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Cost analysis and evaluation of nosocomial infections in intensive care units

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Background/aim: The purpose of this study was to evaluate nosocomial infections occurring in our hospital intensive care units (ICUs) and the risk factors for these, and to determine the effect of these infections on mortality and cost.

Materials and methods: This retrospective study was performed via infection control committee surveillance data, ICU records, and information processing data between 1 January and 31 December 2013 at the Kanuni Education and Research Hospital.

Results: A total of 309 nosocomial infections were observed in 205 out of 566 patients. The density of nosocomial infections was 25.4 in 1000 patient days. Hospitalization was prolonged, and APACHE II and Charlson comorbidity scores were high in patients developing nosocomial infections ($P < 0.001$). Of the patients diagnosed with a nosocomial infection, 170 died. Infections were determined as the cause of death in 62 (36.5%) of the nonsurviving patients with a nosocomial infection. *Acinetobacter baumannii* was identified in 46 (74.2%) of the patients that died from nosocomial infections. The mean cost in patients developing a nosocomial infection was 15,229.30 Turkish lira (TL), compared to 9648.00 TL in patients without a nosocomial infection ($P = 0.002$).

Conclusion: Regular infection control education sessions need to be held and the number of nurses needs to be increased in order to be able to reduce this high mortality, morbidity, and cost.

Key words: Nosocomial infections, intensive care units, cost analysis

1. Introduction

Nosocomial infections are one of the world's most significant health problems, leading to prolongation of hospitalization and increased morbidity, mortality, and treatment costs. Nosocomial infections are most common in intensive care units (ICUs). These are units intended to treat patients requiring intensive care due to severe function compromise in one or more organ systems. They are furnished with high-tech equipment and are provided with 24-h vital sign monitoring and patient care (1,2).

The purpose of this study was to evaluate nosocomial infections occurring in our hospital ICUs and the risk factors for these, and to determine the effect of these infections on mortality and cost.

2. Materials and methods

2.1. Study design

The study was performed retrospectively at the Kanuni Education and Research Hospital, Turkey, which has a 605-bed capacity, including 46 adult ICU beds. Our hospital contains four adult ICUs (Anesthesia and Reanimation, Surgical, Medical, and Neurology). Due to nurse shortages, the nurse/patient ratio in our ICUs ranges between 1:3 and 1:4, and may even rise to 1:6 on some nights. The physical criteria also do not meet the recommended criteria. The patients hospitalized in the ICUs for more than 2 days between 1 January and 31 December 2013 were enrolled in the study. Each patient's medical file, infection control committee surveillance data, ICU records, pharmacy records, and information processing data were used. Patients were divided into two groups: those developing nosocomial infections (Group A) and those not developing nosocomial infections (Group B). The diagnosis of nosocomial infection was based on the Centers for Disease Control and Prevention criteria (3). Nosocomial infection density was calculated via the formula [(number of nosocomial infections/patient days) × 1000]. Device-associated infection rate (DAIR) was

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calculated via the formula [(number of device-associated infections/device-days) × 1000]. Device utilization (DU) was calculated via the formula (number of device days/ patient days).

The Acute Physiology and Chronic Health Evaluation (APACHE) II scores used were those calculated within the first 24 h of hospitalization (4). Charlson comorbidity index scores were obtained through the examination of all patients' medical records (5). The identification of microorganisms and testing for antimicrobial susceptibility were conducted via the Phoenix system (Becton Dickinson), the disk diffusion test, and classic methods. Polymicrobial infection was defined as the presence of two or more agent microorganisms.

Cost in the study was based on the cost of treatment to the patient (invoice cost). Cost for each patient was obtained from our hospital's information processing center data. Invoices were examined in detail, and comparisons were made by calculating patients' treatment costs. In performing these comparisons, costs were divided into five groups: drug costs, expendable supplies costs, medical services costs (laboratory test charges, surgery charges, blood center charges, and consultation charges), other costs, and total costs. When the total cost was determined, this was also calculated in terms of Euros and US dollars based on that day's exchange rate. Physician, nurse, and care attendant charges were not included in cost calculations.

