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Nosocomial infections and risk factors in the intensive care unit of a teaching and research hospital: A prospective cohort study

Authors' Contribution:

- A** Study Design
- B** Data Collection
- C** Statistical Analysis
- D** Data Interpretation
- E** Manuscript Preparation
- F** Literature Search
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Background:

To evaluate the incidence, risk factors and etiology of nosocomial infections (NIs) in the intensive care unit (ICU) of our hospital in order to improve our infection control policies.

Material/Methods:

A 1-year prospective cohort study of nosocomial infection (NI) surveillance was conducted in our ICU in 2008.

Results:

Out of 1134 patients hospitalized in the ICU for a period of 6257 days, 115 patients acquired a total of 135 NIs distributed as follows: 36.3% bacteremia, 30.4% ventilator-associated pneumonia (VAP), 18.5% catheter-associated urinary tract infection, 7.4% central-line infection, 5.9% cutaneous infection, and 1.3% meningitis. The incidence rate of NI was 21.6 in 1000 patient-days, and the rate of NI was 25.6%. Length of ICU stay, central venous catheterisation, mechanical ventilation and tracheostomy were statistically significant risk factors for NI. Of all NI, 112 (83%) were microbiologically-confirmed and 68.8% of the isolates were Gram-negative, 27.6% were Gram-positive, and 3.6% were fungi. 23 (17%) were clinically-defined infections. The most frequently isolated organism was *P. aeruginosa* (25%), followed by *S. aureus* (21.4%), *E. coli* (18.7%) and *A. baumannii* (16.9%).

Conclusions:

The bloodstream was the most common site and Gram-negatives were the most commonly reported causes of ICU infections.

key words:

intensive care unit • infection • risk factors

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BACKGROUND

Nosocomial infections (NIs) constitute an important health problem with high incidence, morbidity and mortality rates worldwide. NIs have become particularly prominent in intensive care units (ICUs), where the incidence is 2 to 5 times higher than in the general hospitalized population [1]. Intensive care unit patients are at greater risk of developing NI because of several reasons including presence of underlying diseases, longer stay, invasive diagnostic and monitoring procedures performed, impaired host defences, and colonization by resistant microorganisms.

Determination of risk factors for developing infection in ICU patients is an important step for implementation of necessary precautions for prevention of infection. Initial empirical antimicrobial treatment should be targeted against the most likely local pathogens, when a NI is suspected. Therefore, the major concern of our study was the prospective assessment of the etiology and risk factors of NIs in the ICU of our hospital during a 1-year period.

MATERIAL AND METHODS

We conducted a 1-year prospective cohort study of nosocomial infection surveillance in a total 25-bed combined medical and surgical ICU of the Kartal Teaching and Research Hospital, which is a 700-bed teaching hospital in Istanbul, Turkey. Infection surveillance was implemented for all patients staying longer than 48 hours in the ICU during the study period from January 1, 2008, to December 31, 2008. Patients coming from ICUs of other hospitals or transferred to the ICU from another clinic in the same hospital, or staying less than 48 hours in the ICU were excluded. A total of 450 patients were included in the study.

Hematological and biochemical tests were performed for all patients once daily. Chest radiography was performed two times a week. Deep tracheal aspirate and urine samples were taken for culture on admission and repeated once a week. Blood samples and/or removed intravascular catheter tips were cultured upon suspicion of bloodstream or catheter-related infection (i.e., fever, leucocytosis). Any other samples (from wounds, cerebrospinal fluid, etc.) were taken for culture when necessary on clinical indication. An infectious diseases specialist regularly visited the ICU daily, followed all the patients there and collected data such as age, gender, cause of ICU admission, underlying diseases, applied invasive procedures (nasogastric tube, endotracheal intubation, mechanical ventilation, tracheotomy, urinary and intravenous catheterization, surgical operation), the Acute Physiology and Chronic Health Evaluation II (APACHE II) score, length of stay, drug use, results of cultures, and administered antibiotics. By means of the CDC definitions of nosocomial infections [2], the decision of NI was made with a combination of both clinical evidence and laboratory findings. An appropriate antimicrobial therapy was administered to the patients based on local surveillance data and antibiotic susceptibility patterns of isolated microorganisms. The nosocomial infection rate was calculated as the number of all infections per 100 patients and per 1000 patient-days.

Samples were cultured for isolation of bacteria using standard microbiological methods. Isolated bacteria were

identified by conventional methods and tested for antibiotic susceptibility by the Kirby-Bauer disc diffusion technique according to Clinical and Laboratory Standards Institute (CLSI) specifications [3]. For each case of ICU-acquired nosocomial infection, the responsible microorganisms were recorded. Only the initial isolates were considered in the study and repeat isolates from the same sites were excluded.

