Evaluation of nosocomial infections and risk factors in critically ill patients

Burcin Ozer¹, Cagla Ozbakıs Akkurt²,3, Nizami Duran¹, Yusuf Onlen¹, Lutfu Savas³, Selim Turhanoglu²

¹ Department of Medical Microbiology, School of Medicine, Mustafa Kemal University, Hatay, Turkey
² Department of Anesthesiology and Reanimation, School of Medicine, Mustafa Kemal University, Hatay, Turkey
³ Department of Infectious Diseases, School of Medicine, Mustafa Kemal University, Hatay, Turkey

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Summary

Background:
Nosocomial infections are one of the most serious complications in intensive care unit patients because they lead to high morbidity, mortality, length of stay and cost. The aim of this study was to determine the nosocomial infections, risk factors, pathogens and the antimicrobial susceptibilities of them in intensive care unit of a university hospital.

Material/Methods:
The patients were observed prospectively by the unit-directed active surveillance method based on patient and the laboratory.

Results:
20.1% of the patients developed a total of 40 intensive care unit-acquired infections for a total of 988 patient-days. The infection sites were the lower respiratory tract, urinary tract, bloodstream, wound, and the central nervous system. The respiratory deficiency, diabetes mellitus, usage of steroid and antibiotics were found as the risk factors. The most common pathogens were Enterobacteriaceae, Staphylococcus aureus, Candida species. No vancomycin resistance was determined in Gram positive bacteria. Imipenem and meropenem were found to be the most effective antibiotics to Enterobacteriaceae.

Conclusions:
Hospital infection rate in intensive care unit is not very high. The diabetes mellitus, length of stay, usage of steroids, urinary catheter and central venous catheter were determined as the risk factors by the final logistic regression analysis. These data, which were collected from a newly established intensive care unit of a university hospital, are important in order to predict the infections and the antimicrobial resistance profile that will develop in the future.

key words: intensive care unit • nosocomial infection • risk factors

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Author's address: Burcin Ozer, Department of Medical Microbiology, School of Medicine, Mustafa Kemal University, 31100 Hatay, Turkey, e-mail: burcinozer@yahoo.com
The intensive care units are treatment units that provide the vital support to the critically ill patients. Nosocomial infections (NIs) are one of the most serious complications in intensive care unit (ICU) patients because they lead to high morbidity, mortality, length of stay and cost [1]. Although only 5–10% of all hospitalized patients are treated in ICUs, they account for approximately 25% of all NIs [2]. Patients hospitalized in ICUs are 5 to 10 times more to acquire NIs than other hospital patients [3]. Patients admitted into ICUs are susceptible to infection because of their underlying diseases or invasive monitoring and they are disposed to the infections after exposure to broad-spectrum antimicrobials [2]. The high rate of nosocomial infection in ICU leads to use broad spectrum antibiotics and emergence of antibiotic resistant microorganisms. The mortality and treatment cost of the infection caused by the resistant strains is very high compared with the mortality and treatment cost infection caused by the susceptible strains [3]. On these grounds it is important to monitor and control of the NIs in ICUs.

The aim of this study was to determine the nosocomial infections, risk factors, causative agents and the antimicrobial susceptibilities of these agents in ICU of Mustafa Kemal University Hospital.

**Material and Methods**

This study was approved by Hospital Ethics Committee. All patients included in the study were admitted to the 10 bed mixed ICU for more than 48 hours during period of study from March 2007 to August 2007. The patients admitted to the ICU were observed prospectively by the unit-directed active surveillance method based on patient and the laboratory. Patients who stayed in ICU less than two days were excluded. They were prospectively followed up including five days after discharge from ICU. Infections that developed 48 hours after admission into the ICU were considered ICU acquired. The presence and criteria of infection were assessed daily on the ward round together with an infectious disease specialist. Urine bacterial culture was routinely performed on admission. Microbiological samples of blood, urine, tracheobronchial secretions, and any suspected infection focus were always obtained when a new infection was suspected. The definitions of infections were based on the definitions proposed by the Centers for Disease Control and Prevention. The risk factors were selected in the light of a review summarizing previously published articles about nosocomial infections in ICUs [2]. The following information was collected for all study patients: age, gender, cause of admission, severity of underlying diseases and organ dysfunction on admission as assessed by means of the Acute Physiology and Chronic Health Evaluation (APACHE) II, presence of ischemic heart disease, chronic obstructive pulmonary disease, diabetes mellitus, chronic renal or hepatic failure, intoxication, foreign body and prosthesis, underlying malignancy, general body trauma, recent use of immunosuppressive therapy, elective or emergency operations, previous antimicrobial therapy, prior hospitalization, parenteral nutrition, transfusion.