2.2. Statistical analysis

Descriptive statistical analysis was performed for all parameters. The Kolmogorov–Smirnov test was used to determine eligibility of variables. The data in conformity with normal distribution were analyzed using Student's t-test, and those not conforming to normal distribution were analyzed using the Mann–Whitney U test. The data obtained by measurements are given as mean ± standard deviation. The data obtained by counting are given as number (%); analyses were performed using the chi-square test. In addition, multivariate analyses were performed using logistic regression. The results of the analysis are presented as P-values, odds ratio (OR), and 95% confidence interval (95% CI). $P < 0.05$ was regarded as significant.

3. Results

A total of 810 patients were hospitalized and treated in our hospital's adult ICUs in 2013, 566 being hospitalized in the ICUs for more than 2 days. Of these patients, 310 patients were male and 255 female, with a mean age of 69.6 ± 17.7 years. The mean duration of hospitalization was 21.5 ± 24.3 days. The Charlson comorbidity index score was 3.0 ± 1.9 and the APACHE II score 19.1 ± 3.1. The urinary catheter (UC) use rate was 0.89%, central venous catheter (CVC) use rate 0.64%, and mechanical ventilator (MV) use rate 0.56. Furthermore, 309 nosocomial infections were observed in 205 of the 566 patients. Nosocomial infection density was 25.4 in 1000 patient days. One hundred thirty-two (42.7%) of the nosocomial infections were primary bacteremia (101 catheter-related blood stream infections (CR-BSIs)), 86 (27.8%) were pneumonia (73 ventilator-associated pneumonia (VAP) cases), 48 (15.5%) were urinary tract infections (UTIs) (all of the infections were UTI related to urinary catheter (UC-UTI)), 24 (7.8%) were surgical site infections, 16 were soft tissue infections, and 3 were central nervous system infections. Hospitalization was prolonged and APACHE II and the Charlson comorbidity scores were high in patients developing nosocomial infection ($P < 0.001$). The incidence of nosocomial infection was 1.73 times higher in patients with APACHE II scores above 20 ($P = 0.002$). Nosocomial infections were more common in patients with trauma, cerebrovascular disease, diabetes mellitus, and kidney diseases ($P < 0.05$). Days of MV, CVC, and UC use were higher in patients developing nosocomial infections ($P < 0.001$). Lower rates of infection occurred in patients receiving enteral nutrition and were higher in patients undergoing surgery, receiving parenteral nutrition, and using vasopressors ($P < 0.05$). The demographic and clinical characteristics of patients with or without nosocomial infection in the ICUs are shown in Table 1. In multivariable analysis, a high Charlson comorbidity index score (OR: 1.82), length of hospitalization (OR: 1.26), and presence of diabetes mellitus (OR: 2.43) were determined to be risk factors for nosocomial infections (Table 2).

Of the 309 nosocomial infections observed in our hospital ICUs, 224 gram-negative microorganisms, 83 gram-positive microorganisms, and 24 *Candida* spp. were identified as agents (Table 3). Polymicrobial agents were identified in 35 nosocomial infections, while no agent could be identified in 18 infections. The most common agents were *Acinetobacter baumannii* (n = 72), *Pseudomonas aeruginosa* (n = 57), and *Staphylococcus aureus* (n = 51). Carbapenem resistance was present in 66 (91.7%) *A. baumannii* cases, while no colistin resistance was observed. While no piperacillin/tazobactam or amikacin resistance was observed in *P. aeruginosa* cases, resistance to carbapenems was identified in 21 (42.1) cases. Extended spectrum beta-lactamase (ESBL) was positive in all *K. pneumoniae*, but not in two *E.coli* cases. The most effective antibiotics for *E.coli* and *K. pneumoniae* were carbapenems and amikacin. Methicillin resistance was determined in 23 (45.1%) of *S. aureus* cases and all cases of coagulase-negative staphylococci (CNS). Vancomycin resistance was present with one *Enterococcus* strain.

