An Overall View on Nosocomial Infections in an Intensive Care Unit

Yoğun Bakım Ünitesinde Hastane Enfeksiyonlarına Kapsamlı Bir Bakış

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ABSTRACT Objective: The purpose of this study was to determine the pathogenic agents in nosocomial infections and measure their antimicrobial sensitivity in the intensive care unit. **Material and Methods:** Between January and October 2007, 250 patients were examined in the intensive care unit of the 1st Internal Medicine Department of Atatürk Training and Research Hospital, which was opened in January 2007. Active and prospective surveillance method based on laboratory data and patients' diagnosis was used for 95 of these patients with hospital-acquired infections. **Results:** During the study period, 137 infection episodes were determined in 95 patients with a diagnosis of nosocomial infections according to the criteria of Centers for Disease Control (CDC). The infection rate was 38%. Urinary tract infection was the most common infection followed by pneumonia and bacteremia. All patients with urinary tract infection had urinary catheterization, 42.5% of the patients with pneumonia had mechanical ventilation and 68.4% with primary bacteremia had central intravenous catheterization. In these infections, 59.1% of the isolated pathogens were gram-negative bacilli, 38.6% were gram-positive bacteria and the remaining 2.1% were *Candida spp. Escherichia coli, S. aureus, P. aeruginosa* and coagulase-negative staphylococci were the most common pathogens identified. In urinary tract infections *E. coli* and in pneumonia and bacteremia *S. aureus* was the most common responsible pathogen. Among the gram-positive bacteria and gram-negative bacilli, high antimicrobial resistance was observed. Resistance to teicoplanin was 14.6% and linezolid was 11.1%, in *S. aureus*, whereas resistance to ciprofloxacin was 88.8% and vancomycin was 11.1% in *Enterococcus spp.* Imipenem was determined as the most effective agent against the isolated gram-negative bacteria, followed by cefepime, however, 16.6% of the *Acinetobacter spp.* and 17.6% of the *P. aeruginosa* were resistant to imipenem. **Conclusion:** In order to prevent or reduce the nosocomial infections, surveillance methods must be carried out in intensive care units and in the entire hospital.

Key Words: Intensive care units; cross infection; anti-bacterial agents

ÖZET Amaç: Bu çalışmada, yoğun bakım ünitemizdeki nozokomiyal enfeksiyonların patojen tiplerini belirlemek ve antibiyotik duyarlılıklarını ölçmek amaçlandı. **Gereç ve Yöntemler:** Atatürk Eğitim ve Araştırma Hastanesi'nin Ocak 2007 tarihinde hizmete açılan 1. Dahiliye Kliniği Yoğun Bakım Ünitesinde, Ocak-Ekim 2007 tarihleri arasında toplam 250 hasta takip edildi. Bu hastalardan hastane enfeksiyonu tanısı alan 95 hasta için aktif, ileriye dönük, hasta ve laboratuar bulgularına dayalı sürveyans metodu kullanıldı. **Bulgular:** Çalışma sürecinde Hastalık Kontrol ve Önleme Merkezi (CDC) kriterlerine uygun olarak nozokomiyal enfeksiyon teşhisi konulan 95 hastada 137 enfeksiyon atağı tespit edildi. Enfeksiyon oranı %38 olarak bulundu. Üriner sistem enfeksiyonu en sık görülen enfeksiyon iken, bunu pnömoni ve bakteriyemi takip etti. Üriner sistem enfeksiyonu saptanan hastaların %100'ünde üriner kateterizasyon, pnömoni saptanan hastaların %42.5'inde mekanik ventilasyon ve primer bakteriyemi saptanan hastaların %68.4'ünde santral venöz kateter kullanımı vardı. Bu enfeksiyonlardan izole edilen patojenlerin %59.1'i gram negatif basil, %38.6'sı gram pozitif bakteri ve %2.1'i kandida türü mantarlardı. En sık *Escherichia coli*, *Staphylococcus aureus, Pseudomonas aeruginosa* ve koagülaz negatif stafilokoklar tespit edildi. Üriner sistem enfeksiyonlarında *E.coli*; pnömoni ve bakteriyemide *S. aureus* en sık gözlenen sorumlu patojenlerdi. Hem gram pozitif hem de gram negatif bakterilerde yüksek oranda antibiyotik direnci saptandı. *S. aureus*'ların %14.2'sinde teikoplanine ve %11.1'inde linezolide, *Enterococcus* türlerinin %88.8'inde siprofloksasine ve %11'inde vankomisine direnç saptandı. İzole edilen gram negatif bakterilere karşı imipenem ve sefepim en etkin ajanlar olarak tespit edildi, ancak *Acinetobacter* suşlarının %16.6'sı ve *P. aeruginosa* suşlarının %17.6'sı imipeneme dirençliydi. **Sonuç:** Hastane enfeksiyonlarını önlemek ya da azaltmak amacıyla başta yoğun bakımlar olmak üzere tüm hastane bünyesinde sürveyans çalışmalarına yer verilmelidir.

