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Nosocomial infections and risk factors in intensive care unit of a university hospital

Bir üniversite hastanesi yoğun bakım ünitesindeki hastane enfeksiyonları ve risk faktörleri

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ABSTRACT

Objective: The aim of this study is to evaluate nosocomial infections (NIs) in intensive care unit (ICU) in terms of site of infection, distribution of pathogens and risk factors for developing infection.

Methods: 80 patients staying for more than 48 hours in the ICU were included in the study. Epidemiologic characteristics of the patients, invasive procedures and other risk factors were noted. Cultures, identification of isolates and antibiotic susceptibility tests were made by standard microbiologic methods.

Results: Of 56 patients who have developed NIs, 26 (50%) had pneumonia, 15 (28.8%) had bloodstream infections and 6 (11.5%) had urinary tract infections. *Klebsiella pneumoniae* (23.5%), *Pseudomonas aeruginosa* (19.6%), and *Acinetobacter* spp. (15.6%) were the most frequently isolated microorganisms, respectively. For *Klebsiella pneumoniae* isolates, extended spectrum beta lactamase (ESBL) rate was 91.6%, carbapenem resistance rate was 15.6% and for *Pseudomonas aeruginosa* and *Acinetobacter spp*. carbapenem resistance rates were 60% and 100% respectively. Hemodialysis, enteral nutrition, total parenteral nutrition and prolonged hospitalization for more than 10 days were determined as independent risk factors for developing NI. Additionally Acute Physiology and Chronic Health Evaluation (APACHE) II score, length of ICU stay and lenght of hospital stay before ICU were found to be high in the NI group.

Conclusion: Pneumonia is the most common NI and carbapenem resistance in Gram-negative bacilli was remarkably high in our ICU. It was considered that infection control measures must be applied carefully, invasive procedures should be used in correct indications and we should avoid long-term hospitalization if unnecessary. *J Clin Exp Invest 2015; 6 (3): 233-239*

Key words: Intensive care unit, nosocomial infections, carbapenem resistance

ÖZET

Amaç: Bu çalışmada yoğun bakım ünitesindeki (YBÜ) hastane enfeksiyonlarının (HE) enfeksiyon odağı, patojenlerin dağılımı ve risk faktörleri açısından değerlendirilmesi amaçlandı.

Yöntemler: YBÜ'de 48 saatten fazla kalan 80 hasta çalışmaya dahil edildi. Hastaların epidemiyolojik özellikleri, invaziv girişimler ve diğer risk faktörleri kaydedildi. Kültürler, patojenlerin tanımlanması ve antibiyotik duyarlılık testleri standart mikrobiyolojik yöntemlerle yapıldı.

Bulgular: HE gelişen 56 hastanın 26 (%50)'sında pnömoni, 15 (%28,8)'inde kan dolaşımı enfeksiyonu ve 6 (%11.5)'sında üriner sistem enfeksiyonu saptandı. *Klebsiella pneumoniae* (%23.5), *Pseudomonas aeruginos*a (%19,6) ve *Acinetobacter* spp. (%15,6) sırasıyla en sık saptanan etken mikroorganizmalar idi. *Klebsiella pneumoniae* izolatlarında genişlemiş spektrumlu beta laktamaz (GSBL) oranı %91,6, karbapenem direnci %15,6, *Pseudomonas aeruginosa* ve *Acinetobacter* spp. izolatları için de karbapenem direnci sırasıyla %60 ve %100 olarak saptandı. Hemodiyaliz, enteral beslenme, total parenteral beslenme, 10 günden uzun süreli yatış HE gelişimi açısından bağımsız risk faktörleri olarak saptandı. "Acute Physiology and Chronic Health Evaluation" (APACHE) II skoru, YBÜ'de yatış süresi ve YBÜ öncesi hastanede yatış süresi de HE gelişen grupta daha yüksek bulundu.

Sonuç: Hastanemiz YBÜ'de pnömoni en sık görülen HE olarak saptandı ve Gram-negatif basillerdeki karbapenem direnci dikkat çekici ölçüde yüksek bulundu. Enfeksiyon kontrol önlemlerinin dikkatli bir şekilde uygulanması, invaziv girişimlerin doğru endikasyonlarda uygulanması ve gereksiz uzun dönem yatışlardan kaçınılması gerektiği düşünüldü.