Microbiologically documented BSI required 1 of the following: 1) recognized pathogen in the blood and pathogen not related to an infection at another site; or 2) fever, chills, or hypotension and any of the following:

- a. a common skin contaminant isolated from at least 2 blood cultures drawn on separate occasions, and the organism is not related to infection at another site;
- b. a common skin contaminant is isolated from blood culture in a patient with an intravascular device, and the physician institutes appropriate antimicrobial therapy [2].

Risk factors for nosocomial infection were recorded as age, sex, cause of admission to the ICU, the Acute Physiology and Chronic Health Evaluation II (APACHE II) score of patients on admission to the ICU, any underlying diseases, surgical history, use of H₂ receptor antagonists, central and/or peripheral intravenous access, nasogastric or endotracheal intubation, mechanical ventilation, urinary catheter, tracheostomy, and the length of stay in the ICU.

Statistical analysis

Statistical analysis was done with SPSS (Statistical Package for Social Sciences) software, version 10.0 (SPSS). Chi-square test, Mann-Whitney U test and logistic regression analysis tests were used. All p values <0.05 were considered significant.

RESULTS

A total of 1134 patients were admitted to our ICU during the study period. The data collected in this study belonged to 450 patients who stayed >48 h in the ICU with 6257 patient-days during one year. Of the 450 patients, only 115 patients acquired nosocomial infections and the remaining 335 patients were non-infected. Of the 450 patients, aged between 6 months and 91 years, 267 (59.3%) were male and 183 (40.7%) were female. The median age was 47.25±23.17 years. There were no significant differences in age and gender between patients with or without ICU-acquired nosocomial infections. Of the 450 patients, only 160 (35.5%) patients had one or more underlying diseases. The most frequent underlying diseases were neoplasia, neurological disease and chronic obstructive pulmonary disease. No significant difference was observed when infected and non-infected cases were compared in terms of underlying diseases (p=0.07). The most frequent causes of admission to ICU were respiratory failure (31.1%), trauma (24.7%) and neurologic disease (22.9%) (Table 1).

The APACHE-II scores ranged between 5 and 40, with a median of 20.46±5.6, with no significant difference between infected and non-infected patients (p=0.26)

Duration of stay in the ICU was between 3 and 165 days, with a median of 15.45±19.18 days in total study patients, 33.92±27.02 days in the infected patients, and 8.12±6.08 days

Table 1. Demographic characteristics, comorbidities and diagnosis on admission of ICU patients.

	Infected patients N (%) 115	Non infected patients N (%) 335	Total N (%)
Female/male	49/66	134/201	450
Age			
<20 years	17 (14.8)	66 (19.7)	83 (18.4)
20-40 years	24 (20.8)	58 (17.3)	82 (18.2)
40-60 years	33 (28.7)	92 (27.5)	125 (27.8)
>60 years	41 (35.7)	119 (35.5)	160 (35.6)
Admission diagnosis			
Trauma	41 (35.7)	70 (20.9)	111 (24.7)
Respiratory failure	34 (29.6)	106 (31.6)	140 (31.1)
Cardiovascular disease	–	28 (8.4)	28 (6.2)
Neurological disease	30 (26.1)	73 (21.8)	103 (22.9)
Intoxication	–	25 (7.5)	25 (5.5)
Comorbidities			
Diabetes mellitus	11 (9.5)	12 (3.6)	23 (5.1)
Cardiovascular disease	7 (6.1)	13 (3.9)	20 (4.4)
COPD	5 (4.3)	22 (6.6)	27 (6)
Uremia	5 (4.3)	16 (4.8)	21 (4.7)
Neoplasia	7 (6.1)	32 (9.5)	39 (8.7)
Neurological disease	14 (12.2)	16 (4.8)	30 (6.7)
APACHE II Score	20.39±6.59	20.37±4.92	

COPD – chronic obstructive pulmonary disease.

in the non-infected patients. Longer ICU stay was a significant risk factor for development of NI ($p=0.00$).