Anahtar Kelimeler: Yoğun bakım üniteleri; çapraz enfeksiyon; antibakteriyel ajanlar

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Although nosocomial infections can be seen in every unit of a hospital, they are more common in intensive care units and they cause higher morbidity and mortality. Usually pneumonia is the most common infection and urinary tract and other infections follow it.

The purpose of this study is to determine the pathogenic agents of nosocomial infections and measure their antibiotic sensitivity in our intensive care unit patients.

Hospital-acquired infections are defined as diseases that are not in the incubation stage at the time of admission and appear after 48-72 hours of hospital stay or infections which begin in hospital, but become visible after discharge.[1,2]

Hospital-acquired infections are crucial problems in our country as in the rest of the world. The incidence ranges between 5-15%.[2,3] Besides causing increased mortality and morbidity, hospital-acquired infections cause prolongation of hospital stay and increase in treatment costs.[4,5] In the USA, a new infection arises in almost 5% of the inpatients, and every year, about 2 million new nosocomial infections are reported that lead to additional 2 billion USD treatment cost.[6]

Hospital-acquired infections are seen at various rates in all units of the hospitals with higher rates in patients staying in the intensive care units. Although these patients constitute 10-15% of all the inpatients, 25% of all hospital-acquired infections as well as 45% of all nosocomial pneumonia and bacteremias are observed in intensive care units.[7,8] Invasive diagnostic and therapeutic procedures, impairment of host defense due to underlying disease, inappropriate antibiotic use and the type of intensive care unit are the influential factors in nosocomial infections at varying degrees.[8]

Although infection rates differ with respect to the type of the intensive care unit, pulmonary and urinary system infections are the most common infections, and others follow them.[9-11] The frequency of microorganisms causing hospital-acquired infections and their sensitivity to antibiotics alter between hospitals and among different units of the same hospital. Besides, some differences occur within the same hospital over time. Factors responsible for hospital-acquired infections show different characteristics such as outer factors, and resistance to these factors develops more quickly. As a result, multiple resistant bacteria are more frequently observed within the hospital. In the future, an increase in hospital-acquired infections is expected.[12,13]

In 1958, American Hospital Association (AHA) declared the necessity of establishing a "Hospital Infection Control Committee" in each hospital in order to minimize the nosocomial infections.[14] A training program for infection control nurses was developed by Centers for Disease Control (CDC) with consequent Comprehensive Hospital Infections Project (CHIP) and National Nosocomial Infections Study (NNIS) in which the basic concepts were determined, the significance of nosocomial infections was described and the positions of "Hospital Epidemiologist" and "Infection Control Nurse" were clarified.[14] In the project of Study on the Efficacy of Nosocomial Infection Control (SENIC) developed by CDC, the importance of surveillance was approved, and nosocomial infections were reported 32% less in hospitals using an active surveillance program compared with the hospitals not using such a program.[15]

Likewise, such activities started in the leadership of Hacettepe University Medical Faculty in our country in 1984 and others followed it.[16]

In this study, we investigated the hospital-acquired infections in patients admitted to our intensive care unit with different underlying diseases, infection types with related pathogens, antibiotic sensitivity/resistance and the risk factors facilitating these infections. Our aim was to contribute, firstly to the proper use of empiric antibiotic therapy by determining the most frequent pathogens in our intensive care unit, secondly to antibiotic resistance to be able to bring recommendations on decreasing the occurrence of resistant microorganisms by preventing unnecessary antibiotic usage, and thirdly to draw attention to the frequency and significance of intensive care unit hospital-acquired infection rates.

MATERIAL AND METHODS

PATIENTS

In this study, 250 intensive care unit patients of internal medicine with different underlying diseases were investigated prospectively for nosocomial infections by surveillance. The intensive care unit was opened in January 2007, included 10 beds and was fully equipped. The follow-up period was between January and the end of October, in 2007.

Patients who had infections developed after 48 hours of admission to intensive care unit and patients who had an infection that was developed in a focus other than the primary infection focus with a different agent were considered to have nosocomial infections and included in the study. Patients with signs of infection at admission or infections which existed before admission but became apparent later were considered as primary infections and were not included in the study. Additionally, patients in whom nosocomial infections were detected, but the pathogenic agents were not identified in clinical materials, were not included.

STUDY PROTOCOL

The study was performed by active and prospective surveillance according to patients' diagnosis and laboratory data.[17] Nosocomial infections were identified by CDC criteria.[18]

In the surveillance form, patient's name and surname, protocol number, age, gender, social insurance, occupation, address, cause of admission, starting date of infection, focus of infection, growing pathogen microorganism(s), type of infection, therapy started on empirical basis, culture(s), antibiotic regimen(s) after culture results, infection duration, interventions, duration of intensive care unit stay and final status of the patient at the end of treatment were recorded. Written informed consent was obtained from all participants.