In this study, 36.7% of patients hospitalized in the ICU for more than 2 days died within 7 days, 16.8% in 8–14 days, 15.5% in 15–30 days, and 10.8% in more than

Table 1. The demographic and clinical characteristics of patients with or without nosocomial infection in the ICUs.

Characteristics	Group A n = 205	Group B n = 361	OR (95% CI)	P
Age	70.3 ± 16.7	69.2 ± 18.3		0.654
Sex (male)	118 (57.6%)	192 (53.2%)	1.19 (0.83–1.71)	0.315
APACHE II	19.9 ± 3.5	18.4 ± 2.5		<0.001
APACHE II >15	196	338	1.48 (0.64–3.53)	0.429
APACHE II >20	98	125	1.73 (1.20–2.49)	0.002
Length of hospitalization	28.1 ± 32.4	17.8 ± 17.1		<0.001
Charlson comorbidity index	3.2 ± 1.4	2.9 ± 2.1		<0.001
Primary and underlying diseases				
Trauma	27	18	2.89 (1.49–5.64)	0.0005
Cardiac disease	7	12	1.03 (0.36–2.86)	0.853
Cerebrovascular disease	45	51	1.71 (1.07–2.73)	0.017
Abdominal disease	25	31	1.48 (0.82–2.67)	0.167
Diabetes mellitus	59	33	4.02 (2.45–6.20)	<0.001
Kidney disease	42	48	1.68 (1.04–2.71)	0.025
Malignity	17	44	0.65 (0.35–1.21)	0.195
Other disease	42	78	0.93 (0.60–1.45)	0.754
Invasive procedures				
Endotracheal intubation	173	291	1.30 (0.80–2.11)	0.261
Ventilator days	18.5 ± 16.0	9.8 ± 11.3		<0.001
Central venous catheter	192	315	2.16 (1.09–4.32)	0.024
Central venous catheter days	21.3 ± 14.7	11.6 ± 7.4		<0.001
Urinary catheter	193	326	1.73 (0.84–3.61)	0.152
Urinary catheter days	25.8 ± 21.3	13.9 ± 10.5		<0.001
Nasogastric catheter	89	154	1.03 (0.72–1.48)	0.861
Enteral nutrition	152	316	0.41 (0.26–0.65)	<0.001
Surgery	61	76	1.59 (1.05–2.40)	0.020
Medication				
Total parenteral nutrition	97	85	2.92 (1.99–4.28)	<0.001
Steroids	36	53	1.24 (0.76–2.02)	0.367
Vasopressor	114	167	1.46 (1.02–2.08)	0.033
Mortality	170	282	1.36 (0.86–2.17)	0.170

30 days. One hundred seventy patients diagnosed with nosocomial infection died. Infections were identified as the cause of death in 62 (36.5%) of the fatal patients with a nosocomial infection. The patients had died before culture growth was reported in 21 (33.9%) of these infections. Empiric treatment-resistant bacterial growth was present in 17 (27.4%) patients that started on such treatment. Treatment was commenced after 3.5 ± 1.1 days in 11 (17.7%) patients. Mortality occurred despite appropriate treatment in 13 (21%). The agent microorganism was *A. baumannii* in 46 (74.2%) of the patients that died due to nosocomial infection.

The mean cost for patients developing nosocomial infections was 15,229.3 ± 23,280.9 Turkish lira (TL), compared to 9648.0 ± 12,031.9 TL for patients without nosocomial infection (P = 0.002) (Table 4). Medical service expenses constituted the highest cost. Medical service costs in patients with nosocomial infections were on average 5000 TL higher than those in patients without nosocomial infection (P = 0.001). Laboratory test charges represented

Table 2. Risk factors of nosocomial infection (multivariate analysis).