A total of 135 nosocomial infections were detected in 115 (25.6%) of 450 patients. The incidence rate of nosocomial infections was 21.6 in 1000 patient-days, and the infection rate of nosocomial infections was 25.6%. The most frequent site of ICU-acquired NI in our study was the bloodstream (49, 36.3%), followed the respiratory system (41, 30.4%), the urinary tract (25, 18.5%), and catheter-related infection was diagnosed only in 10 patients, (7.4%). The distribution of isolated microorganisms by the sites of nosocomial infection is shown in Table 2. Of all nosocomial infections, 112 (83%) were microbiologically-confirmed (culture-positive) and 23 (17%) were clinically-defined (culture-negative) infections. The pathogens of the culture-confirmed nosocomial infections were Gram-negatives in 77 (68.8%), Gram-positives in 31 (27.6%), and fungi in 4 (3.6%). Among the 112 microorganisms, the most frequently isolated was *Pseudomonas aeruginosa* (28, 25%), followed by *Staphylococcus aureus* (24, 21.4%), *Escherichia coli* (21, 18.7%), *Acinetobacter baumannii* (19, 16.9%), and *Klebsiella spp.* (5, 4.5%).

When the infected and non-infected patients were compared according to risk factors with univariate analysis, there was no significant difference with respect to age, gender, APACHE II scores, surgical history, presence of urinary and/or nasogastric catheters, or use of H_2 receptor antagonists ($p>0.05$). Length of ICU stay, central venous catheterization, mechanical ventilation and tracheostomy were identified as statistically significant risk factors for developing nosocomial infection ($p<0.05$). Extrinsic risk factors in infected and non-infected patients are shown in Table 3.

DISCUSSION

Assesment of infections acquired in ICUs, determination of their risk factors and establishment of correct treatment protocols are crucial steps in prevention and management of infections in ICUs. We planned this prospective surveillance study to determine the incidence, etiology and risk factors for NI in ICU patients at the Kartal Teaching and Research Hospital, Istanbul, Turkey.

Table 2. Distribution of isolated micro-organisms by the sites of ICU-acquired infection.

	BSI	Pneumonia	UTI	Central line infection	Other	Total	%
Gram negative bacteria						77	68.8
<i>P. aeruginosa</i>	8	9	7	2	2	28	25.0
<i>E. coli</i>	5	3	10	1	2	21	18.7
<i>A. baumannii</i>	9	3	3	1	3	19	16.9
<i>Klebsiella spp</i>	3		2			5	4.5
<i>E. cloacae</i>	4					4	3.6
Gram positive bacteria						31	27.6
<i>S. aureus</i>	13	3		5	3	24	21.4
<i>Enterococcus spp</i>	3	–	3	1		7	6.3
<i>Candida spp</i>	4	–				4	3.6
Total	49 (36.3%)	41 (30.4%)	25 (18.5%)	10 (7.4%)	10 (7.4%)	112	100.0

Other: (skin-soft infections 8, meningitis 2); BSI – bloodstream infection; UTI – urinary tract infection.

Table 3. Extrinsic risk factors of infected and non-infected patients.

	Infected patients	Non-infected patients	OR	95% CI	p values
Mechanic ventilation	46	225	5.80	1.74–19.29	0.00
Urinary catheterization	115	257	1.44	1.35–1.54	0.56
CVP catheterization	104	184	3.95	2.01–7.77	0.00
NG catheterization	112	181	0.61	0.12–3.11	0.68
Tracheostomy	30	7	8.92	3.76–21.1	0.00
H ₂ antagonist use	114	334	0.34	0.02–5.50	0.45
Operation	35	73	1.33	0.83–2.15	0.26
Apache II Score	20.39±6.59	20.37±4.92	0.73	0.97–1.11	0.26
Duration of stay	33.92±27.02	8.12±6.08	1.68	22.49–29.10	0.00

CVP – Central venous pressure; NG – nasogastric tube; CI – confidence interval; OR – odds ratio.

In general, ICU-acquired infections constitute 20–25% of all hospital-acquired infections [4]. There may be variations in the incidence of ICU infections between centres, depending on the characteristics of patients and ICUs. In a point-prevalence study including 1417 centres in 17 European countries, the infection rate in ICUs was reported to be 20.6%. The infection rates in ICUs in several other studies reported by authors namely were as follows: Legras et al.: 21.6%, Appelgren et al.: 34%, Aly et al.: 10.6%, Ylipatosani et al.: 23.9%, and Urli et al.: 79% [5–10]. When we reviewed the rates of nosocomial infections reported in ICUs in our country, they differed from centre to centre. Meriç et al. reported the infection rate as 39.7%, Esen et al. (who reviewed the data of 56 ICUs in a 1-day point-prevalence study) as 48.7%, and Erbay et al. as 26% [11–13]. The hospital infection

rate per 100 patient admissions in our hospital was calculated as 25.6%.