Specimens from patients with nosocomial infection were obtained each time the body temperature was at or above 38°C. According to the culture results of the specimens, pathogenic microorganism(s) and the type of infection was assessed for each patient. The majority of the specimens were obtained from at least two sources simultaneously, such as; blood and urine, blood and sputum, urine and sputum or blood, urine and sputum etc. If the same bacteria was isolated from different specimens in the same patient at one time, it was considered as "only one bacteria to be isolated", if two different bacteria were isolated from different specimens then it was considered as "two different bacteria isolated" from the same patient. If the same bacteria was isolated from the same source of the specimen in the same patient for a second time, it was not taken into consideration.

Specimens were collected and transported as appropriate. Culture techniques and identification of microorganisms from specimens sent for microscopy and culture were performed in microbiology laboratory by a microbiologist blinded to the study. Blood and Eosin Methylene Blue (EMB) agar, and if indicated anaerobic culture media, were used for the culture of clinical materials such as urine, sputum (obtained by deep tracheal aspiration if the patient was unable to give himself or herself), abscess, wound material, cerebrospinal fluid (CSF), faeces, pleural effusion, peritoneal ascites and intravessel catheter materials. Bactec Plus Aerobic/F was used for blood culture. Sabouraud-dextrose agar was used for fungal culture.

For blood cultures, 10 ml blood was obtained into hemoculture bottles Bactec Plus Aerobic/F with resin as appropriate, then they were inoculated in BACTEC 9120 system for one week and passages to blood and EMB agar were provided from the positive ones.

Antibiotic sensitivities of the bacteria (MIC values) were tested by Sceptor system (Becton Dickinson and Company, USA). In this system different panels were used for different bacteria. In each of the panel used, sensitivities of different bacteria to different antibiotics were evaluated.

STATISTICAL ANALYSIS

Statistical analysis were performed by SPSS for Windows, 10.0. Data were expressed as mean ± SD for numerical variables and numbers and percentages (%) for categorical variables.

RESULTS

Among the 250 patients admitted to the 1st Internal Medicine Department ICU between January and October 2007, hospital-acquired infections were diagnosed in 95 (38%) patients according to the CDC criteria.

Of the 250 patients included in the study, 156 (62.4%) were males, 94 (37.6%) were females and the mean age was 65.1 ± 15.8 years. Social insurance was present in 95.6% of the patients. Sixty eight percent of the cases were living in the urban areas and 32% in the rural areas. Demographic and social characteristics of the patients are presented in Table 1.

The most frequent causes of admission to intensive care unit were; gastrointestinal bleeding 30 (12.0%), congestive heart failure 30 (12.0%), chronic renal failure 24 (9.6%), acute renal failure 22 (8.8%), septicemia 22 (8.8%), pneumonia 18 (7.2%), diabetes mellitus 17 (6.8%), general status disorder 17 (6.8%), chronic obstructive pulmonary disease 11 (4.4%), systemic inflammatory response syndrome 9 (3.6%), hepatic coma 8 (3.2%), coronary artery disease 6 (2.4%), acute pancreatitis 5 (2.0%) and malignancy 4 (1.6%) and the least frequent were urosepsis 3 (1.2%) and acute cholecystitis 3 (1.2%).

More than one facilitating risk factors were present in most of the patients. Interventional procedures were performed to 235 patients in the ICU. The most frequent interventions were urinary catheterization (93.2%), mechanical ventilation (30.4%), and central venous catheterization (27.6%). Hemodialysis was performed in 24 (9.6%) patients and peritoneal dialysis in 10 (4%).

Of 95 patients, hospital-acquired infection developed after 48 hours in 46 (48.4%) patients and 72 hours in 49 (51.6%) patients following their admission to the intensive care unit. One hundred and thirty four hospital-acquired infection attacks were observed in these 95 patients. In 64 patients one nosocomial infection developed, in 29 patients two and in 4 patients three infections occurred.

TABLE 1: Distribution of demographic and social characteristics of the patients.

Characteristics	Patients, n	Patients, %
Age, years		
10-19	2	0.8
20-29	8	3.2
30-39	12	4.8
40-49	21	8.4
50-59	34	13.6
60-69	50	20.0
70-79	84	33.6
80-89	36	14.4
90+	3	1.2
Gender		
Male	156	62.4
Female	94	37.6
Social insurance		
Present	239	95.6
None	11	4.4
Localization		
Urban	170	68.0
Rural	80	32.0
Occupation		
Retired	99	39.6
Housewife	72	28.8
Employed	36	14.4
None	43	17.2

Forty-three (32%) were urinary tract infection, 39 (29.1%) were pneumonia, 37 (27.6%) were bacteremia, 7 (5.2%) were nosocomial wound infection, 4 (2.9%) were surgical wound infection and 4 (2.9%) were peritonitis (Figure 1). We observed that the number of the attacks were correlated with the duration of stay in the ICU. The mean duration of ICU stay was 8.1±6.7 (min 2, max 60) days.