Risk factors	P	OR	95% CI
Charlson comorbidity index	0.014	1.82	1.12–2.98
Length of hospitalization	0.026	1.26	1.10–2.32
Trauma	0.152	3.62	0.82–9.24
Diabetes mellitus	0.020	2.43	1.14–4.10
Total parenteral nutrition	0.218	1.36	0.53–3.92

Table 3. Microorganism agents identified in nosocomial infections in our hospital ICUs.

	Primary bacteremia (n = 132)	Pneumonia (n = 86)	UTI (n = 48)	Other (n = 43)
Microorganism	149	83	48	51
Gram-negative microorganisms	96	66	37	25
Escherichia coli	11	4	11	8
Acinetobacter baumannii	32	29	4	7
Klebsiella spp.	10	5	8	2
Pseudomonas aeruginosa	23	21	6	7
Serratia marcescens	8	2	1	0
Enterobacter spp.	4	3	2	0
Stenotrophomonas maltophilia	4	2	0	0
Proteus mirabilis	3	0	5	1
Burkholderia cepacia	1	0	0	0
Gram-positive microorganisms	40	16	5	22
Staphylococcus aureus	24	16	0	11
CNS	9	0	0	4
Enterococcus spp.	7	0	5	7
Fungi	13	1	6	4
Candida albicans	1	1	2	1
Candida spp.	12	0	4	3

a considerable part of these high costs. The second highest cost component was drug costs. Antibiotics represented a considerable part of the drug costs. Microorganisms being resistant did not affect patients' total costs (P = 0.178). However, while the costs in patients developing infections with resistant microorganisms without mortality in the first 3 days were 21,750 ± 24,676 TL, the costs for patients with sensitive microorganism infection were 12,556 ± 16,547 TL (P < 0.001). The costs of patients developing more than one infection were 24,876 ± 32,738 TL, compared to the costs of 9652 ± 12,496 TL for those with one infection (P < 0.001).

4. Discussion

The type, rate, and agents of nosocomial infections may vary from country to country, hospital to hospital, and unit to unit. These infections are most frequently seen in hospital ICUs. The nosocomial infection rate determined in ICUs is generally 5–10 times higher than the general nosocomial rate. ICU type, length of hospitalization, underlying diseases, severity of disease, and invasive procedures performed play a significant role in high infection rates (6). The National Nosocomial Infections Surveillance (NNIS) report cited an infection rate of 18.7 per 1000 patient days (7). One multicenter study in Turkey

Table 4. Costs of patient with or without nosocomial infection developing in the ICUs.

Costs	Group A n = 205	Group B n = 361	P
Drug costs	3495 ± 4475	2232 ± 3324	<0.001
Expendable supplies costs	1022 ± 1463	571 ± 834	0.001
Medical services costs	13060 ± 20,691	7823 ± 10,284	0.001
Other costs	834 ± 345	761 ± 356	0.286
Mean costs (TL)	15229 ± 23,281	9648 ± 12,032	0.002
Mean costs (dollars)	5439 ± 8315	3446 ± 4297	0.002
Mean costs (Euros)	5060 ± 7735	3205 ± 3997	0.002

1 US dollar = 2.80 TL, 1 Euro = 3.01 TL.

reported a nosocomial infection rate of 33.9 per 1000 patient days (8). The rate of nosocomial infection in our study was 41.2 per 1000 patient days.

