

CoNS (40.5%) represented the most common factor in bloodstream infections. *Acinetobacter* spp. was the most prevalent pathogen found in the respiratory samples and had a high resistance profile. The early initiation of accurate and effective antibiotic therapy positively affects mortality, morbidity, and treatment costs. The study provides important insights into the selection of empirical antibiotic therapy in the respiratory ICU of our hospital.

The present study was designed as a retrospective study, which represents a limitation of this study because of the fact that the same number of antibiograms was not always available for all positive cultures.

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