In the study, 137 pathogenic microorganisms were isolated from the cultures of the patients. In 63 of these cultures a single pathogen, in 25, two pathogens and in eight, three different pathogens were isolated. Of the pathogens isolated, 81 (59.1%) were gram negative bacteria, 53 (38.7%) were gram positive bacteria and 3 (2.2%) were mycoses caused by Candida.

Of the gram positive bacteria isolated, 27 (19.7%) were *Staphylococcus aureus*, 13 (9.4%) were coagulase negative *Staphylococci* (CNS), nine (6.5%) were *Enterococci*, two (1.4%) were *Streptococci* and one (0.7%) was *Kytococcus sedentari-*

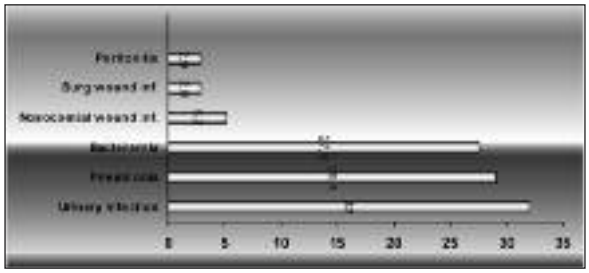

FIGURE 1: Infection types and rates of our patients with the hospital-acquired infections.

us. Eighteen of the *S. aureus* (66.6%) were methicillin-resistant (MRSA), while nine (33.3%) were methicillin-sensitive (MSSA).

Enterobacteriaceae was the most common isolated group in gram negative bacteria (n=43, 31.3%) with *E. coli* (n=30, 21.8%), *K. pneumonia* (n=11, 8%) and *Enterobacter* spp. (n=2, 1.4%), followed by other non-fermentative gram negative bacteria; *P. aeruginosa* (n=22, 16%), *A. baumanii* (n=12, 8.7%), *Flavimonas Oryzihabitans* (n= 2, 1.4%) and *Stenotrophomonas maltophilia* (n=2, 1.4%) (Figure 2).

Frequencies of the isolated microorganisms differed according to the type of the infection.

In urinary infections, *E. coli* (48.8%), *Pseudomonas* spp (23.2%), *candida* (2.2%), *Klebsiella* spp., coagulase negative *Staphylococci*, *S. aureus, Acinetobacter spp.* and *Enterococci spp.* were the most frequently isolated microorganisms, in frequency order. In primary bacteremia, *S. aureus* (27%) and coagulase negative *Staphylococci* (24.3%) were the most common and *Klebsiella spp.*, *E. coli*, *Acinetobacter spp.*, *Enterococci,* and *Flavimonas Oryzihabitans* were the other isolated microorganisms, respectively.

In pneumonia, *S. aureus* (33.3%), *P. aeruginosa* (17.9%) and *Acinetobacter spp.* (15.3%) were the most frequently isolated microorganisms followed by *E. coli spp., Klebsiella spp.,* coagulase negative *Staphylococcus, S. pneumonia and S. maltophilia*, respectively.

In surgical wound infections, one *S. aureus*, two *Enterococcus spp.,* and one *Pseudomonas spp.* and in nosocomial wound infections, two *Pseudomonas spp.,* one *Acinetobacter spp.*, one *S. aureus*, one *Enterococcus,* one *E. coli*, and one *Kytococcus oryzihabitans* were isolated.

Peritonitis was diagnosed in two patients with renal failure who had peritoneal dialysis and in two patients with chronic liver disease in whom ascites was drained several times. *E. coli* and *E. fecalis* were isolated in peritoneal dialysis patients and *K. pneumonia* and *E. fecalis* were isolated in patients with ascites.

Antibiotics were given to patients with primary infections at their admission to the ICU and to patients with nosocomial infections during their stay in the ICU; initially empirical antibiotics were administered. Incase the antibiotic regimen must be used more than three days, then we would have to get the approval of the infectious disease specialist must be obtained. Except 60 patients admitted to the ICU with primary infections, antibiotic therapy was started in 183 (73.2%) of the 250 patients on empirical basis. Among these 183 patients, the most preferred three empirical antibiotics were; ceftriaxone in 74 (40.4%) patients, ciprofloxacin in 36 (19.7%) and cefuroxime axetil in 28 (15.3%) patients, and the most preferred three antibiotics during recommended by the infectious disease specialist were; ceftriaxone in 46 (25.1%) patients, cefoperazone/sulbactam in 27 (14.7%) and ciprofloxacin in 25 (13.6%) patients, respectively. We found that, in 114 (62.3%) of these 183 patients there was inappropriate antibiotic usage and in 35 (30.7%) of these 114 patients unnecessary antibiotics were used. Since bacterial growth was ob-