Certain specific risk factors play important roles in occurrence of infections in ICUs. Several studies have determined the risk factors for ICU-acquired infections. Although some studies reported the patient age over 70 and the presence of underlying diseases to be a risk factor [6,14], the age and underlying diseases of the patients were not statistically significant risk factors for ICU-acquired infections in our study. A positive correlation between rates of nosocomial infections and average length of ICU stay have been reported in various studies [12,14–17]. In accordance with the results of these studies, length of ICU stay was a significant risk factor for ICU-acquired infection both in univariate

Table 4. Prevalence rates of NIs reported from other studies.

	Pneumonia %	Bloodstream infection %	Urinary tract infection %
Vincent et al. [16]	46.9	12.0	17.6
Richards et al. [17]	27.0	19.0	31.0
Richards et al. [19]	31.0	14.0	23.0
Aly et al. [8]	33.0	24.0	11.0
Kallel et al. [20]	58.2	18.2	14.5
Markogiannakis et al. [21]	25.3	36.1	9.5
Esen et al. [12]	28.0	23.3	15.7
Erbay et al. [13]	40.9	30.2	23.6
Meriç et al. [11]	35.4	18.2	11.8
Our study	30.4	36.5	18.5

and multivariate analyses in our study. Each invasive procedure performed poses a risk of infection. There was a direct correlation between central venous catheterization, tracheostomy, mechanical ventilation and the risk of infection in our study, in agreement with the results of other studies [7,11,14,18].

The most commonly reported sites of nosocomial infections in ICUs are the respiratory tract, followed by the urinary tract and the bloodstream, but the distribution of the sites and causes of infection may differ between centres. Table 4 shows the distribution of common NIs reported from ICU studies in various centres. In general, the most common type of infection in ICU is pneumonia, although Markogiannakis et al. reported bacteremia as the most commonly encountered ICU infection followed by pneumonia similar to the results in our study [8,11–13,16,17,19–21].

Our study revealed an unexpectedly higher frequency of BSI compared to other reports.

The higher occurrence of BSI seems to be closely related to specific and well-known risk factors such as the presence of indwelling venous catheters, and one or more critical underlying condition.

In majority of studies, Gram-negative bacteria have been reported as the most common cause of ICU-acquired infections, but there were differences in rates of their distribution at the species level between centres. *Enterobacteriaceae* (25.9%), *P. aeruginosa* (17.2%), *S. aureus* (10.9%) and *Coagulase-negative staphylococcus* (CNS) (4.1%) were the most frequent microorganisms reported by Leon Rosales et al. Similarly, Vincent et al. reported that the most frequent micro-organisms were *Enterobacteriaceae* (34.4%), *S. aureus* (30.1%), *P. aeruginosa* (28.7%), CNS (19.1%) and fungi (17.1%) (5,15). In the study of Tennant et al., *P. aeruginosa* (41.3%) was the most common organism, followed by *Acinetobacter spp* (33.5%), CNS (20%) and *Streptococcus group D* (18.7%) (18). Similarly, various studies on ICU infections performed in our country reported that Gram-negative bacteria were the most frequent pathogens causing ICU infections. Data on distribution of micro-organisms frequently

isolated by Erbay et al. in ICUs of various Turkish hospitals were as follows: *P. aeruginosa* (22.6%), methicillin-resistant *S. aureus* (22.2%) and *Acinetobacter spp.* (11.9%). Esen et al. reported *P. aeruginosa* (20.8%), *Acinetobacter spp* (18.2%), *S. aureus* (18.2%) and *Klebsiella spp* (16.1%) as the common pathogens. Whereas, *S. aureus* (30.9%), *Acinetobacter spp* (26.8%), *P. aeruginosa* (12.4%) were the most frequent etiologic agents reported by Meriç et al. [11–13].

In our study, the most common cause of ICU infections was *P. aeruginosa* (25%), followed by *S. aureus* (21.4%), *E. coli* (18.7%), and *A. baumannii* (16.9%), in decreasing order. The major pathogen causing bloodstream infections was *S. aureus*, whereas in case of pneumonia and urinary tract infection, *P. aeruginosa* and *E. coli*, were the most common bacteria, respectively.

CONCLUSIONS

In conclusion, the bloodstream was the most common site of infection in our ICU. Central venous catheterization, mechanical ventilation, tracheostomy and longer stay in ICU were common risk factors for ICU-acquired infections. Etiologic agents, site and rate of ICU-acquired infections differ from centre to centre. Therefore, each hospital should define their own risk factors for infection, regularly conduct surveillance study of the infectious etiologies of NI, and establish prevention and treatment strategies accordingly, in order to improve the quality of health care.

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