Susceptibility testing of microorganisms was done according to recommended Clinical and Laboratory Standards Institute (CLSI) guidelines [4]. The automated Vitek bacteriology system (bioMerieux Vitek, France) was used for the identification of microorganisms and susceptibility testing.

**Statistical analysis**

Student’s t test, Mann-Whitney U test, χ² and Fisher’s exact χ² tests were used for statistical analysis. P≤0.05 was considered significant. Also a logistic regression model was used in order to evaluate the risk factors of infections.

**Results**

A total of 250 patients were admitted during this 6-month period. 149 patients (61 female and 88 male) with a mean age of 61.1±18.1 (min 15 – max 94) were involved in this study. They stayed a mean of 6.6±5.9 (min 2– max 30) days in ICU. A mean of APACHE II scores was found as 13.2±4.8 (min 4 – max 26).

20.1% (n=30) of the patients developed a total of 40 ICU-acquired infections for a total of 988 patient-days. Nosocomial infection was diagnosed at a mean of 5.4±4.9 (min 2 – max 23) days after the admission in ICU. One event of NI occurred in 23 patients (76.7%), 5 (16.7%) had 2 infections and 2 (6.7%) had 3 or more. The infection sites were the lower respiratory tract (40%), urinary tract (40%), bloodstream (10%), wound (7.5%), and the central nervous system (CNS) infection (2.5%). The sites of infection are summarized in Figure 1.

A total of 52 patients had ischemic heart disease, 32 (21.5%) had undergone surgery before admission whom 23 (15.4%) had emergency, 9 (6%) had elective surgery, 29 (19.5%) had cerebrovascular disease, 19 (12.8%) had diabetes mellitus and 13 (8.7%) chronic obstructive pulmonary disease, 13 (8.7%) had gastrointestinal hemorrhage.

116 patients (77.9%) had a urinary catheter, 37 (24.8%) had a nasogastric tube, 28 (18.8%) were being mechanically ventilated, 25 (16.8%) were being intubated, 8 (5.4%) had a tracheostomy, 7 (4.7%) had an arterial catheter, 6 (4%) had a central venous catheter, 6 (4%) had drenage catheter.

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The respiratory deficiency, diabetes mellitus, usage of steroid and antibiotics were found as the risk factors for nosocomial infection. And male sex, respiratory deficiency, unconsciousness, intubation, mechanical ventilation and colonization of organisms in the lower respiratory tract were found as the main risk factors for lower respiratory tract infection. Only usage of antibiotic was found to be the risk factor for urinary tract infection. Analysis (Table 1) of the clinical characteristics of patients with and without NI denoted that numerous factors were associated with the occurrence of infection.

Final logistic regression analysis showed that diabetes mellitus, length of stay, usage of steroid, urinary catheter and central venous catheter were statistically significant risk factors for nosocomial infection in ICU (Table 2).
Among the total patients, 44 (29.5%) died and 16 (36.4%) was detected with and 28 (63.6%) without NI. The difference in mortality rate between presence of NI and absence of NI groups was significant.

The Table 3 summarizes the organisms isolated from the nosocomial infections. The most common pathogens found were as follows: Enterobacteriaceae (26.1%), Staphylococcus aureus (21.7%), Candida species (16.7%), Pseudomonas aeruginosa (10.9%), Enterococcus species (10.9%), and Acinetobacter species (8.7%).