Anahtar kelimeler: Yoğun bakım ünitesi, hastane enfeksiyonları, karbapenem direnci

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INTRODUCTION

Nosocomial infection (NI) is defined as an infection which is not in the incubation period at the time of admitting to hospital and develops after 48 hours of hospital admission, within 3 days of discharge or 30 days of an operation. These infections cause high mortality and morbidity rates, prolonged hospitalization and high financial burden. Patients in intensive care units (ICUs) are only 10% of all hospitalized patients, but they account for approximately 25% of all NIs, and it has been reported that 45% of all nosocomial bacteremia and pneumonia are seen in ICUs [1,2]. In this study, it was aimed to evaluate NIs in ICU in terms of site of infection, distribution of causative pathogens and their antibiotic susceptibility pattern and the risk factors for developing infection.

METHODS

This prospective study has been conducted in the ICU of Istanbul University Istanbul Faculty of Medicine between March-August 2010 after the study has been approved by the ethics committee. 80 patients over 18 years of age who had stayed more than 48 hours in our ICU were included in the study. The patients who were not followed up from the first day of admission to ICU were excluded. If there was a unit where patients stayed for more than 24 hours before our ICU, these were recorded as internal units, surgical units, emergency unit and units/ICUs of other hospitals.

Epidemiological variables such as age, gender, diagnosis at admission, invasive procedures such as surgical intervention, central vascular line, urinary catheter, nasogastric tube, enteral nutrition, and risk factors such as disease severity at the time of admission (Acute Physiology and Chronic Health Evaluation II [APACHE II] scores), underlying diseases, exposure to antibiotics, duration of hospitalization, and immunosupression were recorded. Patients were followed up in terms of developing NIs and causative pathogens during the hospitalization period. NIs were defined according to CDC (Centers for Disease Control and Prevention) definitions [3].

Clinic samples were taken from the sites of infections. Catheter samples were inoculated on sheep blood agar, sputum, endotracheal aspirates (ETA), pus, bile and various body fluid samples were inoculated on sheep blood agar and MacConkey agar, urine samples were inoculated on sheep blood agar and “eosin methylene blue” (EMB) agar. Isolated bacteria were identified with conventional microbiological methods, and antibiotic susceptibility tests were performed with Kirby-Bauer disc diffusion technique. Extended spectrum β-lactamase (ESBL) producing was shown with double disc synergy test. Blood cultures were performed with BacT/ALERT (bioMérieux, Durham, North Carolina, USA) automatization system.

For statistical evaluation, “Statistical Package for Social Sciences” SPSS 15.0 program was used. Chi-square test, Mann-Whitney U test and logistic regression analysis tests were used. All p values ≤0.05 were considered as significant.

RESULTS

A total of 80 patients who were hospitalized in ICU were evaluated during the study period. Of the 80 patients, 46 (57.5%) were male, and 34 (42.5%) were female. The median age was 57.43±16.50 (23-90) years. Of the 80 patients, 19 (23.8%) were hospitalized in surgical units, 13 (16.3) were hospitalized in internal units, 33 (41.3%) were hospitalized in emergency unit and 15 (18.8%) were hospitalized in other hospitals before admitting to our ICU. The median duration of hospitalization in other units before ICU was 6.58±11.74 (0-80) days. The median duration of hospitalization in our ICU was 28.79±21.29 (4-90) days.

During the follow up, NIs were developed in 52 (65%) patients. Among these patients, 26 (50%) of them had pneumonia, 15 (28.8%) of them had bloodstream infections, 6 (11.5%) of them had urinary tract infections (UTIs), 2 (3.8%) of them had surgical site infections, 2 (3.8%) of them had intraabdominal infections, and 1 (1.9%) of them had skin and soft tissue infection. In two patients who had pneumonia and 2 patients who had bloodstream infections, the pathogen could not be isolated and considered as “clinically-defined pneumonia” and “clinical sepsis”. Also in one patient who had surgical site infection, the pathogen could not be isolated. Gram-negative bacilli were the most common causative pathogens isolated in the patients who had NIs. *Klebsiella pneumoniae* was the most frequent pathogen, and *Pseudomonas aeruginosa, Acinetobacter* spp, and *Escherichia coli* followed respectively (Table 1). Vancomycin-resistant enterococci (VRE) had been isolated in 11.7% of the patients who had NIs and it was the most common pathogen among Gram-positive cocci (Table 1). Fifty seven percent of *E.coli* isolates were ESBL-positive. 91.6% of *Klebsiella pneumoniae* isolates were ESBL-positive and 4 (36.3%) of them were carbapenem-resistant also.