The most prevalent type of infection was pneumonia, with rates of 20%–47%, followed by UTIs and primary bloodstream infection (BSIs) (6,7,9). Esen and Leblebicioglu performed a one-day point prevalence study of ICUs in Turkey in which they observed that pneumonia and lower respiratory tract infection (28.0%), laboratory-confirmed BSI (23.3%), and UTI (15.7%) were the most frequent types (10). In this study, primary BSI was the most common (42.7%) nosocomial infection, followed by pneumonia (27.8%), UTI (15.5%), and surgical site infection (SSI) (7.8%). The majority of these infections in ICUs are linked to the use of invasive devices. One analysis of NNIS Medical-Surgery ICU data reported that 83% of nosocomial infections, 87% of primary BSIs, and 97% of UTIs were linked to the use of invasive devices (7). In our study, all UTIs, 84.9% of pneumonia cases, and 58.3% of BSIs were linked to the use of invasive devices. Our UC and MV use levels were above the 90th percentile according to National Healthcare Safety Network (NHSN) data (11), while CVC and MV use level was close to the 75th percentile. Compared to INICC data (12) and the 2013 report of the National Hospital Infections Surveillance Network (UHESA) in Turkey (13), the UC use rate was compatible with the 75th percentile, and the CVC use and MV use level with compatible with the 50th percentile. The rate of CR-BSIs was 9.9 per 1000 CVC days, compared to 1.8 in the NHSN 75th percentile, 11.7 in the INICC 50th percentile, and 6.9 in the UHESA 75th percentile. The rate of UC-UTIs was 4.4 per 1000 urinary catheter days, compared to 5.2 in the NHSN 90th percentile, 9.1 in the INICC 75th percentile, and 5.3 in the UHESA 75th percentile. The rate of VAP was 10.7 per 1000 ventilator days, 3.9 in the NHSN 90th percentile, 16.5% in the INICC 50th percentile, and 11.9 in the UHESA 50th percentile. These findings show that VAP and CVC-associated BSI rates in our hospital ICUs are high on the basis of the NHSN data and low according to the data from the INICC (Table 5).

Many different risk factors for nosocomial infections, such as a high APACHE II score, lengthy hospitalization, long-term use of invasive devices, total parenteral nutrition, and presence of a comorbid disease, have been reported in the literature (14,15). Vasopressor use contributes to microorganisms' biofilm production, and this plays a significant role in nosocomial infections (16). In terms of the causes of the high infection rate in our study, high APACHE II and Charlson comorbidity index scores ($P < 0.001$), lengthy hospitalization ($P < 0.001$), long-term use of invasive devices ($P < 0.001$), surgery ($P = 0.02$), total parenteral nutrition ($P < 0.001$), and vasopressin use ($P = 0.033$) were more frequent in patients developing an infection. Other adverse factors such as a high number of patients per nurse in ICUs, the lack of isolation rooms,

Table 5. Comparison of invasive device-associated nosocomial infections.

	Our study's rate	UHESA rate (percentile)	INICC rate (percentile)	NNIS rate (percentile)
CR-BSI	9.9	6.9 (75th)	11.7 (50th)	1.8 (75th)
UC-UTI	4.4	5.3 (75th)	9.1 (75th)	5.2 (90th)
VAP	10.7	11.9 (50th)	16.5 (50th)	3.9 (90th)

the low surface area available per bed, and a distance of less than 2 m between beds may also be other reasons for the high level of nosocomial infections. We found that a high Charlson comorbidity index score, prolonged hospitalization, and diabetes mellitus were independent risk factors for nosocomial infections in the multivariable model.

The primary diseases of patients in ICUs, accompanying comorbid conditions and nosocomial infections, affect mortality. Raffin reported that the most important causes of mortality in ICUs are hospital-acquired infections, arrhythmias, kidney failure, liver failure, and heart failure (17). Mortality attributable to nosocomial infections being determined in 36.5% of the fatal patients with nosocomial infections shows the significance of these infections. Delayed culture results in these infections and the resulting rise in mortality due to delays in effective treatment also reveal the need for rapid diagnostic techniques.

The distribution of nosocomial infection agents according to infection type may vary among hospitals or countries. Some pathogens are determined more frequently in some hospitals, and this is helpful in empiric treatment. A multicenter study conducted in Turkey reported *P. aeruginosa* (20.8%), *S. aureus* (18.2%), *Acinetobacter* spp. (18.2%), and *Klebsiella* spp. (16.1%) as agents (10). The most commonly encountered microorganisms in a study from Italy were *A. baumannii* (61.9%), *P. aeruginosa* (22.5%), *E. faecalis* (4.2%), and *C. albicans* (4.2%) (18). The most common microorganisms in a study from Egypt were *Acinetobacter* species (21.8%) and *Klebsiella* species (18.4%), and all *Acinetobacter* strains were multidrug-resistant (19). The most common agents in our study were *A. baumannii*, *P. aeruginosa*, and *S. aureus*.