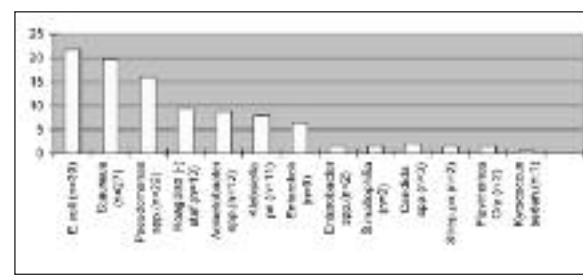

FIGURE 2: Frequencies of the hospital-acquired infection pathogens isolated in our ICU.

served in only 95 of 183 (54%) patients in cultures, 88 patients had used antibiotics in spite of no growth in culture and in 35 (36.8%) of 95 patients with hospital-acquired infections, inappropriate antibiotics were used.

In methicillin resistant *S. aureus* strains isolated in the ICU, sensitivity to vancomycin was almost 100% while sensitivity to trimethoprim-sulfamethoxazole was 71.5%. Seventy percent of the coagulase negative *Staphylococci* (CNS) isolated in the ICU were methicillin resistant. All CNS strains were sensitive to vancomycin and 92.5% were sensitive to teicoplanin, linezolid and oxacillin.

Of the *Enterococcus* species isolated in the ICU, 66.6% were resistant to ciprofloxacin, penicillin and gentamicin. Other antibiotics with low resistance rates were teicoplanin (20%), ceftriaxone (25%), piperacillin/tazobactam (25%), cefaperasone (25%) and aztreonam (25%). Of the pathogens causing a urinary tract infection, 55.5% were sensitive to ceftriaxone and teicoplanin.

Acinetobacter strains isolated in the ICU were sensitive to imipenem (83.4%) and amikacin (72.8%) the most and resistant to aztreonam (77.7%) and ceftazidime (50%) mostly.

Pseudomonas strains isolated in the ICU were most sensitive to cefepime (85%), imipenem (82.4%) and amikacin (82.4%) and were most resistant to ceftriaxone (85.7%) and ceftazidime (83.3%). Aztreonam and ceftriaxone were the antibiotics to which *S. maltophili* showed the highest resistance with 100%.

Of 250 patients followed up during the study, 124 (49.6%) completely recovered, 46 (18.4%) partially recovered and 80 (32%) died during hospital stay. In 45 (56.2%) of the patients who died, nosocomial infections were diagnosed. The most frequent mortality causes were; nosocomial pneumonia (n=23, 51.1%) and septicemia (n=18, 40%).

DISCUSSION

Nosocomial infections affect 5-15% of the inpatients.[4] In intensive care units broad-spectrum antibiotics are commonly used and cross infections and contaminations are seen more frequently in the ICUs than in the other units of the hospital. As a result, frequency of nosocomial infections in the ICUs is 5 to10 times more compared to the other units.[19,20]

In our country, especially in the last 10 years, surveillance and control programs on the prevention and control of nosocomial infections are put into practice in many hospitals, to determine the extent of the infections and to take necessary precautions.[21]

Surveillance can be done in active or passive, patient-based or laboratory-based, prospective or retrospective ways. In passive or only laboratory-based surveillance, the frequency of infections is found lower and it is less reliable. However, laboratory and patient-based active surveillance is a more sensitive method. Although it is reliable, the fact that the person performing the surveillance has to spare most of his/her day for this work, and this is a disadvantage.[17]

It is reported that hospital-acquired infections in the ICUs are observed between 5.3% and 64.6% in our country.[13,22] Our rate was 38% for ten months. If we consider the fact that our ICU is newly established, the rate will get higher.

A multi-center study performed between 1992 and 1998 in 205 ICUs of 152 hospitals in the USA reported hospital-acquired infection rate as 6.1%, while another study performed in the 1417 ICUs in 17 European countries reported this rate as 20.6%.[11,23] In the European Prevalence of Infections in Intensive Care (EPIC) study, the infection rate was 24.7%.[24]

In a study performed in the Ankara University Ibn-i Sina Hospital between 1992 and 1998, hospital-acquired infection rate was found approximately 4% and did not change by years, however, the rate of hospital-acquired infections in the reanimation unit changed between 30 and 64.6% in seven years.[21]

Atatürk University Medical Faculty reported a hospital-acquired infection rate of 4.2% in 27017 patients. The highest infection rates were in the re-

animation unit with 39.5% and in the internal medicine ICU with 9.1%.[25]

In Akdeniz University Medical Faculty Hospital, nosocomial infection rates changed between 1.6% and 47.4% with the highest rates in the reanimation unit 1 (44.7%), unit 2 (%44.6) and internal medicine ICU (17.8%).[26]

In our study, the infection rate in our internal medicine ICU was 38% and in accordance with national and foreign studies. The reason of higher infection rate compared to the other units may be explained by the additional contributing factors to infection development; the majority of patients were in need of pulmonary support, more invasive procedures were applied and worse general status of the patients followed in this unit.