Table 1. Causative microorganisms in the patients with nosocomial infections

Microorganisms	n	(%)
Klebsiella pneumoniae	12	(23.5)
Pseudomonas aeruginosa	10	(19.6)
Acinetobacter spp.	8	(15.6)
Escherichia coli	7	(13.7)
Vancomycin-resistant enterococci	6	(11.7)
Candida spp.	3	(5.8)
Methicilin-resistant Staphylococcus aureus	2	(4.0)
Methicilin-resistant coagulase negative staphylococcus	1	(2.0)
Enterobacter spp.	1	(2.0)
Serratia marcescens	1	(2.0)

Univariate analysis of risk factors for developing NIs revealed that central vascular line, urinary catheter, nasogastric tube, drainage catheter, mechanic ventilation, enteral nutrition, total parenteral nutrition (TPN), hemodialysis, H2 receptor antagonist/proton pomp inhibitor (PPI) exposure during hospitalization, prolonged hospitalization for more than 10 days and antibiotic exposure in last 3 months were significant factors (Table 2).

Multivariate analysis of these factors showed that hemodialysis, enteral nutrition, TPN and prolonged hospitalization for more than 10 days were independent risk factors (Table 3). Among continuous variables APACHE II score, length of stay in ICU and length of stay in other units before ICU were found to be significantly high in the patients with NIs (Table 4).

Table 2. Univariate analysis of effects of invasive procedures and risk factors on development of nosocomial infections

	Patients with NIs (n=52)	Patients without NIs (n=28)	p
	n (%)	n (%)	
Risk factors			
Diabetes mellitus	14 (26.9)	6 (21.4)	0.78
Renal failure	20 (38.4)	7 (25.0)	0.32
Hepatic failure	2 (3.8)	1 (3.6)	1.00
Heart failure	2 (3.8)	2 (7.1)	0.60
History of myocardial infarction	10 (19.2)	6 (21.4)	1.00
Chronic obstructive lung disease	6 (11.5)	2 (7.1)	0.70
Malignancy	14 (26.9)	6 (21.4)	0.78
Transplantation	2 (3.8)	1 (3.6)	1.00
Immunosupression	2 (3.8)	2 (7.1)	0.60
Immunosupressive therapy	2 (3.8)	3 (10.7)	0.33
Advanced age (>65 yaş)	20 (38.5)	10 (35.7)	1.00
Prolonged hospitalization (>10 gün)	44 (84.6)	14 (50.0)	<0.001
Exposure to antibiotics			
Last 3 months	35 (67.3)	12 (42.9)	0.05
Last 6 months	41 (78.8)	17 (60.7)	0.11
Last 1 year	45 (86.5)	19 (67.9)	0.07
Invasive procedures			
Surgical implementation	21 (40.4)	6 (21.4)	0.13
Central vascular line	50 (96.2)	18 (64.3)	<0.001
Urinary catheter	52 (100)	20 (71.4)	<0.001
Nasogastric catheter	46 (88.5)	14 (50.0)	<0.001
Mechanic ventilation	50 (96.2)	16 (57.1)	<0.001
Drainage catheter	26 (50.0)	7 (25.0)	0.03
Hemodialysis	22 (42.3)	4 (14.3)	0.01
Enteral nutrition	47 (90.4)	13 (47.4)	<0.001
Total parenteral nutrition	20 (38.5)	3 (10.7)	0.01
H_2 receptor antagonist/PPI received	52 (100)	24 (85.7)	0.01

NI: Nosocomial infection, PPI: Proton pomp inhibitor

Table 3. Multivariate analysis of effects of risk factors and invasive procedures on development of nosocomial infections

	Patients with NIs (n=52)	Patients without NIs (n=28)	p
	n (%)	n (%)	
Prolonged hospitalization (>10 days)	44 (18.0)	14 (56.7)	0.01
Hemodialysis	22 (20.0)	4 (43.3)	0.05
Enteral nutrition	47 (90.4)	13 (47.4)	0.04
TPN	20 (38.5)	3 (10.7)	0.05