The most important problem in the treatment of *A. baumannii* infection, the levels of which are increasing in the literature, is that almost all strains exhibit resistance to many antibiotics, including carbapenems, leading to a reduction in antibiotic alternatives for use in treatment (20). Akın et al. showed imipenem resistance in *A. baumannii* at a level of 42% in 2004 but of 92% by 2008 (21). Although levels of resistance to antibiotics vary in all centers, the high level of multiresistant strains is worrying. Infections of pan-resistant origins have been reported in recent years (22). Carbapenem resistance was present in 91.7% of *A. baumannii* strains in this study. Mortality occurred in 63.9% of *A. baumannii* infections. Karabay et al. reported mortality in 77% of *A. baumannii* infections (23).

The increase in carbapenem resistance in Turkey, as in many other countries, in recent years has resulted in colistin, the use of which was restricted for many years due to its side-effects, becoming an important treatment option. Studies have reported that colistin cannot be used alone, but only together with another antibiotic (24).

Patient costs in ICUs were considerably higher for patients developing nosocomial infections than those without infections. The cost of medical services represented the most significant part of that high cost. Medical service costs were higher for patients with nosocomial infections than those without. The cost of laboratory tests constituted the highest proportion of medical service costs. Drug costs represent a significant part of the additional expenses caused by nosocomial infections. Antibiotics represent a significant part of drug costs. Some studies have reported that antibiotic expenses constitute half of all costs, while others have reported that additional hospitalization time is the most important contributor to nosocomial infection costs (25,26). Yalçın et al. reported an additional antibiotic cost of $1136 (25). The development of resistance to antibiotics is also emerging as a significant problem. High mortality and morbidity in infections from resistant microorganisms are problematic. It is particularly noteworthy that costs in infections from resistant microorganisms without mortality during the first 3 days are very high. One study from the United States assessed the costs of antibiotics used in sensitive and resistant gram-negative cases and reported high antibiotic costs in resistant microorganisms (27).

The additional costs and deaths resulting from nosocomial infections clearly reveal the need for priority to be given to activities aimed at controlling these infections. The SENIC Project, which demonstrated that nosocomial infections decrease by 32% in hospitals applying infection control programs, represents a solid basis for determination to prevent infections worldwide (28). Yilmaz et al. reported that a 41.7% decrease in intravascular catheter infections was achieved through infection control training (15). Within that context, it will be useful for all health professionals and patients to be made aware of infection control procedures and rational drug use through the arrangement of in-service training programs, which all physicians in a hospital should attend. Savings resulting from the prevention of nosocomial infections are incomparably higher than spending on infection control procedures. The total cost of nosocomial infections as of 2001 in the United States was $5 billion, whereas infection control costs correspond to only 16% of this (29). In one study from Great Britain, gel-form antiseptic containing alcohol was placed by every bedside, the total cost being 5000 pounds sterling. Following the use of the antiseptic, a significant decrease was observed in the incidence of diarrhea caused by hospital-acquired methylene-resistant *S. aureus* (MRSA) and *C. difficile*. The study reported a savings of approximately 208,000 pounds (30). All these studies show that intense work is needed with all sides taking an active part in infection control

procedures in order to reduce nosocomial infection rates and to achieve lower mortality and costs.

In conclusion, as shown by the Charlson comorbidity index and APACHE II scores, serious illnesses are being caused in ICUs. The number of invasive procedures performed on these patients is also therefore very high. The high patient/nurse ratio represents a significant problem. This is a cause of numerous complications, and particularly infections. Nosocomial infections prolong hospitalization times and increase costs. The fact that nosocomial infections can be prevented with an increase in compliance with infection control procedures is important in terms both of morbidity and mortality and of costs. Regular infection control procedure seminars need to be held in Turkish hospitals, and the number of nurses needs to be increased.

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