It was found to have the highest antimicrobial resistance, with 8/10 resistant to methicillin, sulbactam-ampicillin, cefazolin, erythromycin, gentamicin, ciprofloxacine, ofloxacin in the strains of S. aureus. Trimethoprim/sulphamethoxazole, clindamycin, teicoplanin and vancomycin were found to be the most effective antibiotics to S. aureus. Of all the Enterococcus isolates recovered from patients in the ICU, 5/5 of the Enterococcus strains were penicillin and ciprofloxacine resistant and 4/5 of them resistant to tetracycline. No vancomycin resistance was determined in Gram positive bacteria. Imipenem and meropenem were found to be the most effective antibiotics to Enterobacteriaceae. It was found to have the highest antimicrobial resistance, with 9/12 resistant to ampicillin and amoxicillin clavulanic acid. Within the P. aeruginosa strains there was no resistance to amikacin. But ceftazidime, gentamicin, mezlocillin, piperacillin/tazobactam were found to have the highest antimicrobial resistance within P. aeruginosa strains.

The most frequently prescribed antibiotics were third generation cephalosporins (32.9%), quinolones (17.4%), metronidazole (15.4%), first generation cephalosporins (8.7%), and aminoglycosides (8.7%).

**Table 3. The clinical materials from which the pathogens were isolated.**

|                        | Tracheal asp. | Sputum | Urine | Blood | Wound | Cerebrospinal fluid | Total |
|------------------------|---------------|--------|-------|-------|-------|---------------------|-------|
| Enterobacteriaceae     | 4             | 1      | 5     | 1     | 2     | –                   | 12    |
| Staphylococcus aureus  | 7             | –      | 1     | 1     | 1     | –                   | 10    |
| Candida spp.           | –             | –      | 7     | 1     | –     | 1                   | 9     |
| Pseudomonas aeruginosa | 5             | –      | –     | –     | –     | –                   | 5     |
| Enterococcus spp.      | 2             | –      | 2     | 1     | –     | –                   | 5     |
| Acinetobacter spp.     | 3             | –      | 1     | –     | –     | –                   | 4     |
| **Total**              | 21            | 1      | 16    | 4     | 3     | 1                   | 46    |

It is important to know and control the risk factors for nosocomial infection. The risk factors for NIs in ICU were investigated in internal and overseas studies. In this study the finding of a relationship between diabetes mellitus, usage of steroid, antibiotics and nosocomial infection was in accordance with the literature (17). The finding of a relationship between respiratory deficiency, unconsciousness, intubation, mechanical ventilation and lower respiratory tract infection were found in accordance with the literature (18,19).

Urinary catheterization was recognized as the main risk factor for nosocomial infection by Girou et al. [20] and mechanical ventilation was recognized as the main risk factor for nosocomial pneumonia by McCusker et al. [21] and Gusmão et al. [19] in previous studies. Leone et al. [22], reported that female sex, length of ICU stay and duration of catheterization were associated with an increased risk of urinary tract infection. Apostolopoulou et al. [23] reported that duration of mechanical ventilation ≥5 days was risk factor for ventilator
associated pneumonia. Meric et al. [24] reported into a study from our country, a length of stay in ICU (>7 days), respiratory failure as a primary cause of admission, sedative medication and operation (before or after admission to ICU) as significant risk factors for NIs in ICU.

Girou et al. [20] reported that nosocomial infection rates were significantly higher in those who had equal or a higher than 21 APACHE II score, and Apostolopoulos et al. [23] reported the equal or a higher than 18 APACHE II score as a risk factor for nosocomial infections. We did not find significant relation between APACHE II score and NI contrary with Girou et al. [20] and Apostolopoulos et al. [23].

The spectrum of potential pathogens and the predominant bacterial flora can vary considerably in different ICU settings. In this study Enterobacteriaceae was found the most common pathogens, S. aureus and P. aeruginosa were the predominant pathogens in lower respiratory tract infections. Candida spp. and E. coli were the predominant pathogens in urinary tract infections. In the surveillance studies from European countries, S. aureus and coagulase negative staphylococci among the gram positive bacteria and P. aeruginosa and E. coli among the gram negative bacteria were reported to be isolated [25,26]. Candida species are causative agents of urinary tract infections of the patients who are under consistent antibiotic treatment and have urinary catheter [22]. There are studies which reported fifth Candida species or less than fifth [8]. In our study Candida species were isolated with third frequency. In our study one Candida spp. was determined to be caused by meningitis. In a normally way Candida spp. is not isolated from the CNS infections. In this study it was isolated from the patient who had a shunt.