NI: Nosocomial infection, TPN: Total parenteral nutrition

Table 4. Effects of continuous variables on development of nosocomial infections

	Patients with NIs (n=52)	Patients without NIs (n=28)	p
	Mean ± SD	Mean ± SD	
Age	57.5 ± 16.8	57.1 ± 16.0	0.91
APACHE II	21.3 ± 6.82	12.7 ± 7.9	<0.001
Length of ICU stay (day)	36.1 ± 21.49	15.2 ± 12.6	<0.001
Stay in other units before ICU (day)	8.6 ± 13.5	2.8 ± 5.9	<0.001

SD: Standard deviation, APACHE: Acute physiology and chronic health evaluation, ICU: Intensive care unit, NI: Nosocomial infection

DISCUSSION

Since NIs have high mortality, morbidity rates and financial burden, and may be partially prevented with basic implementations, it has became an important health problem within the recent 30 years. In our country, dimension of infections was investigated and precautions were taken by surveillance programs for prevention and control of NIs in many hospitals in recent 10 years. The most important point in follow-up of patients staying in ICU is prevention of NIs as well as treatment of their primary diseases.

"The European Prevalence of Infection in Intensive Care" (EPIC) working group conducted a study in 1417 ICUs from 17 countries in 1992 and determined the rate of NIs as 24.7% [4]. After 15 years from this study, EPIC II which was a point prevalence study has been conducted, and the rate of infections in 1265 ICUs from 75 countries was found as 51%. However, unlike the previous study the rate of all infections was reported as 51% in EPIC II study, differentiation of community-acquired infections and NIs was not performed [5]. In Brazil, Oliveira et al. reported the infection rate in ICU as 20.3%; and in a study conducted in China between 2003-2007 NIs rate was reported as 26.8% [6,7]. In our country, infection rates in ICUs differed from centre to centre and were found in a wide range such as 5.3-65.3% [8,9]. Erol et al. reported the rate of NIs in ICU as 53.5%, Palabıyıkoglu et al. reported as 95.7% and Çelik et al. reported as 72% [9,10,11]. In spite of these high rates, in the study conducted by Arslan et al. rate of NIs in internal and surgical ICUs was reported as 5.3% [12]. In a study conducted by Willke et al. it was reported that ICUs were the units where NIs were most frequently seen (30%-64.6%) for 7 years [13]. In our study, NIs developed in 65% of 80 patients.

In majority of studies, the most commonly reported sites of nosocomial infections in ICUs are respiratory and urinary tracts. Pneumonia is the most frequent (50%) NI in our ICU, consistent with many studies that performed in our country and also in the world [5,14-17]. Then, the most frequent infections were found as bloodstream infections (28.8%), UTIs (11.5%), surgical site infections (3.8%), intra-abdominal infections (3.8%) and skin and soft tissue infections (1.9%), respectively. Most studies report that Gram-negative bacteria are the most common cause of NIs in ICU [5,17]. In our study, *K.pneumoniae* was the most common pathogen (23.5%), followed by *P.aeruginosa* (19.6%), *Acinetobacter* spp. (15.6%) and *E.coli* (13.7%) respectively. According to the results of studies conducted in our country; Çelik et al. and Erbay et al. reported that *P.aeruginosa* and *Staphylococcus aureus*, Tüfek et al. reported that *Acinetobacter* spp. and *P.aeruginosa* were the most common pathogens