The most frequent nosocomial infections in the ICUs are generally pneumonia and urinary tract infection.[11,23] Richards et al. reported that 86% of the nosocomial pneumonias were related to mechanical ventilation, 87% of the primary bacteremia were related to venous catheterization and 95-97% of the urinary tract infections were related to urinary catheterization with generally used open systems. It was reported that in open end catheters bacteriuria developed in less than 4 days, while in closed system catheterization it was delayed until 30 days.[23] In different studies performed in the ICUs of our country, incidence of nosocomial pneumonia was reported between 6 and 50%.[27,28]

In our study we found that the rates of urinary tract infection was 32%, pneumonia was 29.1% and bacteremia was 27.6% in the ICU. Mechanical ventilation was performed in 42.5% of the patients with pneumonia, central venous catheter was present in 68.4% of the patients with bacteremia and arterial catheter was present in 14 patients (36.8%). Our surgical wound infection rates (2.9%) were similar with Spencer et al. (8%) and Richards et al. (3%).[11,23]

In 2004, Ege University Medical Faculty concluded that in 29 of the138 patients in the ICU 38 infection attacks developed (21%) and the majority were bacteremia (9.14%), pneumonia (6.5%) followed by urinary tract infections (3.6%).[29] In another study performed in the ICU of GATA Medical Faculty in 2004, bacteremia was the most common infection with a rate of 31.7%.[30]

The distribution of infectious agents causing-hospital-acquired vary among hospitals and even among the units of the same hospital.[11] In the last 20 years, there have been great changes in the responsible microorganisms of ICU infections and the sensitivity status of these pathogens. Gram negative bacilli were reported as the most important pathogens in 1960 and 70s, however, with the introduction of broad-spectrum cephalosporins and increase in the interventions, a shift occurred towards gram positive microorganisms. In the EPIC study, authors reported that gram positive and negative agents were equally isolated in ICU infections, and *S. aureus* (30%) and *P. aeruginosa* (29%) were the most commonly isolated agents.[22] In Turkey, the recent studies showed that the distribution of isolated bacteria from ICU infections was comparable with the distribution in the EPIC study. In our country the most common isolated nosocomial pathogens in ICU infections were *S. aureus* (19.7-37.6%), *P. aeruginosa* (17.3-32%) followed by *E. coli, Klebsiella* spp., *Acinetobacter* spp. and CNS in varying rates.[4,13]

In multi-center trials performed in Europe, the most common isolated pathogens were *S. aureus* (11.8 and 30.1%), *P. aeruginosa* (11 and 28.7%), *Enterobacteriaceae spp.* (34.4%), coagulase negative *Staphylococci* (10.5 and 19.1%), fungi (7 and 17.1%) and *Enterococci* (8.4 and 11.7%), respectively.[11,31,32]

In our study, 59.1% of the isolated pathogens were gram negative aerobic bacteria, 38.6% were gram positive aerobic bacteria and 2.1% were *Candida spp.* Most commonly isolated gram positive bacteria were *S. aureus* (19.7%) and CNS (9.4%); gram negative bacteria were *Pseudomonas spp.* (16%), *Acinetobacter spp.* (8.7%), while the most common enterobacteriaceae was *E. coli* (21.7%) and *Klebsiella spp.* (8%). Our findings are consistent with the findings reported in the USA,[23] Europe[24] and previously in our country.

Most commonly isolated pathogens in nosocomial urinary tract infections in the ICUs were *Candida spp., E. coli, Enterococci* and *P. aeruginosa*.[11,23] In a study performed by Akdeniz University Medical Faculty, *Candida* was the first pathogen in urinary tract infections and *E. coli, Klebsiella spp.* and *Pseudomonas spp.* followed it.[33] In our study *E. coli* (48.8%), *Pseudomonas spp.* (23.2%), *Candida, Enterococcus spp., Klebsiella spp.* and *S. aureus* were the most commonly isolated pathogens in urinary tract infections, in rank order.

S. aureus and *P. aeruginosa* are the primary responsible pathogens in nosocomial pneumonias in the ICUs.[11,23] *Enterobacter spp.*, *K. pneumoniae*, fungi and *Acinetobacter spp.* follow them. Viruses are reported in only 0.2% of the cases.[23] Similarly, *S. aureus* with 33.3% and *Pseudomonas spp.* with 17.9% were the most commonly isolated microorganisms followed by *Acinetobacter spp.*, *E. coli* and *Klebsiella spp.* in nosocomial pneumonias in our study.

Nosocomial wound infection agent *Kytococcus sedentarius* is a gram-positive bacteria and mostly isolated from diabetic foot wounds. In our study, its rate was 0.7%, and though sensitive to many antibiotics, it was resistant to erythromycin 100%.