In the multicenter studies, high resistance rates were determined. But there was a great difference between the centers [25,26]. For this reason every hospital needs to determine their own resistance patterns.

The antimicrobial resistance rates of the microorganisms isolated in nosocomial infections are higher than that isolated from the outpatients and the percentage of resistant isolates from the patients in ICU is also higher than that from outpatients or the other wards [27,28].

Concerning resistance pattern for S. aureus, 8/10 were resistant to meticillin and all of them had susceptible to vancomycin. Among the strains of Acinetobacter none revealed sensitivity higher than 2/4 to any antimicrobial tested. Amikacin was found to be the most effective antibiotic to the strains of P. aeruginosa. These data confirm that the organisms develop maximum resistance against the antibiotics which are most frequently prescribed.

Conclusions

In this study hospital infection rate in ICU is not very high, being similar to rates previously reported from other units of our country. The respiratory deficiency, diabetes mellitus, usage of steroid and antibiotics were found as the risk factors for nosocomial infection. And male sex, respiratory deficiency, unconsciousness, intubation, mechanical ventilation and colonization of organisms in lower respiratory tract were found as the main risk factors for lower respiratory tract infection. Only usage of antibiotic was found to be the risk factor for urinary tract infection. The diabetes mellitus, length of stay, usage of steroid, urinary catheter and central venous catheter were determined as the risk factors for nosocomial infection in ICU by the final logistic regression analysis. These data, which were collected from a newly established ICU of a university hospital, are important in order to predict the infections and the antimicrobial resistance profile that will develop in the future.

Conflict of interest

There are no conflicts of interest.

References:

1. Rosenthal VD, Guzman S, Orellano PW: Nosocomial infections in medical-surgical intensive care units in Argentina: attributable mortality and length of stay. Am J Infect Control, 2003; 31: 291–95
2. Eggmann P, Pittet D: Infection control in the ICU. Chest, 2001; 120: 2059–93
3. Weber DJ, Raasch R, Rutala WA: Nosocomial infections in the ICU: the growing importance of antibiotic-resistant pathogens. Chest, 1999; 115: 345–41S
4. Clinical and Laboratory Standards Institute. Performance Standards for Antimicrobial Susceptibility Testing: Ninth Informational Supplement. CLSI document M100-S9. Clinical and Laboratory Standards Institute, Wayne, Pennsylvania, USA, 2009
5. Alberti C, Brun-Buisson C, Burchardi H et al: Epidemiology of sepsis and infection in ICU: patients from an international multicentre cohort study. Intensive Care Medicine, 2002; 28: 108–21
6. Vincent JL, Rello J, Marshall J et al: EPIC II Group of investigators: International study of the prevalence and outcomes of infection in intensive care units. JAMA, 2009; 302(21): 2321–29
7. Uri U, Perome G, Acquarolo A et al: Surveillance of infections acquired in intensive care: usefulness in clinical practice. J Hosp Infect, 2002; 52: 130–35
8. Klavs I, Lužnik TB, Škerl et al: Prevalence of and risk factors for hospital-acquired infections in Slovenia: results of the first national survey. J Hosp Infect, 2003; 54: 149–57
9. Pekka Vippolaxi P, Ala-Kokko TI, Laurila J et al: Intensive care acquired infection is an independent risk factor for hospital mortality: a prospective cohort study. Critical Care, 2006; 10: 1–6
10. Cetin BC, Turgut H, Kafeli I et al: Nosocomial infections in the intensive care unit of the University Pammukale University Medical School. Turkish J Hosp Infect, 2002; 2: 98–101
11. Mutlu B, Akhan SC, Gündüz S et al: Prevalence of nosocomial infections in intensive care unit of Kocaeli University Hospital. Turkish J Clinim, 2001; 11(4): 89–90
12. Ozer B, Tatman-Oktun M, Memis D, Oktun M: Nosocomial infections and risk factors in intensive care unit of a university hospital in Turkey. Cent Eur J Med, 2010; 5(2): 203–8
13. Kallel H, Damak H, Bahoul M et al: Risk factors and outcomes of intensive care unit-acquired infections in a Tunisian ICU. Med Sci Monit, 2010; 16(8): PH69–75
14. Junior CT, HovnanianALD, Franca SA, Carvalho CRK: Prevalence rates of infection in intensive care units of a tertiary teaching hospital. Rev Hosp Clin Fac Med São Paulo, 2005; 58(5): 254–59
15. Eshay H, Yalcin AN, Serin S et al: Nosocomial infections in intensive care unit of Kayseri University hospital: a 2 year survey. Intensive Care Med, 2003; 29: 1482–88
16. León-Rosales SP, Molinar-Ramos F, Dominguerezchi F et al: Prevalence of infections in intensive care units in Mexico: a multicenter study. Crit Care Med, 2000; 28(5): 1516–21
17. Pelizzer G, Mantoan P, Timilero L et al: Prevalence and Risk Factors for Nosocomial Infections in Hospitals of the Veneto Region, North-Eastern Italy. Infection, 2008; 36(2): 112–19
18. Carrilho CM, Grion CM, Bonametti AM et al: Multivariate Analysis of the Factors Associated With the Risk of Pneumonia in Intensive Care Units. Braz J Infect Dis, 2007; 11(3): 339–44
19. Gusmão MEN, Dourado I, Fiaccone RL: Nosocomial pneumonia in the intensive care unit of a Brazilian university hospital: an analysis of the time span from admission to disease onset. Am J Infect Control, 2004; 32(4): 209–14
20. Girou E, Stephan F, Novara A, Safar M: Risk factors and outcome of nosocomial infections: results of a matched case-control study of ICU patients. Am J Crit Care Med, 1998; 157: 1151–58
21. McCasker ME, Périsse ARS, Roghmann MC: Severity of illness markers as predictors of nosocomial infection in adult intensive care unit patients. Am J Infect Control, 2002; 30(3): 139–44
22. Leone M, Garnier F, Avidan M, Martin C: Catheter-associated urinary tract infections in intensive care units. Microbes Infect, 2004; 6: 1026–32
23. Apostolopoulou F, Bakakos P, Katostaras T, Gregorakos I: Incidence and risk factors for ventilator-associated pneumonia in 4 multidisciplinary intensive care units in Athens, Greece. Respir Care, 2003; 48(7): 681–88
24. Meric M, Wilke A, Caglayan C, Toker K: Intensive care unit-acquired infections: incidence, risk factors and associated mortality in a Turkish university hospital. Jpn J Infect Dis, 2005; 58(5): 297–302
25. Fluit AC, Verhoef J, Schmitz FJ, the European SENTRY participants: Frequency of isolation and antimicrobial resistance of gram-negative and gram-positive bacteria from patients in intensive care units of 25 European University Hospitals participating in the European Arm of the SENTRY Antimicrobial Surveillance Program 1997–1998. Eur J Clin Microbiol Infect Dis, 2001; 20: 617–25
26. Jones ME, Draghi DC, Thornberry C et al: Emerging resistance among bacterial pathogens in the intensive care unit: a European and North American Surveillance Study (2000–2002). Ann Clin Microbiol Antimicrobals, 2004; 3(14): 1–11
27. Khorvash F, Mostafavizadeh K, Mobasherizadeh S, Behjati M: Susceptibility pattern of E. coli-associated urinary tract infection (UTI): a comparison of spinal cord injury-related and nosocomial UTI. Med Sci Monit, 2009; 15(11): CR579–82
28. Archibald L, Phillips L, Monnet D et al: Antimicrobial resistance in isolates from inpatients and outpatients in the United States: increasing importance of the intensive care unit. Clin Infect Dis, 1997; 24(2): 211–15