respectively [11,16,18]. In a cross-sectional study conducted in hospitals located in Aegean region, *Acinetobacter* spp. and *S.aureus* were reported as the most common pathogens [19]. *Enterobacteriaceae* (notably *E.coli, K.pneumoniae*), *S.aureus* and *P.aeruginosa* were reported as the most common pathogens in EPIC study [4]. In our study, frequency of *S.aureus* infections have been found as 4%, relatively low compared with the other studies. Furthermore, it is extremely remarkable that VRE had been found at a rate of 11.7% and it was the most common pathogen among Gram-positive cocci. It was found that carbapenem resistance is quite high in Gram-negative bacilli. 60% of *P.aeruginosa* species, 33.3% of *K.pneumoniae* species and 100% of *Acinetobacter* species were resistant to carbapenem. In a study conducted in the ICUs of a training and research hospital, Bilman et al. reported carbapenem resistance rates as 85% (meropenem) and 87% (imipenem) for *Acinetobacter* spp. and, 35% (meropenem) and 36% (imipenem) for *P.aeruginosa* [20]. In another study conducted by Yolbaş et al. carbapenem resistance rate for *Acinetobacter* spp. was reported as 87% [21]. In our study, 100% resistance to carbapenem for *Acinetobacter* species suggest us a clonal spread, and also it constitutes an evidence for increasing carbapenem resistance in every year in *Acinetobacter* spp.

While various invasive procedures such as mechanical ventilation, central vascular line, TPN, urinary catheter, hemodialysis, surgical intervention applied in ICUs are important for survival of patients, they are risk factors for development of NIs since they may be an entrance for the causative microorganisms. In a retrospective study in which Ding et al. evaluated the NIs in ICU between 2003-2007, they found that 3/4 of patients with pneumonia had tracheotomy or mechanical ventilation, more than half of the patients with USI and bloodstream infections had urinary catheter and intravenous catheter before the development of infections [7]. It was reported that NIs are correlated with invasive procedures in many other studies [22,23]. In univariate analysis, use of mechanical ventilation, hemodialysis, central vascular line, urinary catheter, nasogastric catheter, drainage catheter, enteral nutrition, TPN, H2 receptor antagonist/PPI exposure were found significantly higher in the group with NIs (Table 2). When logistic regression analysis was applied in these variables; it was seen that hemodialysis, enteral nutrition and TPN were the independent risk factors for development of NIs (Table 3). It was previously shown that gastric colonization increased as a result of dilution of gastric content by enteral nutrition and increasing of pH [24]. In various studies, it was shown that enteral nutrition increases gastroesophageal reflux and risk of aspiration, and aspiration is a major risk factor for development of pneumonia [25,26]. In our study, enteral nutrition was found as one of the independent variables increasing development of NIs.

In various studies it has been reported that patients who are below the age of 1 and above the age of 60 are at increased risk for development of NIs [2,27]. Brawley et al. found that risk for development of infections increases with age [28]. In our study, no statistically significant correlation was found between development of NIs and age. APACHE II scoring system which is used for evaluating the severity of acute disease, is known as having a good correlation with mortality and development of NIs. Akkus et al. observed that patients whose APACHE II score is higher than 15, are at increased risk for development of NIs [29]. However, several studies have determined that APACHE II score is not an independent risk factor for development of NIs [30,31]. In our study APACHE II score was found as 21.3±6.8 in the patients with NIs and 12.7±7.9 in the patients without NIs, difference between two groups was statistically significant (Table 4). Patients in ICUs are exposed to many invasive procedures and, are at increased risk for development of NIs associated with prolonged hospitalization. It was seen that lenght of ICU stay is significantly higher in the patients with NIs in our study, consistent with the other studies conducted in our country [8,31-33]. In several studies also conducted in United States and Europe, it was shown that there is a significant correlation between length of ICU stay and development of NIs [5,6,22,34]. We had determined that 63.5% of patients with NIs (33/52) had a history of hospitalization in other units before the ICU stay and when compared with the group without NIs, this finding was statistically significant. Also, it was seen that length of stay in other units before ICU is significantly longer in the group with NIs compared with the group without NIs (Table 4).

In conclusion, it was seen that the most frequently encountered NI was pneumonia in our ICU, followed by bloodstream infections and UTIs. *Klebsiella pneumoniae, Pseudomonas aeruginosa* and *Acinetobacter* spp. were found as the most frequent causative microorganisms, respectively. VRE was found the most common pathogen among Gram-positive cocci, and all of the *Acinetobacter* species were found to be resistant to carbapenems. It was determined that high APACHE II score, prolonged

hospitalization in ICU, prolonged hospitalization in other units before ICU, hemodialysis, enteral nutrition and TPN are independent risk factors for development of NIs. It was considered that each hospital should apply infection control measures by determining own causative microorganisms, antibiotic resistance patterns and risk factors with regular surveillance cultures and should apply invasive procedures in correct indications.

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