In primary bacteremia, the most common responsible pathogens are coagulase negative *Staphylococci, S. aureus* and less often *Enterococci* and *Candida spp.* It was reported that gram negative aerobic bacteria was less often isolated.[23] In a multi-center study in Europe, isolation rate of *Acinetobacter spp.* was 8%.[32] In our study, the rates were as follows; *S. aureus* was 27%, CNS was 24.3%, *Klebsiella spp.* were 13.5%, *Acinetobacter* spp. were 8.1% and *Flavimonas oryzihabitans* was 1.4%.

Except for urinary tract infections, our results on the bacteria isolated from nosocomial infections were similar to the results of the multi-center studies. For the urinary tract infections, though bacteria and fungi species were similar, the rates were different.

The most important problem is antibiotic resistance for many pathogens responsible for nosocomial infections isolated in ICUs and increased resistance in time. Colonization of the resistant strains and cross contamination caused by the hospital staff complicates the problem. Antibiotic resistance is a significant issue for both gram positive and gram negative bacteria.[34]

In particular, methicillin resistance in *S. aureus* strains among the whole gram positive bacteria and natural resistance to many antibiotics as well as resistance to aminoglycosides and vancomycin in *Enterococcus* strains have been reported in the recent years, and they are gradually increasing in the ICUs.[34]

Resistance to methicillin in *S. aureus* strains in the Mediterranean countries has a higher incidence compared to the incidence in the European and American countries. Saltoglu et al. reported the resistance to methicillin as 90% in *S. aureus* strains in the ICUs.[13] In the ICU of Akdeniz University Medical Faculty, resistance to methicillin was 78% in overall *Staphylococci* origins, 80.7% in *S. aureus* and 64.7% in CNS.[33] In a multi-center study performed in Europe, 272 (59.6%) of the 456 *S. aureus* strains detected in ICUs were resistant to methicillin and the rate changed between 0% for the Northern Europe and 80% for Italy and France. In the EPIC study, 60% of all *S. aureus* infections were related with MRSA strains. According to National Nosocomial Infections Surveillance (NNIS) data, resistance to methicillin was 55% in *S.aureus* and 87% in CNS.[31,35]

Vancomycin was found to be effective in all strains of *Staphylococci*. Another antibiotic to which MRSAs were sensitive was trimethoprim-sulfamethoxazole with 75 and 76%, however, a high resistance to ciprofloxacin, amikacin and gentamicin was detected.[13]

In our study, we detected that the isolated *S. aureus* strains had 94.8% sensitivity to vancomycin, 88.9% to linezolid, 85.8% to teicoplanin and 100% resistance to methicillin and 92% to oxacillin. Although reported in the literature, vancomycin-resistant *Staphylococci* have not been reported

in Turkey, but teicoplanin-resistant *S. aureus* strains have been described.[36]

In our study, all of the CNS were sensitive to vancomycin with 100%, though resistance to teicoplanin was 7.6%, methicillin was 76.9%, ceftriaxone was 85.7%, penicillin was 83.3% and trimethoprim-sulfametaxasole was 80%. We may say that the high resistance rates are due to inappropriate and excessive use of antibiotics. In a multi-center study in Europe, among 279 CNS isolated 70.1% were resistant to methicillin, 9.3% to teicoplanin and 3.5% to vancomycin.[24]

The rates of vancomycin-resistant *Enterococci* (VRE) infections reported in National Nosocomial Infections Surveillance related to CDC was %0.4 in 1989 and 13.6% in 1993 with a 34-fold increase. In many of the study centers, 90-96% of *Enterococci* were found sensitive to nitrofurantoin and it was used successfully in the treatment of urinary tract infections.[35]

In Turkey, the first vancomycin-resistant *E. faecium* strain was reported in the Akdeniz University in 1998 and others followed it.[33] Excessive use of antibiotics in our hospitals suggests that nosocomial VRE infections will become an important problem in the near future. In our study, resistance to vancomycin was 11.1% in *E. fecalis* of the *enterococci spp.* In *Enterococci spp.,* resistance to ciprofloxacin was 88.8% and penicillin was 77.7%.

In another multi-center study in Turkey, *P. aeruginosa*, *Acinetobacter* spp., *E. coli* and *Klebsiella spp.* were the most commonly isolated aerobic gram negative bacteria with 74.6% sensitivity to imipenem. There was relative sensitivity to amikacin and ciprofloxacin approximately 40% was detected to these antibiotics.[22] In our study, resistance to amikacin and ciprofloxacin was 29.4% and 33.3% for *Pseudomonas spp.* and 36.3% and 33.3% for the following microorganisms. Imipenem and piperacillin/tazobactam were the most effective antibiotics for *P. aeruginosa* while the overall sensitivity to cefepime, ceftazidime and ciprofloxacin were 43%.

In Belgium, a study between 1996 and 1999 revealed that, gram negative isolates from ICU infections were mostly sensitive to ciprofloxacin, amikacin, gentamicin and imipenem, but were less sensitive to ceftriaxone and amoxicilin/clavulanate.[37] In the same study, the most sensitive antibiotic to *Klebsiella spp.* was imipenem with 94%. In our study, resistance to imipenem was 10% and ciprofloxacin 22.2% for *Klebsiella spp.*, and 7.1% and 26.9% for *E. coli*, respectively.

It is reported that the most sensitive antibiotic to *Acinetobacter spp.* is imipenem, but 44.5% resistance is present even to this antibiotic. In our study, resistance to imipenem was 16.6%, cefepime and teicoplanin were 30% for *Acinetobacter spp..* In the Akdeniz University ICU, ceftazidime resistance was 62%, cefepime 51% and imipenem 39% for *Pseudomonas spp.*, ceftazidime resistance was 88%, cefepime 78% and amikacin 80% for *Acinetobacter spp.* and ceftazidime resistance was 62%, and imipenem resistance was 3% for *Klebsiella spp.*[26]

For acquired infections in ICUs, the most important factors on the etiology are inappropriate use of antibiotics, invasive procedures, cross-contamination and duration of stay in the ICU.

The inappropriate use of antimicrobial agents is a common worldwide problem. It was reported that about 30% of the patients staying in hospitals were using antibiotics and 25 to 65% of antibiotic use was inappropriate. In Akdeniz University Hospital, inappropriate use of antibiotics was 43%[26] and in our study, inappropriate use of antibiotics was 36.8%. Multiple antibiotic resistance in gram negative bacteria (*Enterobacter spp., P. aeruginosa, K. pneumoniae* and *Acinetobacter spp.*) cause treatment problems that are often challenging in ICUs. These pathogenic microorganisms induce serious infections and increase mortality.[38] Antibiotic policies are particularly important for ICUs which use more antibiotics compared to other units. Both for gram negative and positive bacteria, a close association has been noticed between previous antibiotic use and resistance development. Precautions for using the antibiotics in efficient amounts and in an

alternative manner may delay development of higher resistance rates. In the ICUs, antibiotic usage requires a multidisciplinary approach. In our unit, we are now in touch with the infection control committee more frequently than in the past to avoid inappropriate and extensive use of broad-spectrum antibiotics.

There are many studies reporting that invasive interventions like urinary and venous catheterization and mechanical ventilation increase the risk of infections. In urinary catheterization, the most common route of bacterial entry is the space between catheter outer surface and urethral mucosa. To prevent this risk, closed drainage sets should be used and care should be taken not to deteriorate the system integrity.[9,10] In our unit, we take utmost care while opening the catheter drainage tube junction, removing the urine collection and during irrigation. The related risk of sepsis with central venous catheters is between 3 and 5% and is fairly high compared to peripheral catheters. Colonization and contamination around the entry regions are important for infection development. In central venous catheterization, infection risk is higher in femoral regions than in jugular or subclavian regions.[9,10] However, in our unit, we still use the femoral route for catheterization since it is easier and quicker to find the vessel than the other routes.

As mentioned in many other studies, the hands of all staff responsible in patient care are the most important factors in disseminating microorganisms from a patient to another. It should be noted that, during patient care and between the care of two patients, hand washing with a hygienic soap and water and using gloves if necessary are the most important factors for infection control. In studies and as in our unit, incompliance of healthcare staff to hand washing protocols is considered to be associated with lack of knowledge and motivation. Workload and deficiency in hand washing and drying equipments aggravate the problem.[20] In ICUs, existence of long staying patients, close contact with caring personnel, neglecting precautions for infection control and hand washing and microorganisms resistant to external environment facilitate the cross-contamination.[10]

As the duration of stay in ICU gets longer, the infection risk gets higher. The rate of infection increases 3-fold by staying three and 4 fould by staying 4 days in the ICU than staying one two days; and 33-fold by staying 21 days. Besides, with long duration of stay, colonization and infection risk with resistant bacteria gets high. Although stay durations according to infection types were not calculated, the duration of stay in patients with infection was found 9.85±6.99 days longer than the patients without infection in the ICU in our study.

The mortality rates in patients with infection in ICUs are between 15 and 25%. The most important mortality causes are nosocomial pneumonia and sepsis. In 2004, the mortality rate was 24.1% in patients with infection and 22% in patients without infection in the Internal Medicine ICU of Ege University. The most important mortality causes were pneumonia (48%) and sepsis (42%) (29). In our study, overall mortality rate was 32% (80 out of 250 patients). In 45 (56.2%) of 80 patients who died, nosocomial infections were diagnosed. The most frequent mortality causes were nosocomial pneumonia (51.1%) and septicemia (40%).

In our unit, we have to continue the work on surveillance and apply recommendations for the infection control according to the proposals of the infection control committee of our hospital.

CONCLUSION

Every health center, including our hospital, should investigate its own ICU infections and determine preventive measures according to its own results.

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